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COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

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Errata

For the United States International Trade Commission *COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities*, Investigation No. 332-596, USITC Publication 5469, October 2023.

- On pages 50, 68, 69, 101, 105, 106, 111, and 180, footnote references to the United States Patent and Trademark Office report by Toole et al., *Diagnosing COVID-19: A Perspective from U.S. Patenting Activity*, were updated to change the publication date from “forthcoming” to “October 2023”; on pages 53, 91, 123, and 230, bibliography entries were updated to give the publication date and URL (<https://www.uspto.gov/about-us/news-updates/diagnosing-covid-19-perspective-us-patenting-activity>).
- On page 197, a space was added between footnotes 582 and 583 to correct a formatting error.
- On page 211, the text was corrected to read “About the time of issuance of the CL for the hepatitis C pharmaceutical, however, Gilead expanded its VLs for the treatment to include Malaysia, reportedly as a result of Malaysia’s pursuit of the CL” rather than “Shortly after the issuance of the CL for the hepatitis C pharmaceutical, however, Gilead expanded its VLs for the treatment to include Malaysia, reportedly as a result of the CL.”
- On page 211, a reference to the USITC hearing transcript in footnote 679 was corrected to read “USITC hearing transcript, March 29, 2023, 117–118 (testimony of Sangeeta Shashikant, TWN), 215 (testimony of Melissa Barber); ...” rather than “USITC hearing transcript, March 29, 2023, 117–118 (testimony of Sangeeta Shashikant, TWN), 215 (testimony of Anu Osinusi, Gilead);”
- On page 252, figure 6.3 inaccurately represented Chile, a high-income country, as an upper-middle-income country. The figure was replaced, and the shading now accurately reflects the data provided for upper-middle-income countries.
- On page 252, the title of figure 6.3 was changed to read “UMICs where COVID-19 therapeutics cannot be offered for sale under voluntary license agreements or procured through multilateral programs according to MPP or Gilead’s access partnerships” rather than “UMICs where COVID-19 therapeutics cannot be offered for sale under voluntary license agreements or procured through multilateral programs.”
- On page 498, table J.21 was corrected to provide the underlying data for figure 6.3.

December 20, 2023

Table of Contents

Abbreviations and Glossary	17
Executive Summary	21
Chapter 1 Introduction	41
Approach and Scope	41
Country Classification by Income.....	43
Time Period Covered in the Report	44
Information Sources.....	47
Organization of the Report	51
Bibliography	52
Chapter 2 Background on Intellectual Property and Regulations	57
Introduction	57
Intellectual Property and the TRIPS Agreement.....	57
Patents under the TRIPS Agreement	59
Undisclosed Information and Test Data under the TRIPS Agreement	59
TRIPS Agreement Flexibilities	61
Compulsory Licensing under the TRIPS Agreement	63
The 2022 Ministerial Decision on the TRIPS Agreement	64
Patent Landscape for COVID-19 Diagnostics and Therapeutics	68
Patenting of COVID-19 Diagnostics: Landscape and Examples	68
Patenting of COVID-19 Therapeutics: Landscape and Examples.....	71
Trade Secrets and COVID-19 Diagnostics and Therapeutics	73
Regulations to Bring Diagnostics and Therapeutics to Market	75
National Regulatory Authorities	75
World Health Organization	78
Status of U.S. COVID-19 Diagnostics and Therapeutic Approvals and EUAs	81
Bibliography	84
Chapter 3 Definitions and the Universe of COVID-19 Diagnostics and Therapeutics 99	
Introduction	99
Identifying the Range of Definitions for Diagnostics and Therapeutics	100
Diagnostics	100
Therapeutics.....	101
Identifying the Universe of COVID-19 Diagnostics and Therapeutics	102
Existing COVID-19 Diagnostics	104
Existing COVID-19 Therapeutics.....	106
Relevant COVID-19 Diagnostics and Therapeutics	110

Bibliography	118
Chapter 4 COVID-19 Diagnostics and Therapeutics Manufacturing Supply Chain and Trade.....	131
Introduction	131
Information Sources and Data Gaps.....	131
Overview of Manufacturing Supply Chains for COVID-19 Diagnostics and Therapeutics.....	132
Diagnostics	133
Therapeutics.....	135
Production, Market Segmentation, and Trade.....	137
Diagnostics	138
Therapeutics.....	149
Bibliography	166
Chapter 5 Approaches to Access the Intellectual Property Associated with COVID-19 Diagnostics and Therapeutics.....	177
Introduction	177
Intellectual Property Agreements from Research and Development to Commercialization	178
R&D Collaboration Agreements for COVID-19 Therapeutics and Diagnostics.....	178
Manufacturing Partnership Agreements and COVID-19 Therapeutics	182
Bilateral License Agreements and COVID-19 Therapeutics.....	183
The Medicines Patent Pool and COVID-19 Therapeutics	188
Access to IP in UMICs, LMICs, and LICs.....	193
Compulsory Licenses.....	197
Overview	197
Advantages and Challenges Associated with the Use of Compulsory Licenses	198
Compulsory Licensing Attempts and Outcomes.....	202
Bibliography	218
Chapter 6 Availability and Consumption of COVID-19 Diagnostics and Therapeutics	235
Introduction	235
Demand for Diagnostics and Therapeutics.....	236
Definition of Demand.....	236
Estimating Need.....	238
Uncertainty of Future Demand.....	242
Prices, Purchases, Donations, and Consumption of Diagnostics and Therapeutics.....	242
Diagnostics	243
Therapeutics.....	248
Factors Affecting Demand and Availability of Diagnostics and Therapeutics	261
Price.....	261
Regulations and Approvals	264

Competing Healthcare Priorities.....	268
Testing and Demand for Treatment	269
Last Mile Delivery.....	271
Other Factors Reported	274
Bibliography	277
Chapter 7 Views of Interested Persons.....	291
Introduction	291
Intellectual Property Protection, R&D, and Jobs.....	292
The Relationship between Intellectual Property Protection and Corporate R&D Expenditures, Taking into Account Other Expenditures, such as Share Buybacks, Dividends, and Marketing.....	292
The Location of Jobs Associated with the Manufacturing of Diagnostics and Therapeutics, including in the United States.....	296
The TRIPS Agreement and Access to Medicine	300
Whether and How Existing TRIPS Rules and Flexibilities Can Be Deployed to Improve Access to Medicines.....	300
Successes and Challenges in Using Existing TRIPS Flexibilities	304
To What Extent Further Clarifications of Existing TRIPS Flexibilities Would be Useful in Improving Access to Medicines	307
The TRIPS Agreement and COVID-19 Diagnostics and Therapeutics	309
How the TRIPS Agreement Promotes Innovation in and/or Limits Access to COVID-19 Diagnostics and Therapeutics	309
The Extent to which Products Not Yet on the Market, or New Uses for Existing Products, Could be Affected by an Extension of the Ministerial Decision to COVID-19 Diagnostics and Therapeutics	312
The Relevance, if Any, of the Fact that Diagnostic and Therapeutic Products Used with Respect to COVID-19 May Also Have Application to Other Diseases.....	313
Bibliography	316
Chapter 8 Literature Review.....	323
Introduction	323
Methodologies.....	325
Descriptive Analysis	326
Structural Economic Models.....	326
Reduced-Form Econometric Models	327
The Effect of Patent Protection on Pharmaceuticals	328
Patent Protection and Innovation in the Health Sector	330
Patent Protection and Access to Medicine.....	340
The Effects of Compulsory Licenses.....	349
Compulsory Licenses and Access	350
Compulsory Licenses and Innovation	351

Compulsory Licenses and Global Health.....	352
The Effects of the Medicines Patent Pool.....	353
Research Gaps.....	354
Bibliography	356
Appendix A Request Letter.....	363
Appendix B Federal Register Notice	369
Appendix C Calendar of Hearing Witnesses.....	375
Appendix D Summary of Views of Interested Persons	387
Appendix E Supplemental Tables for Chapter 3	441
Appendix F Methodology for Estimating COVID-19-Related Pharmaceutical Trade	447
Appendix G Literature Review Sources.....	453
Appendix H Countries Covered by Voluntary Licenses by Treatment Type and Income Level	459
Appendix I Additional Data on the U.S. Pharmaceuticals Industry and U.S. Pharmaceutical Trade	465
Appendix J Data for Figures.....	485

Tables

Table 1.1 International organizations and their roles in access to COVID-19 diagnostics and therapeutics.....	48
Table 2.1 Applicants that have received WHO prequalification for therapeutics.....	80
Table 2.2 FDA EUA and full approval dates for authorized COVID-19 therapeutics	82
Table 3.1 Examples of COVID-19 therapeutics, category, class, and mode of action	107
Table 3.2 Phase III clinical trials for COVID-19 therapeutics, as of July 2023	110
Table 3.3 Examples of virus-directed therapeutics for the treatment of COVID-19	112
Table 3.4 Number of authorized COVID-19 diagnostic tests by region.....	113
Table 3.5 Therapeutics for treatment of COVID-19 that are approved, recommended, or have an EUA as of July 2023, by drug	114
Table 3.6 Therapeutics for treatment of COVID-19 that are approved, recommended, or have an EUA by the WHO or the EEA, July 2023	116
Table 4.1 Available COVID-19 tests in the United States	134
Table 4.2 Virus-directed COVID-19 therapeutics by trade name, international nonproprietary name, form of administration, and category.....	136
Box Table 4.3 Pharmaceutical industry coverage, by NAICS code	138
Box Table 4.4 Six diagnostics manufacturers by U.S. manufacturing locations.....	144
Table 4.5 Global exports of diagnostics, including COVID-19 diagnostics, by major exporting country, 2018–22	149
Table 4.6 Select virus-directed COVID-19 therapeutic producers and location of headquarters.....	157

Table 4.7 Global exports under HS subheadings that include COVID-19 therapeutics, by top exporting countries, 2018–22	165
Table 6.1 Estimate of global need for oral antivirals for COVID-19 treatment in 2022	239
Table 6.2 Estimate of need for oral antivirals in LMICs, 2022	241
Table 6.3 Prices for COVID-19 diagnostics (rapid antigen tests and select automated PCR tests) available through the ACT-A pooled procurement mechanism, 2023	244
Table 6.4 COVID-19 therapeutics: Announced government purchase agreements between March 2020 and December 2022, by treatment and country income level	253
Table 6.5 COVID-19 therapeutics: Announced private sector purchase agreements between March 2020 and December 2022, by treatment and country income level.	254
Table 6.6 COVID-19 therapeutics: Announced multilateral organization purchase agreements between March 2020 and December 2022, by treatment and country income level	255
Table 6.7 COVID-19 Therapeutics: Certain private sector donations between March 2020 and December 2022, by treatment and recipient country income level	259
Table 6.8: Number of courses of nirmatrelvir (+ ritonavir) administered by certain high-income countries (HIC), quarterly, 2022–23.	260
Table 6.9 Number of courses of molnupiravir administered by certain high-income countries (HIC), quarterly, 2022–23.....	261
Table D.1 List parties that submitted written submissions without summaries.....	437
Table E.1 Illustrative list of COVID-19 therapeutics and related patent activity.....	443
Table E.2 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff as of July 2023	444
Table E.3 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff as of July 2023, by region.....	444
Table E.4 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff as of July 2023, by income level.....	444
Table E.5 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff from WHO and EEA as of July 2023	445
Table F.1 HS subheadings, with description, that include COVID-19 diagnostics, 2022	449
Table F.2 HS subheadings, with descriptions that include COVID-19 therapeutics, 2022	450
Table F.3 Therapeutics manufacturing countries and their relevant tariff-line codes.....	451
Table G.1 Sources cited in chapter 8: literature review	455
Table H.1 Developing countries where products can be offered for sale under voluntary license agreements, by treatment type and income level.	461
Table I.1 U.S. pharmaceutical manufacturing employment, by state and industry classification, average October 2022–December 2022.....	469
Table I.2 U.S. states’ share of total employment accounted for by pharmaceuticals, by industry classification, October 2022–December 2022	470
Table I.3 U.S. states’ share of total pharmaceutical employment by industry classification, October 2022–December 2022.....	471
Table I.4 U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	474
Table I.5 Share of value of U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	474

Table I.6 U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	474
Table I.7 Share of volume of U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	475
Table I.8 U.S. imports of pharmaceuticals, by source, 2018–22, January–June 2022, and January–June 2023.....	475
Table I.9 Share of U.S. imports of pharmaceuticals, by source, 2018–22, January–June 2022, and January–June 2023.....	475
Table I.10 U.S. imports of medicinal and botanical manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	476
Table I.11 Share of U.S. imports of medicinal and botanical manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	476
Table I.12 U.S. imports of pharmaceutical preparation manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	476
Table I.13 Share of U.S. imports of pharmaceutical preparation manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	477
Table I.14 U.S. imports of in-vitro diagnostic substance manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	477
Table I.15 Share of U.S. imports of in-vitro diagnostic substance manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	477
Table I.16 U.S. imports of biological product (except diagnostic) manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	478
Table I.17 Share of U.S. imports of biological product (except diagnostic) manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023.....	478
Table I.18 U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	478
Table I.19 Share of value of U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	479
Table I.20 U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	479
Table I.21 Share of volume of U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023.....	479
Table I.22 U.S. exports of pharmaceuticals, by market, 2018–22, January–June 2022, and January–June 2023.....	480
Table I.23 Share of U.S. exports of pharmaceuticals, by market, 2018–22, January–June 2022, and January–June 2023.....	480
Table I.24 U.S. exports of medicinal and botanical manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023.....	480
Table I.25 Share of U.S. exports of medicinal and botanical manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023.....	481
Table I.26 U.S. exports of pharmaceutical preparation manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023.....	481
Table I.27 Share of U.S. exports of pharmaceutical preparation manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023.....	481

Table I.28 U.S. exports of in-vitro diagnostic substance manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023	482
Table I.29 Share of U.S. exports of in-vitro diagnostic substance manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023	482
Table I.30 U.S. exports of biological product (except diagnostic) manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023	482
Table I.31 Share of U.S. exports of biological product (except diagnostic) manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023	483
Table J.1 Examples of different ways to categorize COVID-19 diagnostics	487
Table J.2 Examples of different ways to categorize COVID-19 therapeutics.....	487
Table J.3 Count of manufacturers of COVID-19 diagnostics and therapeutics	488
Table J.4 Courses of COVID-19 therapeutics made available through donation or purchase, by country and region, based on publicly announced supply agreements	488
Table J.5 Economies by World Bank income group.....	490
Table J.6 COVID-19 pandemic: Timeline of notable events and reported COVID-19 deaths by income level, January 2020–May 2023.....	491
Table J.7 Number of reported cases of COVID-19 in 2020, with key dates in the United States for development and approval of COVID-19 diagnostic tests, by month	492
Table J.8 Number of COVID-19 diagnostics manufacturers by country income class and country as of June 30, 2022	492
Table J.9 Diagnostics, including COVID-19 diagnostics: exports and imports by income level of exporter (left) and importer (right), 2022.....	493
Table J.10 COVID-19 virus-directed therapeutics manufacturing, by drug	493
Table J.11 HICs: COVID-19 virus-directed therapeutics manufacturing by production type, as of July 2023	493
Table J.12 UMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023.....	494
Table J.13 LMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023.....	494
Table J.14 Exports and imports of HS subheadings that include COVID-19 therapeutics by income level of exporter (left) and importer (right), 2022	495
Table J.15 UMICs, LMICs, and LICs where COVID-19 therapeutics licensed under MPP licenses or BLAs cannot be offered for sale under the terms of those licenses/agreements, by treatment type and income levels	495
Table J.16 UMICs, LMICs, and LICs where four COVID-19 therapeutics can be offered for sale under MPP licenses and BLAs, by count of treatment types.....	496
Table J.17 Number of public health uses of TRIPS Agreement Art. 31 flexibilities since 2001, by execution status in count of Art. 31 flexibilities	496
Table J.18 Number of public health uses and attempts to use TRIPS Agreement Art. 31 flexibilities since 2001, by country.....	497
Table J.19 COVID-19 average daily testing rates, quarterly by country income class.....	497
Table J.20 Select price ranges for COVID-19 therapeutics by country income groups	498
Table J.21 UMICs where COVID-19 therapeutics cannot be offered for sale under voluntary license agreements or procured through multilateral programs	498

Table J.22 Countries where COVID-19 therapeutics were offered through multilateral programs, as of 2022.....	499
Table J.23 Per capita annual health care expenditure, by income group, 2021	499
Table J.24 Regulatory approvals by country for relevant COVID-19 therapeutics.....	500
Table J.25 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by business size, 2020.....	500
Table J.26 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by industry classification, 2020.....	500
Table J.27 U.S. pharmaceutical employment, by business size and industry classification, 2020.....	500
Table J.28 U.S. pharmaceutical employment by industry classification, 2018–22.....	501
Table J.29 U.S. pharmaceutical shipments, 2018–22, January–June 2022, and January–June 2023	501
Table J.30 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023	501
Table J.31 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023	501
Table J.32 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023	502
Table J.33 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023	502

Figures

Figure ES.1 Examples of different ways to categorize COVID-19 diagnostics	27
Figure ES.2 Examples of different ways to categorize COVID-19 therapeutics.....	28
Figure ES.3 Count of manufacturers of COVID-19 diagnostics and therapeutics.....	29
Figure ES.4 Courses of COVID-19 therapeutics made available through donation or purchase, by country and region, based on publicly announced supply agreements	35
Figure 1.1 Economies by World Bank income group.....	44
Figure 1.2 COVID-19 pandemic: Timeline of notable events and reported COVID-19 deaths by income level, January 2020–May 2023.....	46
Figure 2.1 WHO prequalification process.....	79
Figure 2.2 Average timelines for drug approvals, normal and pandemic, United States.....	82
Figure 2.3 Number of reported cases of COVID-19 in 2020, with key dates in the United States for development and approval of COVID-19 diagnostic tests, by month	83
Figure 4.1 Categories of COVID-19 tests in use	133
Figure 4.2 Overview of COVID-19 test kit manufacturing stages	139
Figure 4.3 Number of COVID-19 diagnostics manufacturers by country income class and country as of June 30, 2022	143
Figure 4.4 Diagnostics, including COVID-19 diagnostics: exports and imports by income level of exporter (left) and importer (right), 2022.....	148
Figure 4.5 Overview of finished dosage form value chain (traditional manufacturing).....	151
Box Figure 4.6 Neutralizing monoclonal antibodies development: identification, selection, and production.....	152

Figure 4.7 COVID-19 virus-directed therapeutics manufacturing, by drug	158
Figure 4.8 HICs: COVID-19 virus-directed therapeutics manufacturing by production type, as of July 2023	159
Figure 4.9 UMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023.....	161
Figure 4.10 LMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023.....	162
Figure 4.11 Exports and imports of HS subheadings that include COVID-19 therapeutics by income level of exporter (left) and importer (right), 2022.....	164
Figure 5.1 UMICs, LMICs, and LICs where COVID-19 therapeutics licensed under MPP licenses or BLAs cannot be offered for sale under the terms of those licenses/agreements, by treatment type and income levels	194
Figure 5.2 UMICs, LMICs, and LICs where four COVID-19 therapeutics can be offered for sale under MPP licenses and BLAs, by count of treatment types.....	195
Figure 5.3 Number of public health uses of TRIPS Agreement Art. 31 flexibilities since 2001, by execution status in count of Art. 31 flexibilities	203
Figure 5.4 Number of public health uses and attempts to use TRIPS Agreement Art. 31 flexibilities since 2001, by country.....	204
Figure 6.1 COVID-19 average daily testing rates, quarterly by country income class.....	248
Figure 6.2 Select price ranges for COVID-19 therapeutics by country income groups	249
Figure 6.3 UMICs where COVID-19 therapeutics cannot be offered for sale under voluntary license agreements or procured through multilateral programs	252
Figure 6.4 Countries where COVID-19 therapeutics were offered through multilateral programs, as of 2022	256
Figure 6.5 Per capita annual health care expenditure, by income group, 2021	262
Figure 6.6 Regulatory approvals by country for relevant COVID-19 therapeutics	267
Figure I.1 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by business size, 2020.....	467
Figure I.2 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by industry classification, 2020.....	467
Figure I.3 U.S. pharmaceutical employment, by business size and industry classification, 2020	468
Figure I.4 U.S. pharmaceutical employment by industry classification, 2018–22.....	468
Figure I.5 U.S. pharmaceutical shipments, 2018–22, January–June 2022, and January–June 2023.....	473
Figure I.6 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023	473

Boxes

Box 2.1 The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and Four Flexibilities Used for Public Health Purposes	62
Box 2.2 IP Protections and Diagnostic Testing Platforms	70
Box 2.3 Buffers, Shortages, and Trade Secrets	73
Box 2.4 Stringent Regulatory Authorities and WHO-Listed Authority	77

Box 3.1 Scope of Diagnostics and Therapeutics in World Trade Organization Members' Proposals	103
Box 4.1 Pharmaceutical Manufacturing in the United States	137
Box 4.2 Instrumentation and Related Supplies for Diagnostics	141
Box 4.3 U.S. Manufacturing and Employment	144
Box 4.4 Differences in the Development of Monoclonal Antibodies Compared to Small-Molecule Antivirals	152
Box 5.1 The Bayh-Dole Act.....	180
Box 5.2 Common Elements of Bilateral License Agreements.....	184
Box 5.3 Least-Developed Country Status	206
Box 5.4 Lessons from the HIV/AIDS Epidemic	215
Box 6.1 Funding of COVID-19 Therapeutics Through Multilateral Organizations	257
Box 6.2 Last Mile Distribution in Zambia	274

Abbreviations and Glossary

Term	Definition
ACT-A	Access to COVID-19 Tools Accelerator (hosted by the World Health Organization)
Airfinity	A healthcare data and analytics company, whose activities include monitoring global market and industry trends, tracking research activities, and following intellectual property developments.
antiviral	A drug directed against a virus.
assay	A scientific experiment to detect the presence of a specific item. In the case of COVID-19, an assay is often synonymous with “test” in that it is an experiment to detect the presence of SARS-CoV-2. When used as a verb, it means to conduct such an experiment.
API	active pharmaceutical ingredient. Any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.
biological product (or biologic)	A pharmaceutical product created by living cells or organisms. Compared to small-molecule drugs, biological products are complex products that are more difficult to characterize.
biosimilar	A biological product that has no clinically meaningful differences in safety and effectiveness compared to a reference biological product.
BLAs	bilateral license agreements. Agreements between licensors or owners of intellectual property (IP) and licensees or users of IP for the authorized development, manufacture, or sale of a product subject to IP protections.
CDC	Centers for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
CL	compulsory license. Authorization granted by a government to allow someone other than the patent holder to use a patented process or produce a patented product without the patent holder’s consent under certain conditions.
COVID-19	coronavirus disease 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
developing countries	Term used in common parlance at the World Trade Organization to refer to low-income countries (LICs), lower-middle-income countries (LMICs), and upper-middle-income countries (UMICs). No official definition has been adopted by the WTO.
EC	European Commission
EDIS	Electronic Document Information System (USITC)
EEA	European Economic Area
EMA	European Medicines Agency (EU)
EU	European Union
EUA	Emergency Use Authorization
EUL	Emergency Use Listing (WHO)
excipient	Constituent of a medicine other than the API. Sometimes referred to as an “inactive ingredient.”
FDA	U.S. Food and Drug Administration
FDCA	Food, Drug, and Cosmetic Act
FDf	finished dosage form
FIND	Foundation for Innovative New Diagnostics. A nonprofit organization based in Switzerland.
FTA	free trade agreement
GDP	gross domestic product
generic product	Often used to mean a copy of a patented drug or drug whose patents have expired.
GNI	gross national income
GTA	Global Trade Atlas (S&P)

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Term	Definition
HIC	high-income country. World Bank classification of economies with incomes per capita above \$13,205.
HIV/AIDS	human immunodeficiency virus/acquired immunodeficiency syndrome
HS	International Harmonized Commodity Description and Coding System, generally referred to as “Harmonized System”
HTS	Harmonized Tariff Schedule of the United States
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
IP	intellectual property
JAK inhibitor	Janus kinase inhibitor. JAK inhibitors are small-molecule drugs that block JAK enzymes, which play a role in certain cell signaling pathways. JAK inhibition is the mode of action for certain COVID-19 therapeutics.
LDC	least-developed country. The United Nations defines least-developed countries as low-income countries confronting severe structural impediments to sustainable development.
LIC	low-income country. World Bank classification of economies with incomes per capita of \$1,085 or less.
licensed production	Production of a therapeutic, or other product, under a voluntary license.
licensee	One who obtains a license or right to make use of specified intellectual property.
licensor	One who grants a license to make use of specified intellectual property.
LMIC	lower-middle-income country. World Bank classification of economies with incomes per capita between \$1,086 and \$4,255.
mAb	monoclonal antibody. A type of biological product that treats disease by activating the immune system.
MICs	middle-income countries. Includes both lower-middle-income countries (LMICs) and upper-middle-income countries (UMICs).
ML&P	Medicines Law & Policy. A nonprofit research organization based in the Netherlands.
MPP	Medicines Patent Pool. A United Nations-backed public health organization working to increase access to, and facilitate the development of, lifesaving medicines for low- and middle-income countries.
MPP license	A license agreement between MPP and the intellectual property owner. MPP then sublicenses to manufacturers to develop the licensed product to be made available in a defined set of countries.
MSF	Médecins Sans Frontières (Doctors Without Borders)
NAICS	North American Industry Classification System
NGO	nongovernmental organization
NIH	National Institutes of Health
NLM	National Library of Medicine
NSAID	non-steroidal anti-inflammatory drug
OECD	Organisation for Economic Co-operation and Development
PATH	(formerly) Program for Appropriate Technology in Health
PCR	polymerase chain reaction. A PCR test is an in vitro test to determine whether a patient’s sample has the presence of the genetic material of a virus. Sometimes referred to as “molecular tests” or “nucleic acid tests.”
PQP	Prequalification of Medicines Program
PVA	People’s Vaccine Alliance. A coalition of over 100 organizations and networks.
rapid antigen tests	An in vitro test to determine whether a patient’s sample has any presence of viral proteins.
R&D	research and development
RNA	ribonucleic acid
SARS	severe acute respiratory syndrome

Term	Definition
Small-molecule drug	A pharmaceutical product that is an organic chemical with low molecular weight. Compared to biological products, small-molecule drugs typically have well-characterized chemical structures.
SME	small and medium-sized enterprise
SRA	Stringent Regulatory Authority. According to the World Health Organization, SRAs are regulatory authorities that have the expertise and resources to adequately evaluate both finished pharmaceutical products and active pharmaceutical ingredients.
traditional medicine	Crude preparations of medicines that are produced according to the principle of traditional medicinal practice.
test kit	A set of reagents and tools used to test for a disease.
TRIPS Agreement	Agreement on Trade-Related Aspects of Intellectual Property Rights (effective January 1, 1995).
TRIPS Agreement flexibilities	According to the World Intellectual Property Organization (WIPO), flexibilities aim to permit developing and least-developed countries to use TRIPS-compatible norms in a manner that enables them to pursue their own public policies.
UMIC	upper-middle-income country. World Bank classification for those economies with incomes per capita between \$4,256 and \$13,205.
UN	United Nations
USPTO	U.S. Patent and Trademark Office
USTR	U.S. Trade Representative
VL	voluntary license. Bilateral license agreements and MPP licenses are voluntary licenses.
WHO	World Health Organization
WHO prequalification	A service provided by the WHO to assess the quality, safety, and efficacy of medical products and their production facilities for priority diseases.
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

Executive Summary

The COVID-19 outbreak that began in early 2020 resulted in millions of infections and slowed economies, disrupted supply chains, and led to more than 6.9 million deaths worldwide, as of July 2023. This global health crisis triggered an exponential increase in demand for testing supplies and medicines and reinforced concern over global inequity in access to medicines. The U.S. Trade Representative (Trade Representative), in a letter to the U.S. International Trade Commission (Commission or USITC) dated December 16, 2022, recognized this concern, and noted the varied and divergent opinions on whether the intellectual property (IP) protections that support the development of new medicines may also act as a barrier to access, particularly in developing countries. She stated that the discussion on global availability of medicines has persisted since the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) entered into force in 1995. Her letter noted that the TRIPS Agreement struck a balance in which innovators could have certain patent protections, but governments would have flexibilities with respect to these rules. During the summer of 2022, the WTO agreed to provide further flexibilities with respect to COVID-19 vaccines, as well as to consider extending those flexibilities to COVID-19 diagnostics and therapeutics, in its Ministerial Decision on the TRIPS Agreement (the 2022 Ministerial Decision). The Trade Representative requested that the Commission examine these issues in a report that addresses COVID-19 diagnostics and therapeutics, supply and demand, and TRIPS Agreement flexibilities.

The Trade Representative's request letter asked the Commission to provide information on a number of issues and factors concerning COVID-19 diagnostics and therapeutics, as well as to identify where significant data and information gaps exist. As requested, the Commission's report includes information on the range of definitions for diagnostics and therapeutics and mechanisms for access to these goods, including the role of IP protections. To the extent practicable, the report also includes information on relevant COVID-19 diagnostics and therapeutics, including (1) overviews of the industry, markets, and trade; (2) information on market segmentation of global demand and consumption, according to the World Bank's classification of economies—high-income countries (HICs), upper-middle-income countries (UMICs), lower-middle-income countries (LMICs), and low-income countries (LICs); (3) information on availability and pricing; (4) actions taken by WTO members to use or attempt to use compulsory licenses (CLs) and any alternatives, including voluntary licenses (VLs) and licensing coordinated by the Medicines Patent Pool (MPP), a United Nations- (UN-) backed public health organization, (5) views from the public on specified topics; and (6) a literature review.

Highlights of this Report

The TRIPS Agreement sets minimum standards for the protection and enforcement of IP rights. It also includes flexibilities. Persons providing input to the Commission disagreed about the extent to which the 2022 Ministerial Decision expands flexibilities and whether the decision should be extended to COVID-19 diagnostics and therapeutics.

Determining a definitive scope of what products are covered by the terms “diagnostics” and “therapeutics” as they pertain to COVID-19 and what constitutes relevant COVID-19 diagnostics and therapeutics covered by patents is complicated and subject to interpretation. Based on definitions in the medical field of “diagnostics” and “therapeutics,” a COVID-19 diagnostic is a good used to diagnose

COVID-19 or identify how patients respond to treatments for COVID-19, and a COVID-19 therapeutic is a good used to treat COVID-19. The universe of COVID-19 diagnostics and therapeutics covered by patents or in development that fall within those definitions is broad and varied. There are various parameters that could be applied, individually or in combination, to identify relevant COVID-19 diagnostics and therapeutics, including whether the product is covered by patent, whether the product is directed to COVID-19 (virus-directed), and whether the product has received regulatory approval or authorization; application of each comes with its own challenges.

The development and commercialization of COVID-19 diagnostics and therapeutics occurred on an extremely compressed timeline. Manufacturing of diagnostics and therapeutics involves multiple stages, each of which requires careful attention to detail and strict quality control measures. The two fields of diagnostics and therapeutics are composed of different producers, inputs, know-how, and so on. Generally, COVID-19 diagnostics can be brought to market faster than COVID-19 therapeutics, and the knowledge and manufacturing base globally for small-molecule drugs is larger than for biologics. Research and development of virus-directed COVID-19 diagnostics and therapeutics primarily occurred in HICs, but manufacturing of diagnostics and therapeutics occurred in countries of all income levels except for LICs. As of summer 2023, China (UMIC) reportedly had the highest number of manufacturers of COVID-19 diagnostics (247), and India (LMIC) had the largest number of reported therapeutics manufacturers (56). It is difficult, however, to ascertain how much COVID-19 diagnostics and therapeutics production came online or is still ongoing.

A variety of advantages and challenges are associated with the use of voluntary licenses to provide access to IP associated with COVID-19 therapeutics and compulsory licenses to access COVID-19 therapeutics and other patented pharmaceutical products. Voluntary licenses and compulsory licenses generally were not used to access IP associated with COVID-19 diagnostics. Voluntary licenses have been an important mechanism that was used to offer COVID-19 therapeutics for sale at reduced prices in LICs, LMICs, and some UMICs; however, many UMICs have been excluded from coverage under voluntary licenses. Voluntary licenses also provided a mechanism for technology transfer and knowledge sharing to support the manufacture and regulatory approval of less expensive licensed products. Compulsory licenses have been used by a small number of countries to access IP associated with certain COVID-19 therapeutics. The primary, commonly cited benefits for countries utilizing compulsory licenses are reduced costs and improved access. Another primary benefit of compulsory licenses reportedly is that they provide leverage to negotiate voluntary licenses. One of the main disadvantages is that they do not provide a basis for sharing knowledge.

The availability of supplies to meet global demand for COVID-19 diagnostics and therapeutics has been a moving target throughout the pandemic. Estimates or calculations of demand for these goods differ depending upon whether the metric is market demand or need. When infection rates rose sharply in early 2021, before manufacturers had scaled up production and regulators had granted approvals, access was limited and available only to a few HICs. During 2021, more products became available for procurement. By early 2022, infection rates and deaths from COVID-19 steadily declined as vaccination rates grew and natural immunity strengthened. By early May 2023, the World Health Organization (WHO) declared that COVID-19 would no longer be classified as a public health emergency of international concern. Today, market demand has waned in some countries, with several manufacturers no longer pursuing regulatory approval and stopping production altogether.

The disparity among countries of different income groups is wide in terms of access and availability to COVID-19 diagnostics and therapeutics. About 80 percent of government procurements were by HICs, 14 percent by UMICs, and 5 percent by LMICs. No government purchases were made by LICs, although

products were made available to them through multilateral organizations. The wide disparity among countries in their ability to access COVID-19 diagnostics and therapeutics is the result of multiple factors, including access to IP, prices and affordability, regulatory approvals, healthcare infrastructure, and the healthcare priorities of governments. The importance of each of these and other factors impacting availability and demand varies greatly among countries, although high prices and the lack of price transparency appear detrimental to many countries seeking access.

Academic literature on the effects of patent protection, compulsory licenses, and the MPP is limited and would benefit from additional research. From the available evidence, patent protection is generally found to be more beneficial to innovation in the health sector for developed countries and less so for developing countries. Patent protection is often found to result in higher prices for medicines, which decrease access, but patent protection can also have some counteracting effects, such as increases in international trade flows of pharmaceuticals and faster drug launches in markets, that help improve access. Researchers have found that compulsory licenses and the MPP are associated with increased generics and lower prices, and increased access to pharmaceuticals. Researchers have not studied the relationship between compulsory licenses and the MPP and access to COVID-19 diagnostics and therapeutics.

Information Sources

In preparing its report, the Commission obtained data and information from primary and secondary sources, including academic articles, official trade statistics, U.S. government publications, and a variety of public and private data sources. In addition, Commission staff held more than 120 informational interviews with stakeholders, both virtually and in-person, including through domestic travel to Maryland, Michigan, and New York and international travel to Bangladesh, Brazil, Malaysia, Mexico, South Africa, Switzerland, and Zambia. The Commission held a public hearing and solicited comments from the public on various issues concerning COVID-19 diagnostics and therapeutics. The hearing occurred on March 29–30, 2023, and included 56 virtual and in-person participants from the United States and 14 other countries. For this investigation, the Commission received 145 prehearing briefs, 22 posthearing briefs, and 168 other written submissions from a total of 195 individuals and organizations.

Information Gaps

As requested by the Trade Representative, the Commission identified significant information gaps, which are noted throughout the report. For manufacturing of COVID-19 diagnostics and therapeutics, information varies greatly by country and region, and it was difficult to determine if announced commercial production had been undertaken or was still active as of the writing of this report. In addition, data are extremely limited with respect to production costs for COVID-19 diagnostics and therapeutics. Major factors impacting overall production costs are known, but the cost of manufacturing a specific input or finished product often is not. These costs are often not publicly disclosed and can vary substantially across producers because the supply chains of each producer differ.

Key information gaps also arise from the lack of transparency surrounding IP-related agreements. Because individual agreements are typically not publicly available, it is difficult to obtain detailed information on the universe of agreements and their terms. As demand for COVID-19 therapeutics waned, licensed producers reportedly terminated or suspended operations; however, the status of

many agreements is unknown or in flux. Complete information on the universe and status of CLs—and the use of the least-developed countries (LDC) exception in the TRIPS Agreement—also is lacking, in part, because of differences in countries' laws and procedures, exemptions from TRIPS Agreement reporting requirements for LDCs, and the role of private actors in using, or attempting to use, CLs.

Finally, there is very little price transparency for COVID-19 therapeutics beyond the tiered-pricing schemes employed by originator companies in purchasing agreements with individual governments. This makes it difficult to fully assess the prices of COVID-19 treatments available in different markets. In terms of availability, data are reported for government procurements, private purchases (including by multilateral organizations), and donations. However, data on actual fulfillment of announced procurements and donations are limited. Further, data on consumption (i.e., the number of tests taken for diagnostics and the number of treatments administered to patients for therapeutics) are limited to just a few HICs, and no data on consumption are available for middle-income countries (MICs) and LICs. Because of these data gaps, the ability to analyze global trends in consumption is limited.

Intellectual Property

Intellectual Property and the TRIPS Agreement

The TRIPS Agreement sets minimum standards for the protection and enforcement of IP rights, including the patents and trade secrets that are particularly relevant to COVID-19 therapeutics and diagnostics. It also states that the protection and enforcement of IP rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology to the mutual advantage of producers and users of technical knowledge and in a manner conducive to promote social and economic welfare, and to a balance of rights and obligations. The TRIPS Agreement incorporates flexibilities that permit countries to issue compulsory licenses in a manner that is compatible with the TRIPS Agreement to improve access to pharmaceutical products. Compulsory licensing enables WTO members to use the subject matter of a patent without the authorization of the patent owner under certain circumstances. It is the most widely used TRIPS flexibility for public health purposes, followed by the extended transition period for LDCs to implement certain protections for pharmaceutical patents and regulatory test data.

The WTO has issued declarations and decisions and modified the TRIPS Agreement itself to enhance flexibilities to use compulsory licenses for pharmaceutical products. The 2022 Ministerial Decision provides additional flexibilities with respect to patents for COVID-19 vaccines, including by relaxing the conditions on the use of compulsory licenses to manufacture products for export. The Commission received substantial public input on the 2022 Ministerial Decision and its possible effects. Some described it as a waiver of important IP rights under the TRIPS Agreement with negative consequences for innovation, competitiveness, and national security. Others described it as making relatively minor changes to the existing compulsory licensing framework with limited negative consequences and potentially positive effects on access.

Intellectual Property Protections for COVID-19 Diagnostics and Therapeutics

Persons providing information to the Commission on COVID-19 diagnostics generally agreed that foundational patents for the two main types of COVID-19 diagnostic tests—polymerase chain reaction (PCR) tests and rapid antigen tests—have expired. Reportedly, the best evidence that patents did not act as a primary barrier to the production of these tests is that many new producers and products, including in developing countries, came online relatively quickly (although other factors reportedly gave rise to access challenges). This is not to say that patents and other IP protections are irrelevant to the diagnostics industry, which is research and development (R&D) intensive. A 2023 patent landscape report on COVID-19 diagnostics prepared by the U.S. Patent and Trademark Office (USPTO) describes inventions in emerging diagnostic technology areas.

Witnesses and information available to the Commission describe substantial patenting related to COVID-19 therapeutics. Industry representatives consider patent protections essential to preserve and obtain a return on large investments in R&D, manufacturing, regulatory processes, and the commercialization of new therapeutics. IP protections also provide a framework for collaboration among different public and private actors, helping to define what each entity brings to the table, what actions they may take, and how IP that is jointly created may be used going forward. On the other hand, some public health advocates and others raise concerns about high prices and access limitations associated with large numbers of primary patents (e.g., for the active pharmaceutical ingredient essential to the product) and secondary patents (e.g., those associated with different uses, combinations, formulations, and processes).

A patent landscape report prepared by the World Intellectual Property Office (WIPO) identifies many patent filings related to small-molecule therapeutics, biological products, and the use of traditional medicines to treat COVID-19. As part of the VLs described in chapter 5, originator companies identified hundreds of patent filings in developed and developing countries related to COVID-19 therapeutics. Patents protect almost all therapeutics recommended by the WHO for the treatment of COVID-19, with the exception of dexamethasone. Trade secrets also play a role in protecting the manufacturing and regulatory know-how needed to bring COVID-19 therapeutics and diagnostics to market.

Definitions and the Universe of COVID-19 Diagnostics and Therapeutics

In the medical field, diagnostics and therapeutics are defined as goods that are used, respectively, to diagnose and treat disease. Therefore, a COVID-19 diagnostic or therapeutic is a good that is used to diagnose or treat COVID-19. Since the emergence of SARS-CoV-2 (the virus that causes COVID-19), hundreds of diagnostics have been produced and hundreds of therapeutics have been studied, all specific to COVID-19, and new research and studies around the world are being added to the pipeline every week. If the diagnostics and therapeutics in development reach the end of the pipeline, the goods then must go through a regulatory approval process. The regulatory ecosystem for COVID-19 diagnostics and therapeutics is composed of a broad assortment of regulatory actors, including national regulatory

authorities, the WHO prequalification program, procurement organizations, and WHO entities that publish WHO guidelines.

The request letter asked the Commission to identify the universe of COVID-19 diagnostics and therapeutics covered by patents and in development. That universe is broad and varied, and identifying the full scope of products that fall within that universe is challenging for many reasons. The full epidemiology of COVID-19 in humans is still being studied, and thousands of diagnostics and therapeutics have been used to diagnose and treat COVID-19, including pharmaceuticals approved for other conditions but repurposed for treating patients infected with COVID-19. Identifying an up-to-date universe of existing and current diagnostics and therapeutics is further complicated by the fact that recommendations and authorizations of tests and medicines for COVID-19 change as the virus mutates and technologies progress. It is possible, however, to provide examples of the relevant diagnostics and therapeutics that have been used to test and treat COVID-19.

The universe of COVID-19 diagnostics generally contains three broad categories: (1) tests used to diagnose an active infection of the SARS-CoV-2 virus, (2) tests that measure an adaptive immune response to the virus, and (3) tests used in the management of patients with COVID-19. All categories of COVID-19 diagnostic tests require a number of ancillary products depending on the requirements of a test's specific protocol, which can include analyzers, cartridges, swabs, and plastic consumables (such as those to hold specimens and/or reagents). The universe of COVID-19 therapeutics includes medical devices and medicines to treat COVID-19. It includes therapeutics that directly target the virus as well as therapies prescribed to treat or manage symptoms of COVID-19 or secondary infections or symptoms that result from complications of SARS-COV-2 viral infection (e.g., inflammation, blood clots, poor pulse oxygen levels).

Patent landscape reports prepared by the USPTO and WIPO describe patent activity around the world for, respectively, COVID-19 diagnostics and therapeutics since the emergence of COVID-19. While the patenting of new diagnostic innovations has occurred, these patents primarily serve to enhance or augment existing diagnostic technologies, rather than supplant them. The foundational patents for PCR and rapid antigen tests have reportedly expired. The National Medical Library provides information on clinical trials and other studies for COVID-19 diagnostics and therapeutics and provides insights on the number of COVID-19 diagnostics and therapeutics in development.

To identify relevant examples of COVID-19 diagnostics and therapeutics, a number of specific parameters, individually or in combination, could be used to construct a more focused group of products. These include whether the products are covered by patent, whether the products are directed at SARS-CoV-2—not for example a test or treatment for a secondary infection or complication that stemmed from the COVID-19 infection—and whether the products are available to patients through authorization, or the equivalent thereof, or approval of a national or international health regulatory body. This report, as requested, uses various applications of these parameters as illustrative examples to provide information on relevant COVID-19 diagnostics and therapeutics.

COVID-19 Diagnostics and Therapeutics

The most common in vitro diagnostic tests for the detection of an active COVID-19 infection are PCR tests and antigen tests (figure ES.1). Used in point-of-care and at-home kits, antigen tests detect the presence of viral proteins in a patient’s sample. PCR tests have greater sensitivity and specificity but require more robust medical infrastructure and capital. Antigen tests are faster and usable in a wider variety of environments but have a greater probability of false negative or false positive results. Globally, more than 700 different brands of PCR tests and more than 1,000 antigen tests are on the market.

Figure ES.1 Examples of different ways to categorize COVID-19 diagnostics

Underlying data for this figure can be found in appendix J, [table J.1](#).

Test	Type	Subtype	COVID-19 test
In vitro	Diagnostic	Molecular	PCR
		Antigen	Rapid tests
		Serology	Antibody
		Other	Breathalyzer
	Immune response	Adaptive response	Genotyping
			T cell immune response
	Management	Biomarker	Immunoenzymatic assay

Source: Compiled by the USITC.

Note: The tests listed here do not represent an exhaustive list of COVID-19 diagnostics.

Relevant therapeutics that are currently available for the treatment of patients infected with COVID-19 may be classified into two distinct categories: (1) small-molecule drugs and (2) biological products (biologics). Both categories of pharmaceuticals have been used during the course of the pandemic, for example antivirals, which are small-molecule drugs, and monoclonal antibodies (mAbs), which are biologics. Examples of the various types are presented in figure ES.2.

Figure ES.2 Examples of different ways to categorize COVID-19 therapeutics

Underlying data for this figure can be found in appendix J, [table J.2](#).

Treatment type	Treatment class	Mode of action	Pharmaceutical	Patient setting
Antiviral	Virus-directed	Nucleoside or nucleotide analogue	Remdesivir	In- and outpatient
		Protease inhibitor	Molnupiravir	Outpatient
			Ensitrelvir	
			Nirmatrelvir (+ ritonavir)	
Anti-inflammatory	Host-directed	Immune suppression	Dexamethasone	Inpatient
		Inhibitor (e.g., JAK or IL-6)	Baricitinib	
			Tocilizumab	
Monoclonal antibody (mAb)	Virus-directed	Neutralizing mAb	Casirivimab and imdevimab	In- and outpatient
			Bamlanivimab and etesevimab	
			Sotrovimab	Inpatient
Other	Adjunctive therapy	Secondary (e.g., NSAID, immunomodulator, anticoagulant)	Heparin	Inpatient
			Ibuprofen	
			Vitamin C	Outpatient

Source: Compiled by the USITC.

Notes: The drugs listed here do not represent an exhaustive list of COVID-19 therapeutics. Patient setting refers to the location of the patient being treated (e.g., the drug in question can be prescribed for the treatment of COVID-19 in patients who are not hospitalized (outpatient) or are hospitalized (inpatient)).

COVID-19 Diagnostics and Therapeutics Manufacturing Supply Chain and Trade

The pharmaceutical industry is multinational in nature, with pharmaceutical companies having presence and operations across multiple countries. For the pharmaceutical industry to have access to and serve various global markets, the establishment of subsidiaries, manufacturing plants (including contract manufacturing), and distribution networks (often through partnerships) in multiple countries is required. Generally, the intricate global network of production and distribution supply chains can optimize costs, use specialized expertise in that region, and help ensure a steadier supply of medicines to global markets. The worldwide presence of pharmaceutical companies also allows for global collaboration, which has been critical during the COVID-19 pandemic.

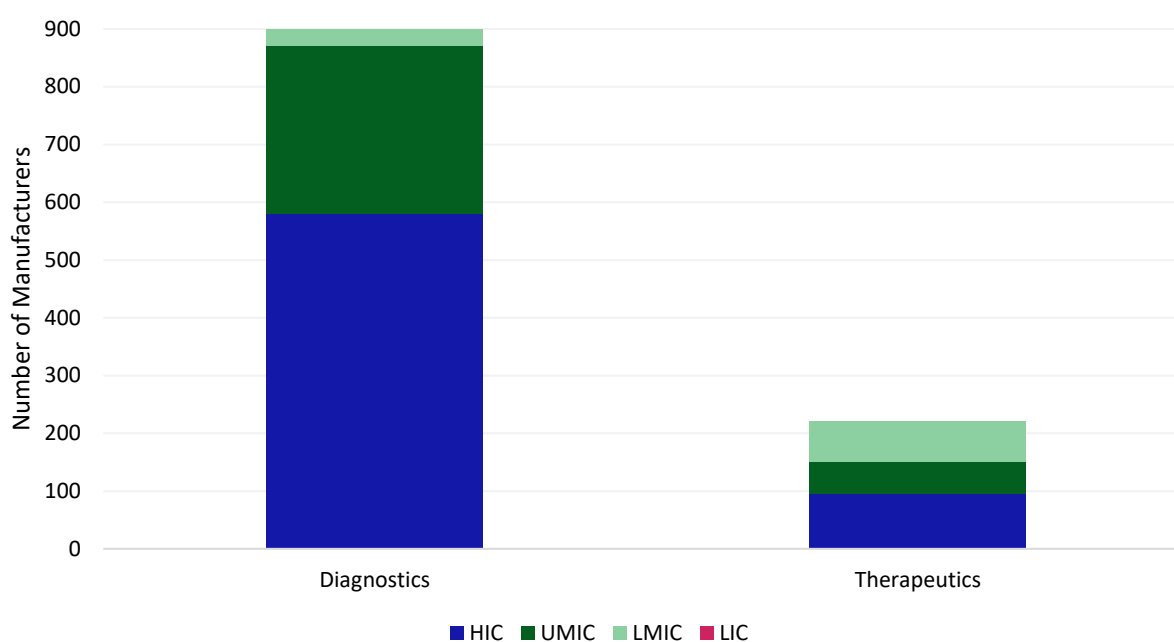
The process of manufacturing COVID-19 tests and synthesizing COVID-19 drugs on a large scale involves multiple stages, each of which requires careful attention to detail and strict quality control measures. Because the relevant COVID-19 diagnostic tests and therapeutics were for the emerging SARS-CoV-2

virus, production at scale of the majority of diagnostics and certain novel therapeutics began prior to regulatory approvals or authorizations.¹

Determining the active level of production for COVID-19 diagnostics and therapeutics is difficult. Figure ES.3 presents an estimate of the number of manufacturers of COVID-19 diagnostics (900) and therapeutics (221) as of June/July 2023. It should be noted, however, that this is based on publicly available information and does not account for production that may be paused or has never started, nor does it show the capacity of these facilities. No production of COVID-19 diagnostics or therapeutics in LICs has been reported.

Figure ES.3 Count of manufacturers of COVID-19 diagnostics and therapeutics

In number of manufacturers. HIC = high-income countries; UMIC = upper-middle-income countries, LMIC = lower-middle-income countries; LIC = low-income countries. Underlying data for this figure can be found in appendix J, [table J.3](#).



Sources: FIND, accessed June 30, 2023; Airfinity, accessed August 28, 2023.

Notes: Additionally, there are 58 manufacturers of serology COVID-19 tests and 1 manufacturer of a COVID-19 saliva test. Manufacturers of COVID-19 diagnostics and therapeutics in this section refer to firms that have produced, announced intention to produce, or are actively producing either COVID-19 diagnostics or therapeutics. For diagnostics, this figure includes the count of developers/manufacturers of the product. For therapeutics specifically, the count of manufacturers only includes those of drugs that are approved, authorized, and/or recommended for the treatment of COVID-19.

Trade in a broader category of goods that includes COVID-19 diagnostics and therapeutics is concentrated among HICs.² In 2022, HICs were the recipient of nearly 85.4 percent (\$314 billion of \$368 billion) of global exports of products including COVID-19-related diagnostics and therapeutics. Similarly, HICs were the source of 91.9 percent (\$338 billion of \$368 billion) of global exports of products including COVID-19-related diagnostics and therapeutics. Switzerland was the top exporter of products

¹ Though not “approved,” these tests and drugs were submitted to regulatory agencies to be considered for approval; until granted approval, some countries employed mechanisms such as “emergency use authorizations.”

² Globally, most HS subheadings are not specific to a COVID-19 diagnostic or therapeutic. Therefore, the trade data in this report reflect large basket categories of products not specific to COVID-19.

including COVID-19-related diagnostics (\$43.7 billion in 2022), and Germany was the top exporter of products including COVID-19-related therapeutics (\$65.1 billion in 2022).

Approaches to Access Intellectual Property Associated with COVID-19 Diagnostics and Therapeutics

Different types of IP-related agreements have been used to help move COVID-19 products to market. These include R&D agreements, manufacturing partnerships, agreements between companies that originate new products and licensed producers (bilateral license agreements), and license agreements involving the MPP. Bilateral license agreements and MPP license agreements are both referred to as voluntary license agreements. Key TRIPS Agreement flexibilities, such as CLs and the LDC exception to the TRIPS Agreement, also have been used with COVID-19 therapeutics. According to information available to the Commission, only R&D agreements were used in connection with COVID-19 diagnostics. Manufacturing partnerships and VLs, as well as CLs and the LDC exception, were not typically used for the production of COVID-19 diagnostic tests.

R&D Collaboration Agreements for COVID-19 Diagnostics and Therapeutics

An R&D collaboration agreement provides the basis for different entities to work together on the R&D underlying a new product or process. Small and medium-sized enterprises (SMEs) played an important role in the R&D associated with COVID-19 therapeutics; reportedly they are responsible for most therapeutic R&D programs in the United States and for most products in the global clinical development pipeline. Large firms, the federal government, and universities also have been prominent in R&D collaborations for the development of COVID-19 therapeutics and diagnostics, either independently or in collaboration with SMEs. For example, the R&D behind molnupiravir and remdesivir, as well as the GeneXpert diagnostic testing platform, involved collaborations among the federal government, SMEs, academic institutions, and large firms. Substantial U.S. government funding and participation in R&D suggest to some commentators that companies should be required to make their products and intellectual property (IP) available at lower prices and more broadly, and that contract terms should be more transparent.

Voluntary Licenses and Access to COVID-19 Therapeutics

VLs provided the framework for the licensed production of COVID-19 therapeutics subject to IP protections for sale in LICs, LMICs, and some UMICs. Licensed products generally can be offered at lower prices than the original for a number of reasons including because the licensed producer does not have to invest in the substantial R&D and regulatory costs associated with the discovery and approval of a new drug. Essential features of VLs include the following:

- **IP description:** VLS typically reference the patented information, know-how, and other technical information to be offered the licensed producer. The technical information may include know-how associated with manufacturing processes needed for production at scale, as well as know-how needed to obtain regulatory approval.
- **Covered territories:** VLS identify the countries where the licensed product may be offered for sale. In practice, these territories generally include most LICs and LMICs and exclude most UMICs. The covered territories for sales may be different than where the licensed product is manufactured.
- **Payment of royalties and pricing:** To make access more affordable, VLS may waive the payment of royalties in general or depending on certain factors. These factors may include the income level of the country where the product is sold and whether the WHO has declared a public health emergency of international concern. Licensed producers generally set prices according to their own needs, without the involvement of the originator company or the MPP.

Advantages and Challenges Associated with VLS

VLS have been an important mechanism used to offer COVID-19 therapeutics for sale at reduced prices in LICs and LMICs; however, most UMICs have been excluded from coverage under VLS. Originator companies began negotiations for licensed production early—before clinical trials and regulatory processes had been completed. This reduced the lag time between the introduction of original products in high-income markets and licensed products in lower-income markets. Another key advantage of VLS is that they provided a mechanism for technology transfer and knowledge sharing. Originator companies provided access not only to patented information but also to technical know-how about manufacturing processes and, in some cases, assistance with regulatory processes. This advantage was not available to countries relying on CLs or the LDC exception to the TRIPS Agreement.

In terms of transparency, VLS through the MPP generally were superior to bilateral license agreements. Model agreements—and executed versions of licenses and sublicenses—generally are available on the MPP website. By contrast, only U.S.-based biopharmaceutical company Gilead Sciences, Inc. (Gilead) published a model version of its license agreement; only limited information on other agreements was publicly available. MPP licenses also may streamline the license negotiation process by eliminating the need for originator companies to identify and negotiate terms with each potential producer. A key difference of VLS, as compared to CLs and the LDC exception, is that the originator company controls what, when, and where products are made available. Efficacious therapeutics are not available at reduced prices in all countries, a particular issue for access to COVID-19 therapeutics in a number of UMICs.

Limits on Territories Where COVID-19 Therapeutics Can Be Sold Under VLS

With limited exceptions, four key COVID-19 therapeutics—ensitrelvir fumaric acid (ensitrelvir), molnupiravir, nirmatrelvir (+ ritonavir), and remdesivir—could be offered for sale in almost all LICs and LMICs under VLS.³ By contrast, 19 of 54 UMICs were not included under VLS for ensitrelvir, 28 of 54 for

³ International nonproprietary names and trade names are as follows: Ensitrelvir fumaric acid (Xocova), molnupiravir (Lagevrio), nirmatrelvir (+ ritonavir) (Paxlovid), and remdesivir (Veklury).

molnupiravir, 41 of 54 for nirmatrelvir (+ ritonavir), and 22 of 54 for remdesivir. Large UMICs not covered by VLs include Argentina, Brazil, China, Colombia, Mexico, Russia, and Turkey. In terms of population, at least one of the four therapeutics could be offered for sale to all, or virtually all, of the LIC and LMIC populations. In UMICs, at least one of the four therapeutics could be offered for sale to 14.7 percent of the UMIC population, leaving 85.3 percent of the UMIC population without access to these COVID-19 therapeutics under the terms of the VLs. COVID-19 infection rates were particularly high for countries excluded from some VLs, as compared to those countries within the coverage territory. Originator companies instead offered their branded products for sale in large UMIC markets, reportedly through a tiered-pricing approach according to country income levels and supply agreements with donor agencies. To expand access to licensed products in UMICs, some commentators suggest the possibility of higher royalty payments under VLs, rather than their exclusion from coverage.

Compulsory Licenses and Access to COVID-19 Diagnostics and Therapeutics

Easing the use of CLs pertaining to COVID-19 vaccines was the primary focus of the 2022 Ministerial Decision; however, as of September 2023, CLs have not been used to access patents pertaining to COVID-19 vaccines. COVID-19 therapeutics have been the subject of CLs in a number of countries, including Hungary, Israel, and Russia. Hungary's CL allowed a domestic manufacturer to begin local production of remdesivir, and Hungary reportedly was able to treat patients and begin clinical trials. Reportedly, Israel's CL led, in part, to the patent holder pledging not to enforce the patent globally while the drug (Kaletra) was being used for COVID-19 treatment. Russia's CL for remdesivir was upheld domestically, but it is unclear what impact the CL had. An Indian firm requested that a CL be granted for baricitinib, and the patent holder ultimately offered a VL to the firm. CLs have not been used to access patents associated with COVID-19 diagnostics.

Advantages and Challenges Associated with the Use of CLs

Like other methods of access, CLs provide certain advantages and disadvantages compared to other options. The primary, commonly cited benefit for countries using CLs is the reduced cost of the products and improved access, as compared to the originator company's product. Another benefit ascribed to the use—or potential use—of CLs is leverage. One of the more prominent ways this leverage can be exercised is in negotiating the inclusion of a VL for a producer in a potential CL-using country. Development of a country's domestic manufacturing capacity is another reported potential benefit from using CLs.

It was commonly identified that countries that use CLs encounter economic and political pressure after granting, or attempting to grant, a CL. Another key challenge to effectively using a CL is that the flexibility only covers patents and does not include know-how, which is often necessary to reproduce more complex pharmaceutical products such as biologics. The potential lack of availability of a qualified manufacturer, either domestically or through a trading partner, can also reportedly pose a challenge. Legal and procedural hurdles in various forms, such as the requirements of the TRIPS Agreement or domestic IP laws, can present another substantial challenge for countries to use CLs. Views are mixed as to the impact of CLs on innovation, but some commentators state that CL usage is detrimental to innovation.

The Least-Developed Country Exception and Access to Intellectual Property

LDC is a special classification of a country, as determined by the United Nations, that receives differential treatment under various WTO agreements. One primary example of this differential treatment is a transition period for the implementation of the majority of obligations under the TRIPS Agreement (commonly referred to as the LDC Exception). An LDC can use this transition period in multiple ways, depending on its domestic laws. For example, until the end of the transition period, an LDC could provide no pharmaceutical patent protection at all or provide protection for a period that is less than the TRIPS Agreement-required 20-year minimum.

Some LDCs, such as Bangladesh, have made substantial use of these flexibilities. In 2008, Bangladesh suspended the issuance of pharmaceutical patents and, in 2022, made pharmaceutical and chemical products exempt from patent protection. Using this flexibility, Bangladeshi manufacturers produce generic versions of nirmatrelvir (+ ritonavir), remdesivir, and baricitinib and export these pharmaceutical products to jurisdictions where the products are not covered by patents or where an applicable CL has been issued. Manufacturers in Laos, Myanmar, and Paraguay also leverage their LDC status to manufacture generic versions of COVID-19 therapeutics. Other LDCs, such as Zambia, have not used the flexibilities to the same degree. For example, Zambia issues pharmaceutical patents, with certain restrictions, despite the LDC transition period. Zambia's patent law, however, previously limited patent protections to 16 years instead of the 20 years required under the TRIPS Agreement with an option for the patent holder to request an extension of the patent protection term; the patent term is now 20 years, however, and the terms of extension are more limited. The law also authorizes the government to declare a period of emergency and subsequently use any patented invention to maintain or secure supplies and services essential to the life of the community.

Availability and Consumption of COVID-19 Diagnostics and Therapeutics

Demand and Need for Diagnostics and Therapeutics

Whether existing production and supplies of diagnostics and therapeutics can meet demand depends on how demand is defined. Two examples of measurement methods are: (1) assessing actual market purchases and donated procurements by countries across all income groups and (2) assessing the population-based public health "need" by estimating the maximum number of people that may benefit from treatment to avoid hospitalization or death. Measuring need is challenging, particularly in the face of multiple epidemiological and policy uncertainties. While there are estimates of need for COVID-19 therapeutics, no studies or reports have been found that provide estimates of need for diagnostics.

Prices, Purchases, Donations, and Consumption of Diagnostics and Therapeutics

Diagnostics: Data on COVID-19 diagnostic prices and purchases are not compiled consistently across test types, manufacturers, regions, or timeframes, so it is challenging to accurately identify trends and disparities. Prices vary significantly across different regions and countries, depending on healthcare systems, economic conditions, and local regulations. Pricing can also vary by the technology used, such as PCR tests or antigen tests.

For COVID-19 diagnostics, various sources point to large government procurement of testing kits, such as the commitment of the U.S. government to make 1 billion self-tests available free of charge. Pooled procurement by multilateral organizations has made tests broadly available across MICs and LICs. Also, governments, the private sector, and philanthropic organizations have donated tests to many MICs and LICs. Although no data are available on global consumption of COVID-19 diagnostics, trends can be inferred by observing testing rates over specific time periods. For example, testing rates fell significantly between the first quarter of 2022 and the second quarter of 2023. By mid-2023, several sources noted that testing appeared to have stopped in most MICs, and testing data were no longer reported for LICs. The fall in diagnostics demand will likely continue with the announced end of the WHO's public health emergency of international concern.

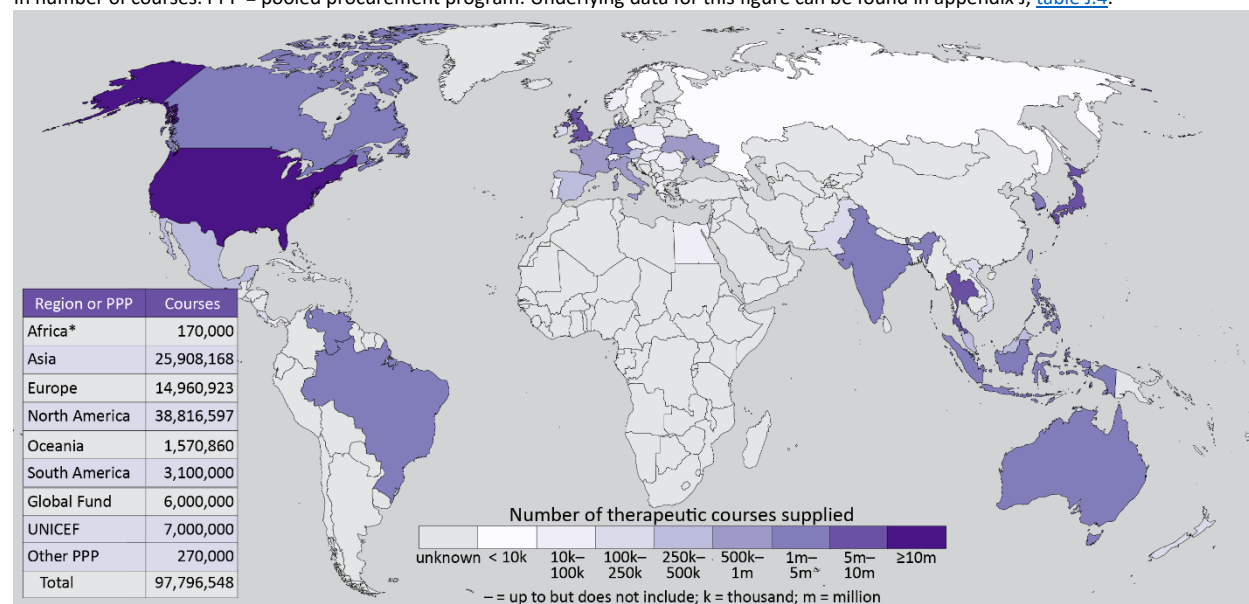
Therapeutics: There is very little price transparency for COVID-19 therapeutics, so it is challenging to identify prices paid by purchasers. The data that are available highlight the tiered-pricing scheme employed by originator companies in which prices are offered to countries according to their income levels. HICs pay the highest prices for therapeutics, but the middle tier, mostly composed of UMICs, faces a price point that is typically half or less than half the HIC price. The third tier is for LMICs and LICs and is sometimes referred to as the “best access price” or “non-profit price” by manufacturers.

Obtaining COVID-19 therapeutics occurs via one of two mechanisms: through donations (pooled procurement or direct) or purchases. Purchases can be further broken down into government or private. Figure ES.4 shows the courses of COVID-19 therapeutics made available either through donation or purchase during the course of the pandemic as determined by publicly announced supply agreements that identify the destination country. Announced purchase agreements of COVID-19 therapeutics are predominantly through governments, accounting for 79 percent of the 98 million treatment courses of COVID-19 therapeutics tabulated from supply agreements announced since 2020. HICs dominated government purchases, which accounted for about 81 percent (or 62.4 million treatment courses), followed by UMICs for 14 percent (11 million courses), and LMICs for 5 percent (3.6 million courses). No government purchases by LICs have been reported. Roughly one-half of all the government purchases (39.9 million courses) were for Pfizer Inc.'s (Pfizer) nirmatrelvir (+ ritonavir).

Pooled procurements of COVID-19 therapeutics by multilateral organizations have been made available broadly across MICs and LICs. The main announced procurements were 6 million courses of nirmatrelvir (+ ritonavir) by the Global Fund and 4 million courses of nirmatrelvir (+ ritonavir) and 3 million courses of molnupiravir by UNICEF. Sources say that the distribution of treatment courses has been slow. A few originators, such as Pfizer; Eli Lilly and Company (Lilly); Merck & Co., Inc. (Merck); and Gilead, have made donations of COVID-19 therapeutics to certain LICs and LMICs.

Figure ES.4 Courses of COVID-19 therapeutics made available through donation or purchase, by country and region, based on publicly announced supply agreements

In number of courses. PPP = pooled procurement program. Underlying data for this figure can be found in appendix J, [table J.4](#).



Source: Airfinity, accessed August 29, 2023.

Note: These numbers represent announced government procurements, private purchases (including by multilateral organizations), and donations. The data do not reflect confirmed deliveries. Not all supply agreements disclose the country or region and are thus not accounted for in the region or PPP table within the figure. For example, not reflected in the map but listed in the tabulation on the bottom left of the figure are announced supply agreements via the Global Fund, which can go to MICs (UMICs or LMICs) or LICs, as well as the supply agreements with UNICEF, which can go to LMICs and LICs. Africa* includes Sub-Saharan Africa and Egypt. Sub-Saharan Africa is home to 22 of 26 countries with LIC designation, and 19 of 54 countries with LMIC designation.

Factors Affecting Demand and Availability of Diagnostics and Therapeutics

Many consider the prices of COVID-19 therapeutics to be a significant barrier to access for many LICs, LMICs, and UMICs. Under the tiered-pricing scheme described above, the prices paid by LICs, LMICs, and UMICs are considerably lower than for HICs but the reduced prices still exceed or comprise a high share of the average per capita annual health care expenditure for LICs, LMICs, and many UMICs. For example, Pfizer's nirmatrelvir (+ ritonavir) is reportedly available to UMICs at roughly \$250 per treatment course, which is about one-half the average annual per capita healthcare expenditure across all UMICs. VLs, such as those facilitated by the MPP, allow for the production of licensed (generic) products that can be lower priced than direct purchases from the originator. However, production of licensed products has been slow to ramp up, and many UMICs are not covered by known voluntary license agreements.

Demand has also been impacted by the waning of the pandemic. For certain drugs, only a small number of licensed manufacturers are producing, and demand for their products has been low with the timing of licensed product availability coinciding with the waning of the pandemic. This also may be the case for supplies available to LICs and LMICs for free through donor funds from international organizations, such as the Global Fund and UNICEF, and private entities. By the time contracts were negotiated between originator companies and procurement organizations, demand for the products was declining.

Regulatory approval processes, including WHO prequalification and national regulatory approvals, are essential for ensuring public health and safety but can lead to delays in bringing diagnostics and therapeutics to market. Lengthy approval processes, limited resources and expertise, and little harmonization within and among regulatory bodies have been considered barriers to accessing diagnostics and therapeutics. For example, many COVID-19 diagnostics and therapeutics did not receive WHO prequalification, guidance, or national regulatory approval until later in 2022 or early 2023, when demand for COVID-19 products had already begun to decline.

Moreover, governments with limited budgets for healthcare expenditures must balance their responses to COVID-19 with efforts to combat other diseases, such as HIV/AIDS, malaria, and tuberculosis. Several representatives of government ministries and multilateral organizations provided anecdotal evidence that once WHO declared in May 2023 that COVID-19 was no longer a public health emergency of international concern, many countries with competing health priorities chose to allocate their limited health budgets to other areas and are now giving a lower priority to their response to COVID-19.

The extent to which last mile delivery can reportedly be a barrier to patient access to COVID-19 diagnostics and therapeutics in developing countries varies among countries by income level. Little evidence shows that last mile delivery challenges have constrained access in HICs and UMICs. Last mile delivery, however, can be a barrier in LMICs and LICs, especially in rural areas, because of factors such as poor roads and distance between health centers.

Views of Interested Persons

In addition to requesting information on the subjects discussed above, the Trade Representative's letter stated that public input would be particularly salient for eight specific topics, which the Commission has grouped into three categories: (1) IP protection, R&D, and jobs; (2) the TRIPS Agreement and access to medicine; and (3) the TRIPS Agreement and COVID-19 diagnostics and therapeutics. The views of interested persons on these topics were summarized from public input provided at the Commission's hearing and through written submissions and are not the views of the Commission.

Intellectual Property Protection, R&D, and Jobs

The relationship between IP protection and corporate R&D expenditures, taking into account other expenditures, such as share buybacks, dividends, and marketing: In discussions about the relationship between IP protection and corporate R&D expenditures, some participants stated that IP protections are necessary to incentivize investments in corporate R&D; these investments made possible the development of COVID-19 diagnostics and therapeutics and will address any future public health crisis. In addition, it was noted that IP protections are important for attracting investment in industry sectors that are high risk and capital intensive, such as the diagnostics and therapeutics industries. Others, however, stated that extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would have a limited effect on corporate R&D expenditures. Participants provided little information about the effect of other expenditures, such as share buybacks, dividends, and marketing on R&D expenditures.

The location of jobs associated with the manufacturing of diagnostics and therapeutics, including in the United States: Reported employment figures vary and often include jobs not directly related to the

manufacture of diagnostics and therapeutics. While the views of interested persons did not provide comprehensive information on jobs associated with the manufacturing of diagnostics and therapeutics, participants provided information on jobs in 26 specific countries, including the United States.

TRIPS Agreement and Access to Medicine

Whether and how existing TRIPS rules and flexibilities can be deployed to improve access to

medicines: Some participants maintained that IP protections, such as those established in the existing TRIPS Agreement rules, increase access to medicine by incentivizing investment in the R&D of new medicines or in finding new uses for existing medicines. According to several participants, IP protections enable access to medicine through VLs and other partnerships because clearly defined IP ownership gives companies confidence to share their knowledge. Other participants, however, asserted that certain characteristics of VLs limit access and that CLs enabled by TRIPS Agreement flexibilities allow production of affordable generic medicines that can increase access to medicine.

Successes and challenges in using existing TRIPS flexibilities: The TRIPS Agreement includes a number of flexibilities, but participants focused their responses on the successes and challenges of using CLs. Participants provided examples of several countries successfully using CLs and noted that CLs are useful bargaining tools to encourage pharmaceutical companies to engage in programs for donations, price negotiations, and VLs. Some participants discussed challenges related to the use of TRIPS Agreement flexibilities such as difficulty establishing local production (in part because CLs do not involve the transfer of knowledge necessary for production) and public safety and quality concerns with local production. Other participants focused on political pressures (including pressure from diagnostic- and pharmaceutical-producing companies), limits on exports of products manufactured using a CL, and complexities of the TRIPS Agreement rules and local regulations.

To what extent further clarifications of existing TRIPS flexibilities would be useful in improving access to medicines: Some participants commented on the extent to which further clarifications of existing TRIPS Agreement flexibilities would be useful in improving access to medicines. Some participants noted where certain improvements could be made. Other participants stated that IP protections were not a barrier to access to medicines and therefore, clarifications were not needed. Multiple participants mentioned that clarifications could be useful at the national or regional level where regulations are often too complex to implement TRIPS Agreement flexibilities in a timely manner during a crisis.

TRIPS Agreement and COVID-19 Diagnostics and Therapeutics

How the TRIPS Agreement promotes innovation in and/or limits access to COVID-19 diagnostics and therapeutics: Some participants asserted that IP protections are fundamental to innovations in medicine, including by fostering the decades-long R&D and partnerships necessary for innovation that supported the foundational research for COVID-19 diagnostics and therapeutics. Other participants, however, stated that patents and other IP protections create monopolies that result in products that are not affordable for widespread purchase in developing countries, reducing access to diagnostics and therapeutics.

The extent to which products not yet on the market, or new uses for existing products, could be affected by an extension of the Ministerial Decision to COVID-19 diagnostics and therapeutics: A common argument among some participants was that waiving or weakening IP rights on COVID-19 diagnostics and therapeutics would reduce incentives to invest in the R&D of tests and treatments for future pandemics. It was also noted that, to address future pandemics more quickly, companies need IP protections that allow them to realize reasonable returns on their investments. Other participants stated that for the best public health outcomes, an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics should apply to products that will be developed in the future, including in some cases combination drugs.

The relevance, if any, that diagnostic and therapeutic products used with respect to COVID-19 may also have application to other diseases: Some participants expressed concern that an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would cover an overly broad set of diagnostics and therapeutics and reduce incentives for companies to look for COVID-19 applications for their products. Other participants stated that it would be possible to limit the scope of an extension of the 2022 Ministerial Decision or that a broader interpretation of covered products would be best to increase access to medicine.

Literature Review

As requested by the Trade Representative, the Commission conducted a literature review that catalogs academic research and provides a critical and detailed assessment of the literature covering the effects of IP rules on different outcomes for pharmaceuticals. The review covers four main topics. The first two topics explore innovation in the health sector and access to medicines in relation to patent protections, providing information on these issues as they relate to LICs, LMICs, UMICs, and HICs, when available. The third topic covers the outcomes of using CLs by WTO members for pharmaceuticals, including available information on product access, innovation, and global health. The fourth topic summarizes the effect, or lack thereof, of the MPP on access to COVID-19 diagnostics and therapeutics. Across the four topics, the literature can be broadly summarized as being limited and would benefit from additional research on these topics. Researchers face many challenges, including limited data availability and difficulty identifying the causal effect, when studying the effects of patent protection, CLs, and the MPP.

The Effects of Patent Protection on Innovation in the Health Sector

At the center of the debate regarding the use of patent protection is the relationship between incentives for innovation and the inaccessibility of this innovation during the period of market exclusivity. Responses to firm-level surveys from the literature generally provide strong support for the importance of patent protection for innovation in the health sector, especially for pharmaceuticals. Although firm-level survey data attempt to provide context on whether patent protection leads to further innovation, this evidence is only suggestive and not conclusive. In addition, this survey evidence has generally focused on HICs, with less known about UMICs, LMICs, and LICs. Model-based analyses often find mixed results on the relationship between patent protection and innovation in the health sector. Some cross-country studies provide evidence that patent protection supports innovation in the

health sector in more developed countries and had little to no effect on innovation in developing countries. Country-specific studies do not always follow these general trends.

The Effects of Patent Protection on Access to Medicines

When studying patent protection and access to medicine, researchers have used a range of different measures related to access. Studies have generally found that patent protection results in higher prices for medicine, with the magnitude of these price premiums varying across different studies. Little evidence on pharmaceutical sales is available. Trade flows of pharmaceuticals are often found to have increased because of patents, with differences in outcomes depending on the development status of countries and the direction of trade flows. Patent protection is generally associated with faster launches of medicine, with some variation in results depending on the type of patent protection and the development level of countries. The diffusion of pharmaceuticals tends to be limited in LICs; however, researchers have noted that factors other than patent protection are important determinants for the diffusion of medicine in these markets. Two studies on India gave estimates of negative welfare effects due to patent protection, with most of the negative effects being faced by local consumers.

The Effects of Compulsory Licenses

The TRIPS Agreement establishes flexibilities such as CLs to help address concerns that patents and monopolistic pricing limit access to pharmaceuticals. Empirical evidence on the effects of compulsory licensing on pharmaceuticals is limited because identifying the effect of CLs is challenging. For example, it is difficult to identify the effect of CLs separated from other country and industry characteristics. Researchers have generally found that CLs are associated with decreased prices and that CLs increased the number of people with access to patented products. Two studies from the literature provide evidence that CLs may encourage innovation; there is one study that provides evidence that CLs can increase consumer welfare in the country using CLs. However, because this research is for specific countries it is difficult to generalize findings.

The Effects of the Medicines Patent Pool

Academic research has not studied the relationship between the MPP and access to COVID-19 diagnostics and therapeutics. The limited literature on the relationship between the MPP and access to other pharmaceuticals generally focuses on HIV/AIDS drugs. Overall, these studies showed that the MPP increased access to generic drugs and encouraged technology diffusion.

Chapter 1

Introduction

In a letter dated December 16, 2022, the U.S. Trade Representative (Trade Representative) asked the U.S. International Trade Commission (USITC or Commission) to conduct a factfinding investigation and provide a report on global access to COVID-19 diagnostics and therapeutics.⁴ In her letter, the Trade Representative noted that the COVID-19 pandemic renewed the longstanding concern over sufficient global access to medicines and the difficult question of how best to balance the need for equitable global access with protections for intellectual property (IP).

Her letter acknowledged the varied and divergent opinions on whether the IP protections that support the development of new medicines may also act as a barrier to access, particularly in developing countries. The issue of IP and access to COVID-19-related goods was formally brought before the World Trade Organization (WTO) in October 2020, when India and South Africa submitted a joint communication to the WTO Council for Trade-Related Aspects of Intellectual Property Rights (TRIPS Council)—“Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19.” This document asked the WTO to allow all countries to choose to neither grant nor enforce patents and other IP related to COVID-19 vaccines, therapeutics, diagnostics, and other technologies for the duration of the pandemic.⁵

Following negotiations and discussion, on June 17, 2022, at its 12th Ministerial Conference, the WTO adopted the Ministerial Decision on the TRIPS Agreement (the 2022 Ministerial Decision), which included clarifications and a waiver of certain compulsory licensing rules in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) for the production of COVID-19 vaccines for developing countries.⁶ This investigation is intended to provide information as WTO members consider whether to extend the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics.

Approach and Scope

The Trade Representative’s letter asked the Commission to provide information on issues and factors concerning COVID-19 diagnostics and therapeutics, as well as identify where significant data and information gaps exist, to inform WTO members’ consideration of extending the 2022 Ministerial Declaration to COVID-19 diagnostics and therapeutics. The Commission’s report primarily covers the period from December 2019 to July 2023 and presents information by country income level when possible (see below). In keeping with the Trade Representative’s request, to the extent practicable and where data are available, this report:

- Identifies the range of definitions for “diagnostics” and “therapeutics” in the medical field.

⁴ The request letter is available in appendix A.

⁵ WTO TRIPS Council, “Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19,” IP/C/W/669, October 2, 2020.

⁶ WTO, “Ministerial Decision on the TRIPS Agreement,” WT/MIN(22)/30, June 22, 2022.

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

- Identifies and defines the universe of existing COVID-19 diagnostics and therapeutics covered by patents as well as COVID-19 diagnostics and therapeutics in development.
- Provides a broad overview of relevant COVID-19 diagnostics and therapeutics, including a description of the products and any intellectual property protections, and containing, to the extent practicable and where data are available:
 - An overview of production and distribution, including key components, the production processes, key producing countries, major firms, operational costs, a description of the supply chain, and the level of geographic diversification within the supply chain;
 - An overview of demand, including key demand factors, an assessment of where unmet demand exists, supply accumulation and distribution, and the impact of the relationship between testing and demand for treatment, if any exists;
 - Information on market segmentation of global demand and consumption, which may be delineated by low-income countries (LICs), lower-middle-income countries (LMICs), upper-middle-income countries (UMICs), and high-income countries (HICs);
 - Information on availability and pricing (or manufacturing costs in the cases where goods are donated) for COVID-19 diagnostics and therapeutics, if available; and
 - Global trade data for COVID-19 diagnostics and therapeutics or diagnostics and therapeutics in general if specific data are not available.
- Catalogs, to the extent practicable based on available information and a critical review of the literature:
 - The reasons for market segmentation and barriers to a more diverse geographical distribution of the global manufacturing industries for COVID-19 diagnostics and therapeutics;
 - The relationship between patent protection and innovation in the health sector and between patent protection and access to medicine in LICs, LMICs, UMICs, and HICs;
 - Actions taken by WTO members to use or attempt to use compulsory licenses (CLs) for the production, importation, or exportation of pharmaceutical products and the outcomes of those actions, including the effect on product access, innovation, and global health;
 - A description of any alternatives to compulsory licensing available to WTO members, such as voluntary licenses (VLs), including through the Medicines Patent Pool (MPP); multilateral programs, including the Global Fund and United Nations Children’s Fund (UNICEF); government-to-government programs; and private sector donations; and
 - The effect, or lack thereof, of the MPP on access to COVID-19 diagnostics and therapeutics.

The Trade Representative also stated in her letter that public input would be particularly salient on the following topics:

- How the TRIPS Agreement promotes innovation in or limits access to COVID-19 diagnostics and therapeutics;
- Successes and challenges in using existing TRIPS flexibilities;
- The extent to which products not yet on the market, or new uses for existing products, could be affected by an extension of the Ministerial Decision to diagnostics and therapeutics;

- Whether and how existing TRIPS rules and flexibilities can be deployed to improve access to medicines;
- To what extent further clarifications of existing TRIPS flexibilities would be useful in improving access to medicines;
- The relationship between intellectual property protection and corporate research and development expenditures, taking into account other expenditures, such as share buybacks, dividends, and marketing;
- The relevance, if any, of the fact that diagnostic and therapeutic products used with respect to COVID-19 may also have application to other diseases; and
- The location of jobs associated with the manufacturing of diagnostics and therapeutics, including in the United States.

The Trade Representative requested that the Commission hold a public hearing and solicit views from foreign governments, nongovernmental health advocates, manufacturers, and other interested persons on these factors, as well as on certain topics related to the TRIPS Agreement.

Country Classification by Income

As requested by the Trade Representative and to the extent possible, the Commission provides information on market segmentation, which is presented throughout the report according to income categories of economies defined by the World Bank. The World Bank classifies economies into four groups according to income, as measured by gross national income (GNI) per capita.⁷ These income groups are updated annually, with the most recent groupings based on data from 2021. The first group, low-income countries (LICs), had an income per capita of \$1,085 or less. The second group, lower-middle-income countries (LMICs), had an income per capita between \$1,086 and \$4,255. The third group, upper-middle-income countries (UMICs), had an income per capita between \$4,256 and \$13,205.⁸ Finally, the fourth group, high-income countries (HICs), had an income per capita above \$13,205 (figure 1.1).⁹ The term “developing country” is used at the WTO, and in common parlance, when speaking about the first three groups.¹⁰ The term “least-developed country” (LDC), a designation provided by the UN, does not correspond to a particular World Bank classification. LDCs are defined as countries confronting severe structural impediments to sustainable development and that are highly vulnerable to economic and environmental shocks and have low levels of human assets.¹¹ Furthermore,

⁷ GNI is gross domestic product (GDP) plus net receipts from abroad of compensation of employees, property income, and net taxes minus subsidies on production. The GNI used for these thresholds is expressed in U.S. dollars, converted from local currencies using the Atlas method. OECD Data, “Gross National Income (Indicator),” accessed August 25, 2023; World Bank, “What Is the World Bank Atlas Method?,” accessed February 8, 2023.

⁸ LMICs and UMICs may be referred to as middle-income countries (MICs).

⁹ For more information on the World Bank’s methodology for choosing these income thresholds, see World Bank, “WDI—Classifying Countries by Income,” accessed February 8, 2023.

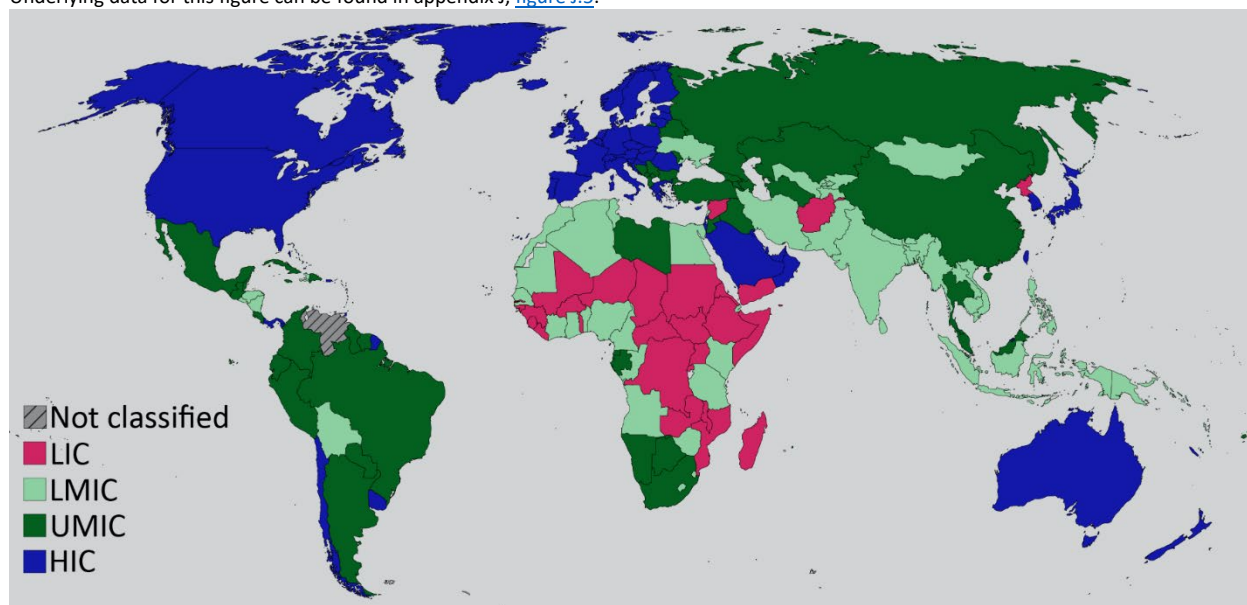
¹⁰ According to the WTO, a majority of members are developing countries. The WTO has no definitions for “developed” or “developing.” Although members announce their status for themselves, other members can challenge the decision to make use of WTO provisions applicable to developing countries. WTO, “Who Are the Developing Countries in the WTO?,” accessed July 18, 2023.

¹¹ UNDESA, “Least Developed Countries (LDCs),” accessed July 17, 2023.

some sources group LICs and LMICs together, but wherever possible, the Commission has attempted to present data and information separately for the four World Bank income groups.

Figure 1.1 Economies by World Bank income group

HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries. Underlying data for this figure can be found in appendix J, [figure J.5](#).



Source: Hamadeh, Van Rompaey, Metreau, “New World Bank Country Classifications by Income Level,” July 1, 2022. Country classifications are for calendar year 2021 or World Bank fiscal year 2023.

Notes: Venezuela was classified as a UMIC until July 2021, after which it was recategorized as “not classified” by the World Bank. Although country classifications were updated by the World Bank on July 1, 2023 (resulting in a change in classification for American Samoa, El Salvador, Guinea, Guyana, Indonesia, Jordan, West Bank and Gaza, and Zambia), the USITC uses fiscal year 2023 classifications to maintain consistency with Airfinity data used throughout the report.

Time Period Covered in the Report

The SARS-CoV-2 virus (the strain of coronavirus that causes COVID-19) was first identified in Wuhan, China, in December 2019. In March 2020, after confirmation of more than 118,000 cases in 114 countries, the World Health Organization (WHO), a United Nations (UN) agency focused on international health and safety, declared COVID-19 a global pandemic. By early August 2023, the WHO had reported about 769 million confirmed cases of COVID-19 worldwide and almost 7 million deaths.¹² Cases of COVID-19 continue to fluctuate. After their peak in January 2021, and following the widespread distribution of COVID-19 vaccines and the introduction of treatments, deaths have fallen significantly.¹³ On May 5, 2023, the WHO declared an end to COVID-19 as a public health emergency of international

¹² Nearly 275 million COVID-19 cases were confirmed in Europe, 206 million cases in western Pacific countries, 193 million cases in the Americas, 61 million cases in Southeast Asia, 23 million cases in eastern Mediterranean countries, and nearly 10 million cases in Africa. WHO, “WHO Coronavirus (COVID-19) Dashboard,” accessed August 10, 2023. Members of the WHO are grouped according to regional distribution. WHO, “Countries,” accessed August 10, 2023.

¹³ WHO, “WHO Coronavirus (COVID-19) Dashboard,” accessed June 2, 2023.

concern, although the virus is still active in many communities and, therefore, now considered to be endemic.¹⁴

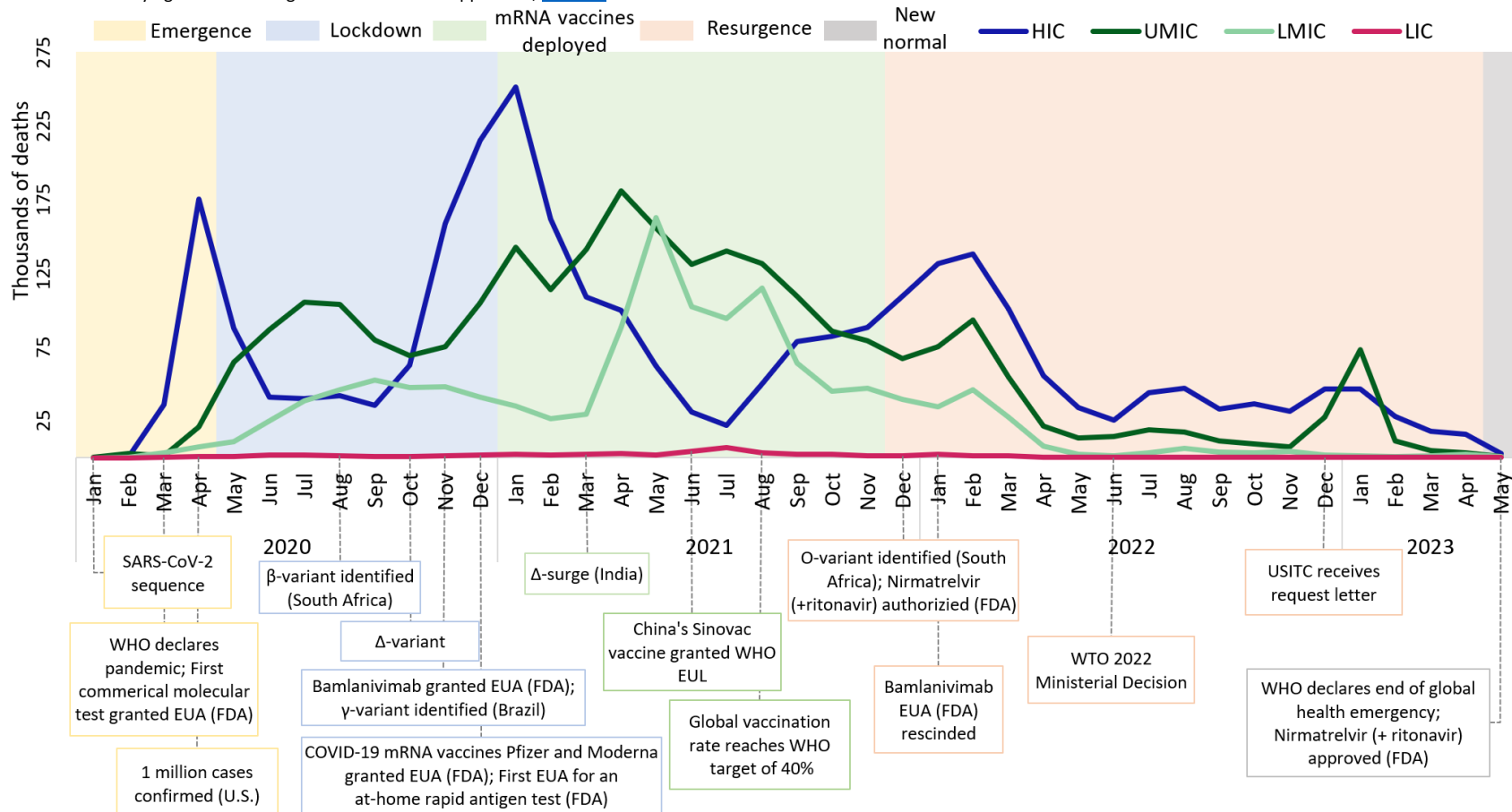
In the report and when feasible, the Commission has generally provided data and information for the time period of the pandemic, from emergence of the SARS-CoV-2 virus in late 2019 through approximately July 2023.¹⁵ Other parts of the report, such as the section on CLs, cover a broader period of time to provide context. Key events and trends during this timeframe (figure 1.2) provide important context to the topics discussed, including the supply chain, demand, consumption, and availability, and illustrate how timing plays a role in these topics.

¹⁴ WHO, “WHO Director-General’s Opening Remarks at the Media Briefing,” May 5, 2023.

¹⁵ The USITC gathered information for the investigation primarily from December 2022 through July 2023; however, the specific data and information presented in the report vary by availability. In some cases, trade data before 2020 are provided for reference.

Figure 1.2 COVID-19 pandemic: Timeline of notable events and reported COVID-19 deaths by income level, January 2020–May 2023

In thousands of deaths. WHO = World Health Organization; WTO = World Trade Organization; EUA = Emergency Use Authorization; EUL = Emergency Use Listing; FDA = U.S. Food and Drug Administration. β , δ , γ , \omicron , Δ = high-income countries; IC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries. Underlying data for this figure can be found in appendix J, [table J.6](#).



Sources: WHO, “WHO Coronavirus (COVID-19) Dashboard,” accessed June 2, 2023; Wellcome, “What Is a Variant?,” accessed August 10, 2023; Kay and Pandya, “How Errors, Inaction Sent a Deadly Covid Variant,” December 29, 2021; WHO, “WHO Validates Sinovac COVID-19 Vaccine for Emergency Use,” June 1, 2021; KFF, “KFF Global COVID-19 Vaccine Coverage Tool,” July 24, 2023.

Notes: WHO data on COVID-19 deaths are an aggregation of data reported by countries, territories, and areas. Stages—emergence, lockdown, mRNA vaccine deployment, resurgence, and new normal—are denoted by colors in the background of the plot and are largely based on key events and trends in the United States. The income categories shown are defined by the World Bank. As discussed in the text, official counts of COVID-19 deaths depend on jurisdictional testing capabilities, reporting standards, and records management systems, and may therefore be understated for LICs relative to other income levels shown in the figure.

Information Sources

The Commission obtained data and information in this report from primary and secondary sources, including sworn testimony presented at the Commission’s public hearing, written submissions to the Commission, official trade statistics, U.S. government publications, a literature review, a variety of public and proprietary data sources, and staff interviews with stakeholders in the United States and around the world. The Commission also received hearing testimony and submissions on the topics where the Trade Representative indicated that input from the public would be particularly salient. As requested in the letter from the Trade Representative, the report includes a critical review of the literature on topics related to IP protections, innovation, access to medicines, CLs, VLs, and the MPP.

The Commission held a public hearing in this investigation on March 29–30, 2023.¹⁶ Participants at the hearing included 56 witnesses who appeared in-person or virtually from the United States and 14 foreign countries.¹⁷ The witnesses represented a variety of organizations and entities, including foreign governments, civil society organizations, pharmaceutical companies and associations, U.S. national and state trade-promotion organizations, nonprofit research organizations, investment firms, and academia. In addition, interested persons were given the opportunity to submit written submissions for the record. The Commission received more than 335 written submissions, including 145 prehearing briefs, 22 posthearing briefs, and 168 other written submissions related to the investigation. The Commission used the information received in these submissions, as appropriate, throughout this report.

Additionally, Commission staff interviewed representatives from more than 120 entities through virtual meetings and fieldwork to gain insight and understanding of the issues and the global value chains for COVID-19 diagnostics and therapeutics. Fieldwork included domestic travel to Maryland, Michigan, and New York and international travel to Bangladesh, Brazil, Malaysia, Mexico, South Africa, Switzerland, and Zambia. The locations of fieldwork meant that at least one country for each of the World Bank income groups was visited: LIC (Zambia),¹⁸ LMIC (Bangladesh), UMICs (Brazil, Mexico, and South Africa), and HICs (Switzerland and the United States). During fieldwork, Commission staff interviewed persons at a variety of firms, organizations, and government agencies, including persons at diagnostics and therapeutics manufacturers, civil society organizations, international health organizations, national ministries of health, WTO member delegations, and nonprofit organizations.

Among the entities interviewed by Commission staff were key international organizations, including the U.S. Agency for International Development (USAID), WHO, the World Intellectual Property Organization (WIPO), and entities specifically named in the Trade Representative’s request letter: MPP, Foundation for Innovative New Diagnostics (FIND), UNICEF, and the Global Fund. Several entities are involved in the

¹⁶ The *Federal Register* notice is available in appendix B; the USITC Calendar of Public Hearing is available in appendix C. A list of statements submitted to the Commission in response to the *Federal Register* notice about the investigation, as well as 500-word summaries, is available in appendix D.

¹⁷ Hearing witnesses appeared virtually from Brazil, the Democratic Republic of the Congo, Fiji, Ghana, Guatemala, India, Malaysia, Mexico, the Netherlands, South Africa, Switzerland, Uganda, the United Kingdom, and Uruguay. See appendix C for a complete list of public hearing witnesses.

¹⁸ Zambia was classified as a LIC for calendar year 2021 or World Bank fiscal year 2023 (FY23). Country classifications were updated by the World Bank on July 1, 2023, resulting in Zambia changing classification from LIC to LMIC. The Commission uses FY23 classifications to maintain consistency with Airfinity data used throughout the report.

access and regulation of COVID-19-related products that are discussed across multiple chapters of the report. The responsibilities of key organizations and their roles in facilitating access to COVID-19 diagnostics and therapeutics, most of which were interviewed for this report, are listed in table 1.1.

Table 1.1 International organizations and their roles in access to COVID-19 diagnostics and therapeutics

Organization	Description	Role in access to COVID-19 diagnostics and therapeutics
Access to COVID-19 Tools Accelerator (ACT-A)	Hosted by the WHO, ACT-A is co-convened by multiple agencies, including the Coalition for Epidemic Preparedness Innovations, FIND, Global Alliance for Vaccines and Immunization, Global Fund, UNICEF, Unitaid, Wellcome, WHO, World Bank, and the Bill & Melinda Gates Foundation.	ACT-A develops and distributes essential health products for combating COVID-19, seeking to ensure equitable access. ACT-A operates across three pillars of Diagnostics, Therapeutics, and Vaccines (COVAX), with a cross-cutting Health Systems and Response Connector.
ACT-A Diagnostics Pillar	Jointly led by the Global Fund and FIND, the ACT-A Diagnostics Pillar aims to improve timely availability of low-cost and quality-assured COVID-19 diagnostics worldwide.	The Diagnostics Pillar works to scale up equitable access to COVID-19 diagnostic technologies and tools (for both rapid antigen and polymerase chain reaction (PCR) tests) through investments in development of new and better diagnostics, manufacturing, and distribution of tests.
ACT-A Therapeutics Pillar	Jointly led by Unitaid, the Global Fund, and Wellcome, the ACT-A Therapeutics Pillar aims to enhance the development, manufacturing, procurement, and distribution of COVID-19 treatments for populations in LICs and LMICs.	The Therapeutics Pillar supports field trials and funding research efforts to develop new therapeutics against COVID-19. It also supports pooled procurement of COVID-19 therapeutics for both inpatient and outpatient treatments.
Americares	Americares is a health-focused relief and development organization whose mission is to save lives and improve health for people affected by poverty or disaster.	Americares is an implementing partner in the COVID Treatment Quick Start Consortium.
Bill & Melinda Gates Foundation	A private, charitable foundation, the Bill & Melinda Gates Foundation provides grants and makes strategic investments to fight poverty, disease, and inequity around the world.	The foundation has provided a variety of grants for the global COVID-19 response, including founding the COVID-19 Therapeutics Accelerator, which works within the ACT-A Therapeutics Pillar to provide support to identify drugs and treatments that can help prevent cases of COVID-19 among vulnerable populations and treat mild and moderate cases of the disease.
Clinton Healthcare Access Initiative (CHAI)	CHAI is a global health organization committed to saving lives and reducing the burden of disease in LICs and MICs.	Among other initiatives, CHAI reached agreements with generic manufacturers to make generic versions of COVID-19 therapeutics available in LICs and MICs.

Organization	Description	Role in access to COVID-19 diagnostics and therapeutics
COVID Treatment Quick Start Consortium	COVID Treatment Quick Start Consortium is a public-private partnership that brings together Duke University, CHAI, COVID Collaborative, and AmeriCares as implementing partners, with support from the Open Society Foundations, Pfizer, and the Conrad N. Hilton Foundation.	The consortium is working to support test-to-treat demonstration programs, as well as to introduce and scale up access to COVID-19 oral antiviral therapies in high-risk populations in 10 LICs and MICs.
Direct Relief	Direct Relief is a global humanitarian aid organization that provides emergency medical assistance and disaster relief in the United States and internationally.	Direct Relief is providing emergency medical resources—vaccines, antibody therapies, personal protective equipment, medical-grade oxygen, and other critical items—to medical facilities across the world.
Foundation for Innovative New Diagnostics (FINN)	FINN is a global nonprofit organization connecting countries and communities, funders, decisionmakers, healthcare providers, and developers to spur diagnostic innovation and make testing an integral part of sustainable, resilient health systems.	FINN is a co-lead of the ACT-A Diagnostics Pillar. It also tracks the development and commercialization of SARS-CoV-2 tests (immunoassays and molecular) for COVID-19 and provides a fully searchable directory that includes performance data (sensitivity and specificity).
Global Fund	The Global Fund is a multilateral financing organization that raises and invests resources to end HIV/AIDS, tuberculosis, and malaria worldwide and strengthen health systems in over 100 countries.	In April 2020, it established the “COVID-19 Response Mechanism,” which allows recipients to use some of their funding for responding to COVID-19. The COVID-19 Response Mechanism is the main channel for providing grant support to LICs, LMICs, and UMICs to purchase COVID-19 tests, treatments, and personal protective equipment.
Medicines Patent Pool (MPP)	The MPP is a UN-backed public health organization that aims to increase access to, and facilitate the development of, life-saving medicines for LICs and MICs through an innovative approach to voluntary licensing and patent pooling.	In 2020, the MPP temporarily expanded its mandate to include COVID-19 treatments. It has licensed COVID-19 therapeutics to make generic versions of these products available in LICs and MICs.
United Nations Children’s Fund (UNICEF)	UNICEF is a global humanitarian organization focused on the welfare of children. Its programs cover child health and nutrition, safe water and sanitation, education, HIV/AIDS prevention and treatment, protection of children and adolescents from violence and exploitation, and providing emergency relief in response to disasters.	The UNICEF response to COVID-19 is mostly through providing access to COVID-19 vaccines through the ACT-A COVAX pillar. UNICEF supports the procurement of COVID-19 vaccine doses, as well as helps to transport, store, and rollout in LICs and MICs. In addition, UNICEF assists in delivery of diagnostics, therapeutics, personal protective equipment, and other essential items.

Organization	Description	Role in access to COVID-19 diagnostics and therapeutics
Unitaid	Unitaid is a global health initiative with three strategic objectives: (1) accelerate the introduction and adoption of key health products; (2) create systemic conditions for sustainable, equitable access; and (3) foster inclusive and demand-driven partnerships for innovation.	Unitaid co-leads the ACT-A Therapeutics Pillar and is at the forefront of global efforts to ensure equitable access to treatments for COVID-19. It is also a part of the ACT-A Diagnostics Pillar, working with partners to ensure that LICs and MICs have access to COVID-19 tests.
World Health Organization (WHO)	The WHO is the UN agency that connects nations, partners, and people to promote health, keep the world safe, and serve the vulnerable. The WHO leads global efforts to expand universal health coverage, directs and coordinates the world’s response to health emergencies, and promotes healthier lives.	The WHO hosts ACT-A (see above).

Sources: ACT-Accelerator, “ACT-Accelerator: Access to COVID-19 Tools,” accessed August 10, 2023; WHO, “The Access to COVID-19 Tools (ACT) Accelerator,” accessed August 10, 2023; WHO, *ACT-Accelerator Investment Case*, June 26, 2020, 1–8; ACT-Accelerator, “Diagnostics,” accessed June 11, 2023; ACT-Accelerator, “Therapeutics,” accessed August 10, 2023; Bill & Melinda Gates Foundation, “How We Work,” accessed August 11, 2023; COVID-19 Therapeutics Accelerator, “Frequently Asked Questions,” accessed August 11, 2023; CHAI, “About Us,” accessed August 11, 2023; Milic, “Press Release: CHAI Announces Agreements,” May 12, 2022; COVID Treatment Quick Start Consortium, “10-Country Partnership in Africa and Southeast Asia—to Introduce COVID Oral Antivirals and National Test-and-Treat Programs—Announced by New Public-Private Consortium,” September 7, 2022; Direct Relief, “Direct Relief,” accessed August 11, 2023; Americares, “Frequently Asked Questions,” accessed August 11, 2023; The Global Fund, *The Global Fund Strategy 2017-2022*, April 27, 2016, 1–40; UNICEF, *UNICEF Annual Report 2021*, May 2022, 1–16; FIND, “FIND: About Us,” accessed August 10, 2023; FIND, “FIND: COVID-19 Diagnostics and Testing,” accessed August 10, 2023; Unitaid, “Strategy—Unitaid,” accessed August 10, 2023.

The Commission reviewed patent landscape reports published by WIPO and the U.S. Patent and Trademark Office (USPTO) for descriptions of patent activity surrounding COVID-19 diagnostics and therapeutics.¹⁹ The WIPO report, originally published in March 2022 and updated in April 2023, provides a global landscape of patenting activity related to COVID-19 therapeutics and vaccines.²⁰ The USPTO report focuses on U.S. patenting activity related to COVID-19 diagnostics.²¹ The Commission also obtained patent and licensing information from the Medicines Patents and Licences Database,²² published by the MPP, and other resources. The TRIPS Flexibility Database, published by the nonprofit research organization Medicines Law & Policy, was used to track CLs and other TRIPS flexibilities used by WTO members for public health purposes.²³

¹⁹ Patent landscape reports provide a snapshot of the patent situation related to specific technologies based on state-of-the-art searches in selected patent databases. WIPO, “Patent Landscape Reports,” accessed August 1, 2023.

²⁰ WIPO, *COVID-19 Related Vaccines and Therapeutics: Preliminary Insights*, 2022, 1–83; WIPO, *COVID-19 Related Vaccines and Therapeutics: Preliminary Insights*, 2023.

²¹ Toole et al., “Diagnosing COVID-19,” October 2023, 4.

²² MPP, The Medicines Patents and Licences Database, accessed July 30, 2023.

²³ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

The Commission obtained official trade statistics for COVID-19 diagnostics and therapeutics from USITC DataWeb/Census and the S&P Global Market Intelligence Global Trade Atlas.²⁴ In addition, the Commission obtained data and information on the global pharmaceutical market, including licensing, pricing, and production of pharmaceutical products, from FIND and PATH (formerly the Program for Appropriate Technology in Health) for COVID-19 diagnostics and from Airfinity Infectious Disease Analytics for COVID-19 therapeutics.²⁵ Airfinity collects publicly available information on the market for COVID-19 diagnostics and therapeutics. However, it is not possible to know how comprehensively this public information covers the market. Information on clinical trials and research studies related to products in development is from the National Institutes of Health (NIH) U.S. National Library of Medicine (NLM) database.²⁶

Organization of the Report

The remainder of the report is organized as follows: Chapter 2 provides background and context for the IP issues raised in the request letter and information on regulations to bring diagnostics and therapeutics to market. It provides an overview of the TRIPS Agreement, as well as a description of IP protections for COVID-19 diagnostics and therapeutics, with examples of how patent and trade secret protections operate in practice. Chapter 3 provides the range of definitions of diagnostics and therapeutics in the medical field; identifies the universe of existing COVID-19 diagnostics and therapeutics covered by patents, including products in development; and gives an overview of relevant COVID-19 diagnostics and therapeutics. Chapter 4 gives an overview of the development, production, and trade of certain COVID-19 diagnostics and therapeutics. Chapter 5 focuses on mechanisms for manufacturers to get access to IP rights. Chapter 6 presents information on availability and consumption of COVID-19 diagnostics and therapeutics. Chapter 7 summarizes views and information provided by interested persons on the topics specified in the Trade Representative’s request letter where she deemed public input to be particularly salient. Finally, chapter 8 provides a critical review of the literature on the relationship between patents and innovation in the healthcare sector, the relationship between patents and access to medicines, the outcomes of using CLs, and the effects of the MPP on access to COVID-19 diagnostics and therapeutics.

²⁴ USITC DataWeb provides U.S. international trade data retrieved from the U.S. Census Bureau. The Global Trade Atlas provides global trade data. The report generally covers the timeframe from the beginning of the pandemic to the most current data available at the time of publication. In some cases, trade data before 2020 are provided for reference and analysis.

²⁵ Airfinity is a healthcare data and analytics company, whose activities include closely monitoring global market and industry trends, tracking research activities, and following intellectual property developments. Airfinity, “COVID-19,” accessed various dates.

²⁶ NIH, NLM, ClinicalTrials.gov, accessed August 1, 2023.

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Chapter 2

Background on Intellectual Property and Regulations

Introduction

This chapter provides background and context for the intellectual property (IP) issues raised in the request letter, as well as information on the regulatory environment for COVID-19 diagnostics and therapeutics. It begins with an overview of the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and its requirements for the protection of patents and trade secrets—protections particularly relevant to COVID-19 therapeutics and diagnostics. It next describes key flexibilities under the TRIPS Agreement, including compulsory licensing. The chapter then describes IP protections for COVID-19 diagnostics and therapeutics, including examples of how patent and trade secret protections operate in practice. The chapter addresses in summary form, with more targeted discussions in later chapters, the following elements of the request letter: the TRIPS Agreement framework; intellectual property protections for COVID-19 diagnostics and therapeutics; and the relationships among patent protection, innovation, and access to medicine in countries at different income levels. This chapter then presents information on regulations to bring diagnostics and therapeutics to market including national regulatory authorities and the World Health Organization (WHO) Prequalification of Medicines Program, which is relevant background for understanding the information on COVID-19 diagnostics and therapeutics discussed in chapters 3, 4, and 5.

Intellectual Property and the TRIPS Agreement

IP refers to “creations of the mind.”²⁷ Governments grant creators of IP the right to prevent others from using their creations, and the right to decide who may use the IP and on what terms.²⁸ The TRIPS Agreement, which entered into force on January 1, 1995, is the most comprehensive multilateral agreement on IP.²⁹ Although multilateral agreements protecting IP rights existed before the TRIPS Agreement, the TRIPS Agreement seeks to improve the predictability and stability of trade in IP-related goods and services, and incorporated many of these prior agreements’ protections into the WTO

²⁷ These creations can take many different forms including inventions and undisclosed information such as trade secrets, the protections most relevant to COVID-19 diagnostics and therapeutics. WTO, “Intellectual Property: Protection and Enforcement,” accessed July 31, 2023.

²⁸ WTO, “Intellectual Property: Protection and Enforcement,” accessed July 31, 2023.

²⁹ Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 319 (hereinafter TRIPS Agreement); WTO, “Intellectual Property: Protection and Enforcement,” accessed July 17, 2023.

framework.³⁰ The TRIPS Agreement has five major functions: (1) to apply multilateral principles of trade to IP, such as national treatment and most-favored-nation status;³¹ (2) to set minimum standards of protection in seven IP areas;³² (3) to lay out the available tools a WTO member must provide for enforcing these rights in its territory;³³ (4) to establish dispute settlement procedures;³⁴ and (5) to outline transitional arrangements for the agreement's implementation, such as delayed implementation of certain IP rights by least-developed countries (LDCs).³⁵

Provisions of the TRIPS Agreement that describe its objectives and principles focus on IP rights and promoting innovation and the dissemination of technology. Article 7 states the agreement's objectives:

The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations.³⁶

Article 8 similarly describes the TRIPS Agreement's principles, affirming the rights of members to adopt measures consistent with the agreement and necessary to protect public health and promote the public interest in socioeconomic and technological development. It further states that measures consistent with the TRIPS Agreement may be needed to prevent practices that abuse IP rights, unreasonably restrain trade, or adversely affect international technology transfer.³⁷

To further encourage technology transfer, Article 66.2 requires developed country members to provide incentives to enterprises and institutions in their territories to promote and encourage technology transfer to LDC members.³⁸ Various government officials and nonprofit organizations participating in

³⁰ Note that treaty obligations incorporated by the TRIPS Agreement still exist independently for member states. See TRIPS Agreement, art. 2.2.

³¹ See generally TRIPS Agreement, arts. 3–4; WTO, "Intellectual Property: Protection and Enforcement," accessed July 31, 2023.

³² The standards in the agreement cover the following IP rights: copyright and related rights; trademarks, including service marks; geographical indicators; industrial design; patents; layout-designs (e.g., topographies of integrated circuits); and undisclosed information, including trade secrets. See generally TRIPS Agreement, arts. 9–39; WTO, "Intellectual Property: Protection and Enforcement," accessed July 31, 2023.

³³ See generally TRIPS Agreement, arts. 40–49, 51–61; WTO, "Intellectual Property: Protection and Enforcement," accessed July 31, 2023.

³⁴ See generally TRIPS Agreement, arts. 63–64.

³⁵ TRIPS Agreement, art. 66.1; WTO TRIPS Council, "Extension for the Transition Period under Art. 61 of the TRIPS Agreement for LDCs for Certain Pharmaceutical Obligations with Respect to Pharmaceutical Products," IP/C/73, November 6, 2015; WTO TRIPS Council, "Extension of the Transition Period Under Article 66.1 for Least Developed Country Members," IP/C/88, June 29, 2021.

³⁶ TRIPS Agreement, art. 7; see also Matthews, written submission to the USITC, May 5, 2023, 1 (emphasizing this provision); Health Global Access Project, written submission to the USITC, March 15, 2023, 4; TWN, prehearing brief submission to the USITC, March 20, 2023, 9; WIPO, "Advice on Flexibilities under the TRIPS Agreement," accessed July 29, 2023; see also CAEME, written submission to the USITC, May 19, 2023, 2–3.

³⁷ TRIPS Agreement, art. 8; see also Matthews, written submission to the USITC, May 5, 2023, 1 (emphasizing this provision); Health Global Access Project, written submission to the USITC, March 15, 2023, 4; TWN, prehearing brief submission to the USITC, March 20, 2023, 9; CAEME, written submission to the USITC, May 19, 2023, 2–3.

³⁸ TRIPS Agreement, art. 66.2.

this investigation stated that improved compliance with this technology transfer obligation would be particularly useful for COVID-19 diagnostic and therapeutic technologies.³⁹

Patents under the TRIPS Agreement

The TRIPS Agreement generally requires that WTO members make patents available for inventions—whether products or processes—in all technology areas that are new, nonobvious, and useful (capable of industrial application).⁴⁰ The agreement does permit WTO members to exclude certain inventions from being patented, including those necessary to protect human health or life and diagnostic, therapeutic, or surgical treatment methods.⁴¹ Patents shall confer on the owner exclusive rights, including the right to prevent third parties from making, using, offering, selling, or importing the patented product, or a product produced with a patented process, without the owner’s consent.⁴² The owners of patents shall also have the right to transfer IP rights, including through licensing contracts, which enable the owner to grant others the right to use their patents on specified terms.⁴³

The term of protection may not end before the expiration of a 20-year period, counted from the filing date of the patent.⁴⁴ The TRIPS Agreement does not require the extension of patent terms to compensate for regulatory delays.⁴⁵ In exchange for these patent rights, to facilitate the dissemination of technology, WTO members also shall require that the patent application disclose the invention in a manner sufficiently clear and complete that a person skilled in the art could replicate the invention and may require the applicant to identify the “best mode” for building upon the invention.⁴⁶

Undisclosed Information and Test Data under the TRIPS Agreement

The TRIPS Agreement requires WTO members to protect undisclosed information (commonly referred to as trade secrets). Protectable undisclosed information is information that is secret, has commercial

³⁹ FIND, written submission to the USITC, May 16, 2023, 1; Access to Medicine Foundation, written submission to the USITC, May 4, 2023, 1; Embassy of Bangladesh, written submission to the USITC, April 5, 2023, 3; nonprofit organization representatives, interviews by USITC staff, Switzerland, June 7 and June 8, 2023; government representative, interview by USITC staff, Bangladesh, July 17, 2023.

⁴⁰ TRIPS Agreement, art. 27(1). Generally, patents do not have extraterritorial effect, such that a patent is only recognized by the country that issued it. One notable exception is the European Patent Convention, which provides for a single patent application to obtain a patent recognized by all European Patent Organisation member states. The Patent Cooperation Treaty (PCT), administered by WIPO and discussed in a later section, allows applicants to begin pursuing patent protection in the 157 states that are members of the treaty through a single filing at WIPO.

⁴¹ TRIPS Agreement, art. 27(2–3).

⁴² TRIPS Agreement, art. 28(1).

⁴³ TRIPS Agreement, art. 28(2).

⁴⁴ TRIPS Agreement, art. 33.

⁴⁵ This additional layer of protection is included in U.S. law—and that of other countries—and is included in certain U.S. free trade agreements. USITC, *Economic Impact of Trade Agreements*, June 2021, 70. ’t Hoen, “Protection of Clinical Test Data and Public Health,” 2022, 189.

⁴⁶ This is the so-called “patent bargain”: in exchange for protection for an invention, the inventor agrees to provide sufficient information about it so that others may build upon it. Devlin, “The Misunderstood Function of Disclosure in Patent Law,” October 1, 2010, 401–2; academic representative, interview by USITC staff, February 23, 2023.

value because it is secret, and has been subject to reasonable steps to maintain secrecy.⁴⁷ The information must be protected from disclosure, acquisition, or use by others in a manner that is contrary to honest commercial practices.⁴⁸ Many different types of undisclosed information may be protected including confidential business information, such as a firm's price lists and marketing strategies; know-how, such as facts about manufacturing methods or processes for achieving certain results; and technical information, such as research results and chemical formulas.⁴⁹

The TRIPS Agreement does not specify a particular way of protecting undisclosed information. In practice, WTO members rely on trade secret laws, incorporate trade secret protections into their unfair competition or contract laws, and rely on common law.⁵⁰ Unlike patents, undisclosed information does not need to be registered with or reviewed by an administrative agency for protections to become effective. Whether the information meets the requirements for legal protection is not determined by a patent examiner ahead of time but typically by a judge afterwards in a lawsuit.⁵¹ Also, unlike patents, trade secrets do not have a defined (i.e., time-limited) term of protection. As long as they continue to be subject to reasonable protective measures, they have unlimited duration. Reasonable protective measures may include requiring that employees or third parties enter into license agreements with confidentiality provisions or other contracts that specify the terms under which trade secrets may be accessed and used.⁵²

The TRIPS Agreement further requires the protection against unfair commercial use of undisclosed test data submitted to regulators as a condition for the marketing approval of pharmaceuticals using new chemical entities, provided that generating the data involves considerable effort.⁵³ Although the TRIPS Agreement does not require members to provide exclusive rights to such data, in certain jurisdictions, test data protection takes the form of data exclusivity.⁵⁴ Data exclusivity means that the use of the test data is exclusive to the originator company for a certain period of time. Some countries, however, have introduced waivers to data exclusivity, which can be invoked to ensure that the regulatory authority can

⁴⁷ Trade secret definitions are similar across jurisdictions, generally corresponding to the criteria articulated in Article 39.2 of the TRIPS Agreement. Schultz and Lippoldt, *Approaches to Protection of Undisclosed Information (Trade Secrets)*, January 30, 2014, 7–8.

⁴⁸ TRIPS Agreement arts. 39.2 and note 10.

⁴⁹ Schultz, *Trade Secrecy and Covid-19*, October 5, 2022, 5.

⁵⁰ Schultz and Lippoldt, *Approaches to Protection of Undisclosed Information (Trade Secrets)*, January 30, 2014, 8, 15.

⁵¹ Schultz and Lippoldt, *Approaches to Protection of Undisclosed Information (Trade Secrets)*, January 30, 2014, 7–8; Brant and Lohse, "Trade Secrets: Tools for Innovation and Collaboration," September 25, 2014, 8–9.

⁵² Schultz and Lippoldt, *Approaches to Protection of Undisclosed Information (Trade Secrets)*, January 30, 2014, 7–8; Brant and Lohse, "Trade Secrets: Tools for Innovation and Collaboration," September 25, 2014, 8–9, 13.

⁵³ These test data include data gathered during the research and development and clinical trial processes; these data are later submitted to national regulatory authorities in order to provide evidence of the safety and efficacy of a product. TRIPS Agreement, art. 39.3.

⁵⁴ As with patent term extensions, data exclusivity regimes often are required by free trade agreements. USITC, *Economic Impact of Trade Agreements*, June 2021, 70–71; 't Hoen, "Protection of Clinical Test Data and Public Health," 2022, 189.

proceed with the registration of a generic product⁵⁵ produced or imported under a compulsory license (CL).⁵⁶

TRIPS Agreement Flexibilities

The TRIPS Agreement establishes minimum standards for the protection of patents, trade secrets, and other types of IP. It also incorporates flexibilities. In the context of patents, these flexibilities include Articles 31 and 31*bis* of the TRIPS Agreement. In the words of the World Intellectual Property Organization (WIPO), TRIPS flexibilities

aim to permit developing and least-developed countries to use TRIPS [Agreement]-compatible norms in a manner that enables them to pursue their own public policies, either in specific fields like access to pharmaceutical products or protection of their biodiversity, or more generally in establishing macroeconomic, institutional conditions that support economic development.⁵⁷

In November 2001, WTO members focused on the importance of TRIPS Agreement flexibilities to respond to public health concerns in developing countries by adopting the Declaration on the TRIPS Agreement and Public Health, also known as the Doha Declaration.⁵⁸ The Declaration affirms the primacy of the protection of public health over IP protection:

We agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.

In this connection, we reaffirm the right of WTO Members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose.⁵⁹

The Database on Flexibilities in the Intellectual Property System (TRIPS Flexibilities Database) documents 172 instances in which governments used or attempted to use TRIPS Agreement flexibilities for public

⁵⁵ Generic product is often used to mean a copy of a patented drug or drug whose patents have expired. World Trade Organization (WTO), "What does 'Generic' Mean," September 2006.

⁵⁶ Countries that provide for data exclusivity waivers in medicines regulations, or in relation to the use of compulsory licenses (CLs) to facilitate generic medicine registration and sales where necessary to protect public health, include Malaysia, Chile, and Colombia. 't Hoen, "Protection of Clinical Test Data and Public Health," 2022, 191.

⁵⁷ WIPO, "Advice on Flexibilities under the TRIPS Agreement," accessed July 29, 2023; see also CILFA, written submission to the USITC, May 5, 2023, 117 (explaining importance of flexibilities); CAEME, written submission to the USITC, May 19, 2023, 3.

⁵⁸ WTO, "TRIPS and Public Health," accessed August 1, 2023.

⁵⁹ WTO, "Declaration on the TRIPS Agreement and Public Health," WT/MIN(01)/DEC/2, November 20, 2001, par. 4.

health purposes during the period from adoption of the Doha Declaration in November 2001 through May 2023.⁶⁰ The four flexibilities WTO members used most are described in box 2.1.⁶¹

Box 2.1 The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and Four Flexibilities Used for Public Health Purposes

During the period from November 2001 through May 2023, the most widely used flexibilities were compulsory licensing (122 of 172 instances), the extended transition period for least-developed countries (LDCs) to implement certain IP protections for pharmaceuticals (46 of 172 instances), exceptions to patent rights (3 instances), and parallel importation (1 instance, but according to one source, the practice of parallel importation is likely taking place more often than the database shows).^a These flexibilities are briefly described below:

- **Compulsory licenses:** The TRIPS Agreement Article 31 permits members to allow for the use of the subject matter of a patent, including use by the government or authorized third parties, without the authorization of the patent owner subject to certain conditions.^b For example, Article 31 limits the use of compulsory licensing to predominantly supply the domestic market. Article 31*bis* for pharmaceutical products waives this limitation subject to terms set out in an annex to the article.
- **Extended transition period for LDCs:** Paragraph 7 of the Doha Declaration postpones the obligation of LDC members to grant and enforce pharmaceutical patents and provide data protections.^c LDCs have until January 1, 2033, to implement IP protections for pharmaceutical patents and test data.^d They also are exempt from implementing most other TRIPS Agreement obligations (with the exception of Articles 3, 4, and 5, related to national treatment and most-favored-nation treatment) until July 1, 2034, or until they cease to be an LDC member, whichever date is earlier.^e
- **Exceptions to patent rights:** The TRIPS Agreement Article 30 permits members to provide limited exceptions to exclusive rights if the exceptions “do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.”^f This flexibility may be used, for example, for research and scientific purposes, such as developing generic versions of drugs that can be marketed as soon as possible after a patent expires.^g
- **Parallel importation:** Parallel imports are products marketed by the patent owner—or with the patent owner’s permission—in one country and imported into another country without the approval of the patent owner. The relevant legal principle is exhaustion: once a patent owner has sold a patented product, the associated rights are exhausted and the owner no longer has any rights over what happens to the product.^h Under TRIPS Agreement Article 6 and the Doha Declaration, members are free to establish their own exhaustion regimes without challenge subject to the most-favored-nation and national treatment provisions of the agreement.ⁱ

^a ML&P, written submission to the USITC, May 2, 2023, 5.

^b TRIPS Agreement, art. 31.

^c WTO, “Declaration on the TRIPS Agreement and Public Health,” WT/MIN(01)/DEC/2, November 20, 2001, par. 7.

⁶⁰ ML&P, written submission to the USITC, May 2, 2023, 5; ML&P, The TRIPS Flexibilities Database, accessed August 1, 2023.

⁶¹ These examples of flexibilities are for illustrative purposes only and do not constitute a comprehensive list. For example, countries are free to determine how broadly or narrowly to interpret patentability criteria and to offer patent opposition mechanisms that may result in fewer patents, so long as these actions are consistent with TRIPS Agreement requirements. ML&P, The TRIPS Flexibilities Database, accessed August 1, 2023.

^d TRIPS Agreement, art. 66.1; WTO TRIPS Council, “Extension for the Transition Period under Art. 61 of the TRIPS Agreement for LDCs for Certain Pharmaceutical Obligations with Respect to Pharmaceutical Products,” IP/C/73, November 6, 2015.

^e WTO TRIPS Council, “Extension of the Transition Period Under Article 66.1 for Least Developed Country Members,” IP/C/88, June 29, 2021.

^f TRIPS Agreement, art. 30. See box 5.3, Least-Developed Country Status, in chapter 5 for more information.

^g WTO, “Fact Sheet: TRIPS and Pharmaceutical Patents, Obligations and Exceptions,” September 2006.

^h WTO, “Fact Sheet: TRIPS and Pharmaceutical Patents, Obligations and Exceptions,” September 2006.

ⁱ TRIPS Agreement, art. 6; Doha Declaration, par. 5(d).

Compulsory Licensing under the TRIPS Agreement

Under Article 31, WTO members may allow for compulsory licensing of the subject matter of a patent, subject to certain conditions.⁶² These conditions include requiring the proposed user to first seek authorization from the patent owner on reasonable terms. This requirement may be waived in cases of national emergency or other extreme urgency.⁶³ Conditions also include adequate remuneration for the patent owner and use of a CL “predominantly for the supply of the domestic market.”⁶⁴

This domestic market limitation restricts the quantity of product that can be produced for export under a CL, which may render local production of a drug uneconomical. It also creates difficulties for WTO members with insufficient or no pharmaceutical manufacturing capacities that rely on imports to obtain needed products.⁶⁵ In recognition of these difficulties, Paragraph 6 of the Doha Declaration instructed the TRIPS Council to find an expeditious solution to the problem.⁶⁶ In 2003, WTO members adopted a decision waiving the limitation of CLs to production predominantly for the domestic market for pharmaceutical products exported to certain members in accordance with specified terms. These terms are known as the Paragraph 6 System. The waiver allows for export of pharmaceutical products made under CLs to countries that cannot make the products themselves.⁶⁷ In 2005, WTO members agreed to incorporate the decision into the TRIPS Agreement, subject to the acceptance of two-thirds of members.⁶⁸ The amendment took effect in January 2017 and was implemented in Article 31*bis* of the TRIPS Agreement and the annex and appendix thereto (the Article 31*bis* system).⁶⁹

The Article 31*bis* system contains the following important elements. First, unlike Article 31, which may reach the subject matter of any patent, it applies only to pharmaceutical products defined as:

any patented product, or product manufactured through a patented process, of the pharmaceutical sector needed to address the public health problems as recognized in paragraph

⁶² Trade secrets are not subject to compulsory licensing. But see Prepared Oral Statement of Professors David S. Levine and Joshua D. Sarnoff, submission to the USITC, March 22, 2023, 1 (stating that the TRIPS Agreement does not preclude governments from compelling the sharing of trade secrets).

⁶³ TRIPS Agreement, arts. 31(b) and 31(k).

⁶⁴ These conditions may be modified in cases where the use is permitted to remedy anti-competitive practices. See TRIPS Agreement, arts. 31(f), 31(h), and 31(k).

⁶⁵ WTO, “Obligations and Exceptions,” September 2006; ‘t Hoen, *Private Patents and Public Health*, 2016, 40.

⁶⁶ WTO, “Declaration on the TRIPS Agreement and Public Health,” WT/MIN(01)/DEC/2, November 20, 2001, par. 6; WTO, “TRIPS and Public Health,” accessed August 1, 2023.

⁶⁷ See WTO, “Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health,” WT/L/540, September 2, 2003.

⁶⁸ WTO, “Amendment of the TRIPS Agreement,” WT/L/641, December 8, 2005.

⁶⁹ TRIPS Agreement, art. 31*bis*, annex to the TRIPS Agreement, and appendix to the annex to the TRIPS Agreement; see also WTO, “Amendment of the TRIPS Agreement,” WT/L/641, December 8, 2005; WTO, “WTO IP Rules Amended,” January 23, 2017.

1 of the TRIPS Agreement on Public Health (WT/MIN(01)DEC/2). It is understood that active ingredients necessary for its manufacture and diagnostic kits needed for its use would be included.⁷⁰

Second, the Article 31*bis* system waives the requirement that products be produced predominantly for the domestic market, subject to the following procedures.⁷¹ An eligible importing member must make a notification to the TRIPS Council (1) specifying the names and quantities needed; (2) for members other than LDCs, stating that it has insufficient manufacturing capacities; and (3) if the product is patented in the territory, confirming that a CL will be granted.⁷² For exporting members, the CL must contain the following conditions: (1) only the amount necessary for meeting the needs of the importing member may be manufactured; (2) products shall be clearly identified through specific labeling and marking; and (3) prior to shipment, the compulsory licensee shall post on a website information about quantities, destinations, and distinguishing features of the products.⁷³ Complexities reportedly associated with the use of the Article 31*bis* system are discussed in chapter 5.

The 2022 Ministerial Decision on the TRIPS Agreement

The issue of the balance between IP protection and public health came to the forefront in the context of the COVID-19 global pandemic in October 2020, when India and South Africa submitted a proposal at the WTO to broadly waive TRIPS Agreement obligations in the areas of copyrights, patents, industrial designs, and undisclosed information related to the prevention, containment, or treatment of COVID-19.⁷⁴ After a year and a half of discussions and alternative proposals, the WTO adopted, at the 12th Ministerial Conference, the 2022 Ministerial Decision on the TRIPS Agreement (2022 Ministerial Decision), a substantially narrower decision than the original proposal.⁷⁵ The following sections summarize the terms of the 2022 Ministerial Decision. This is followed by a summary of the views of witnesses who provided input to the U.S. International Trade Commission regarding the decision.⁷⁶

Terms of the 2022 Ministerial Decision

The 2022 Ministerial Decision focuses on rules governing the compulsory licensing of patents for COVID-19 vaccines. It has a duration of five years, with the possibility of extensions, and leaves for later the determination whether to extend the 2022 Ministerial Decision to COVID-19 diagnostics and

⁷⁰ TRIPS Agreement, annex to the TRIPS Agreement, par. 1(a).

⁷¹ TRIPS Agreement, art. 31*bis*, par. 1.

⁷² TRIPS Agreement, annex to the TRIPS Agreement, par. 2.a.

⁷³ TRIPS Agreement, annex to the TRIPS Agreement, par. 2.b.

⁷⁴ WTO TRIPS Council, “Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19,” IP/C/W/669, October 2, 2020.

⁷⁵ WTO, “Ministerial Decision on the TRIPS Agreement,” WT/MIN(22)/30, June 22, 2022. See also Matthews, written submission to the USITC, May 5, 2023, 1 (emphasizing that the 2022 Ministerial Decision is narrow); Rethink Trade, written submission to the USITC, May 5, 2023, 1; TWN, written submission to the USITC, May 5, 2023, 2; KEI, prehearing brief submission to the USITC, March 20, 2023, 7.

⁷⁶ Chapter 7 of this report provides a detailed discussion of views, and appendix D presents the summaries of submissions provided by some participants.

therapeutics.⁷⁷ The 2022 Ministerial Decision states that an eligible member may use the subject matter of a patent required for the production and supply of COVID-19 vaccines, including ingredients and processes necessary to manufacture the vaccine, without the rights holder's consent, in accordance with TRIPS Article 31 "as clarified and waived" in the Decision. The Decision clarifies that an eligible member may authorize use of the subject matter of a patent through any instrument available in the law of the member that permits such an authorization (such as executive orders, emergency decrees, government use authorizations, and judicial or administrative orders) whether or not the member has in place compulsory licensing rules.⁷⁸ The Decision further clarifies that efforts to obtain the rights holder's authorization is not required and provides that eligible members may waive the requirement of Article 31(f) that use be predominantly to supply its domestic market and allow any portion of product manufactured under the CL to be exported to eligible members.⁷⁹ A difference between the 2022 Ministerial Decision and existing TRIPS flexibilities, in particular under Article 31*bis*, is that, while both provide for waiver of the requirement of Article 31(f), the Decision does not require that export be in accordance with the terms set forth in the Annex to Article 31*bis*.

The 2022 Ministerial Decision also includes an understanding that Article 39.3 of the TRIPS Agreement does not prevent an eligible member from enabling the rapid approval of a COVID-19 vaccine produced under the decision.⁸⁰ Article 39.3 requires members—when requiring submission of undisclosed test data for the approval of a pharmaceutical product using new chemical entities—to protect that undisclosed data against unfair commercial use. It also requires members to protect such data from disclosure, except where necessary to protect the public or unless steps are taken to ensure protection of the data from unfair commercial use.⁸¹

Views on the 2022 Ministerial Decision

The Commission obtained public input from a wide range of interested persons—including representatives of industry, academia, nonprofit organizations, civil society organizations, research organizations, and multilateral institutions—regarding the 2022 Ministerial Decision and its possible extension to COVID-19 diagnostics and therapeutics. Industry representatives and others described the 2022 Ministerial Decision as a broad waiver of IP rights, with the possibility of substantial negative consequences if extended to diagnostics and therapeutics. Public health advocates, however, stated that the 2022 Ministerial Decision was narrow in scope and that its extension would not have negative consequences. Participants also provided information on patent protections and diagnostics. Some participants, including representatives of industry, nonprofit organizations, and multilateral institutions, agreed that patents were not a primary barrier to access to COVID-19 diagnostics tests. Key points are summarized below.⁸²

Participants' descriptions of the 2022 Ministerial Decision, and its potential effects, were strikingly different. Most participants, particularly those representing the interests of industry, described it

⁷⁷ WTO, "Ministerial Decision on the TRIPS Agreement," WT/MIN(22)/30, June 22, 2022, pars. 6 and 8.

⁷⁸ WTO, "Ministerial Decision on the TRIPS Agreement," WT/MIN(22)/30, June 22, 2022, par. 1.

⁷⁹ WTO, "Ministerial Decision on the TRIPS Agreement," WT/MIN(22)/30, June 22, 2022, par. 3.

⁸⁰ WTO, "Ministerial Decision on the TRIPS Agreement," WT/MIN(22)/30, June 22, 2022, par. 4.

⁸¹ TRIPS Agreement, art. 39.3.

⁸² Considerations related to different approaches to defining COVID-19 diagnostics and therapeutics are discussed in chapters 3 and 4.

broadly as a waiver of the TRIPS Agreement or of IP rights in general.⁸³ Others, particularly academics, nonprofit, and civil society organizations, described it as making relatively minor changes to existing CL rules.⁸⁴ As for the potential effect of extending the 2022 Ministerial Decision to diagnostics and therapeutics, industry representatives and others stated that IP rights are necessary to support investment and innovation and provide a framework for collaborations.⁸⁵ They further stated that the existing IP rules worked well to incentivize the development and deployment of COVID-19 therapeutics and diagnostics, and that the 2022 Ministerial Decision would disrupt the balance between IP rights and access already contained in the TRIPS Agreement.⁸⁶ They also raised concerns about the negative effects of weakening TRIPS Agreement protections on U.S. innovation, competitiveness, and national security.⁸⁷

By contrast, those who stated that the 2022 Ministerial Decision made relatively minor changes to existing CL rules also asserted that its extension to diagnostics and therapeutics would not undermine the IP and access to medicines balance otherwise supported by the TRIPS Agreement.⁸⁸ In particular, proponents of extension stated that effects on pharmaceutical companies would be minimal because the decision would be time and purpose limited and would not alter TRIPS Agreement obligations

⁸³ See, e.g., Pfizer, written submission to the USITC, May 5, 2023, 3; Merck & Co., Inc. (“Merck”), written submission to the USITC, May 5, 2023, 14; Gilead, written submission to the USITC, May 5, 2023, 2; Lilly, prehearing brief submission to the USITC, March 17, 2023, 1; Novartis, written submission to the USITC, May 5, 2023, 1; BASF, written submission to the USITC, May 4, 2023, 2.

⁸⁴ See, e.g., Matthews, written submission to the USITC, May 5, 2023, 1; Watal, written submission to the USITC, May 3, 2023, 2–3; TWN, written submission to the USITC, May 5, 2023, 1; Rethink Trade, written submission to the USITC, May 5, 2023, 1; KEI, prehearing brief submission to the USITC, March 20, 2023, 5; MSF, written submission to the USITC, May 17, 2023, 1; People’s Vaccine Alliance, written submission to the USITC, May 4, 2023, 1–3; multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023.

⁸⁵ See, e.g., Brant, Schultz, “Unprecedented,” November 2021, 51–52; Pfizer, written submission to the USITC, May 5, 2023, 3; Merck, written submission to the USITC, May 5, 2023, 14; Gilead, written submission to the USITC, May 5, 2023, 2; Lilly, prehearing brief submission to the USITC, March 17, 2023, 1; Novartis, written submission to the USITC, May 5, 2023, 1; BASF, written submission to the USITC, May 4, 2023, 2.

⁸⁶ See, e.g., PhRMA, written submission to the USITC, May 5, 2023, 1; BIO, written submission to the USITC, May 5, 2023, 1; EFPIA, written submission to the USITC, May 4, 2023, 1; Association of the British Pharmaceutical Industry, written submission to the USITC, May 17, 2023, 1; International Federation of Pharmaceutical Manufacturers Association, written submission to the USITC, May 5, 2023, 1; JPMA, written submission to the USITC, May 5, 2023, 1; VFA, written submission to the USITC, May 3, 2023, 1; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representative, interview by USITC staff, Malaysia, July 21, 2023; see also WTO TRIPS Council, “TRIPS Council Discussions on COVID-19 Therapeutics and Diagnostics: Evidence and Questions on Intellectual Property Challenges Experienced by Members,” IP/C/W/693, November 1, 2022.

⁸⁷ See, e.g., U.S. Chamber of Commerce, prehearing submission to the USITC, March 17, 2023, 2; ITIF, prehearing submission to the USITC, March 17, 2023, 14; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 13; Council for Innovation Promotion, prehearing submission to the USITC, March 16, 2023, 5; Abbott and McDaniel, written submission to the USITC, May 4, 2023, 5; Institute for Policy Innovation, written submission to the USITC, May 3, 2023, 5; Alliance for Biosecurity, written submission to the USITC, May 5, 2023, 2; Arizona Chamber of Commerce & Industry, written submission to the USITC, May 5, 2023, 1; Willems, written submission to the USITC, May 5, 2023, 4

⁸⁸ See, e.g., Matthews, written submission to the USITC, May 5, 2023, 1; Watal, written submission to the USITC, May 3, 2023, 2–3; TWN, written submission to the USITC, May 5, 2023, 1; KEI, prehearing brief submission to the USITC, March 20, 2023, 5; MSF, written submission to the USITC, May 17, 2023, 1; People’s Vaccine Alliance, written submission to the USITC, May 4, 2023, 1–3; government representative, interview by USITC staff, Brazil, June 29, 2023.

applicable to developed countries, which are the industry’s source of most revenues.⁸⁹ They also emphasized the historical importance of generic competition, facilitated by CLs, to reducing prices and improving access to medicines in developing countries.⁹⁰

On the issue of diagnostics and patents, nonprofit organizations and industry representatives generally agreed that patents did not act as a primary barrier limiting global access to the two main types of COVID-19 diagnostic tests—polymerase chain reaction (PCR) tests and rapid antigen tests.⁹¹ The foundational patent for PCR tests—the “gold standard”⁹² of COVID-19 tests—reportedly was originally filed in 1987 and expired 20 years later (over 15 years ago).⁹³ Foundational patents for antigen tests also have expired, according to industry and nonprofit sources.⁹⁴ Reportedly, the best evidence that patents did not act as a primary barrier to the production of COVID-19 diagnostic tests is substantial global manufacturing of COVID-19 diagnostic tests—900 producers in 53 countries have produced over 2,000 different COVID-19 diagnostic testing products, as of June 2023.⁹⁵ This does not mean that patents are irrelevant; for example, they may be used to protect testing platforms and associated inputs used in automated testing processes for COVID-19 and other diseases.⁹⁶ There are also emerging diagnostic

⁸⁹ Across the global pharmaceutical market in general, seven high-income countries reportedly accounted for more than 87 percent of sales of new medicines launched during the 2016–21 period. Oxfam, written submission to the USITC, May 5, 2023, 11.

⁹⁰ Oxfam, written submission to the USITC, May 5, 2023, 7; Public Citizen, prehearing brief submission to the USITC, March 20, 2023, 10–11.

⁹¹ See, e.g., FIND, written submission to the USITC, May 16, 2023, 1; FIND, *Diagnostics & Intellectual Property*, November 2022; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 7; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representatives, interviews by USITC staff, March 7, June 14, and June 1, 2023; industry representative, email message to USITC staff, June 16, 2023; industry representative, interview by USITC staff, Brazil, June 28, 2023; government representative, interview by USITC staff, South Africa, June 27, 2023; industry representative, interview by USITC staff, South Africa, June 28, 2023; multilateral organization representative, interview by USITC staff, June 6, 2023; industry representative, interview by USITC staff, Malaysia, July 25, 2023.

⁹² CDC, “COVID-19 Testing: What You Need to Know,” May 11, 2023.

⁹³ FIND, written submission to the USITC, May 16, 2023, 1; FIND, *Diagnostics & Intellectual Property*, November 2022; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 7; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representatives, interviews by USITC staff, March 7, June 1, and June 14, 2023; industry representative, email message to USITC staff, June 16, 2023.

⁹⁴ FIND, written submission to the USITC, May 16, 2023, 1; FIND, *Diagnostics & Intellectual Property*, November 2022; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 7; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representatives, interviews by USITC staff, March 7, June 1, and June 14, 2023.

⁹⁵ See chapter 4 (Production, market segmentation, trade, diagnostics, and global production). See also PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18 (patents for the basic technology have all expired and do not impede the ability of manufacturers to replicate it); Watal, written submission to the USITC, May 3, 2023, 4–5 (India was able to quickly ramp up local production to more than a million PCR test kits per day in 2021 with a nearly tenfold decrease in prices); AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 13–14; multilateral organization representative, interview by USITC staff, June 6, 2023.

⁹⁶ Abbott, “DIAGNOSTICS PATENTS,” accessed August 28, 2023; industry representative, interview by USITC staff, July 5, 2023. See box 2.2, IP Protections and Diagnostic Testing Platforms, below for more information.

technologies, including those identified in the U.S. Patent and Trademark Office (USPTO) patent landscape report, that may be subject to patent protections.⁹⁷

Patent Landscape for COVID-19 Diagnostics and Therapeutics

Two patent landscape reports, one prepared by the USPTO covering COVID-19 diagnostics and the other by WIPO covering COVID-19 therapeutics, describe patent activity since the emergence of COVID-19.⁹⁸ These reports provide snapshots into the volume of patenting, where inventors are seeking protection, who is inventing, and the nature of the inventions for which patents have been sought since the emergence of the pandemic.⁹⁹ The descriptions of patent landscapes are followed by particular examples, views of relevant stakeholders, and a brief summary of available economic literature on patent protections and COVID-19 diagnostics and therapeutics.

Patenting of COVID-19 Diagnostics: Landscape and Examples

The USPTO patent landscape report identifies 824 COVID-19 diagnostic-specific published patent filings at the USPTO between December 2019 and the end of March 2023.¹⁰⁰ These patents are generally for technologies that enhance or augment existing diagnostic approaches including PCR or antigen tests but do not fundamentally change the foundational technologies for which patents have reportedly expired. Published patent filings for COVID-19 diagnostics represented a small share of overall diagnostic patent filings during the same period—2.6 percent at its peak in the fourth quarter of 2021 and tapering to 1.4 percent in the most recent data (2023 Q1).¹⁰¹ Most filings during this period were made by companies (just over 58 percent), followed by universities, research institutes, and hospitals (about 27 percent) and individuals (13 percent).¹⁰² Most filers were based in the United States and qualified as “small entities” for purposes of the USPTO’s criteria for reduced fee programs.¹⁰³

⁹⁷ FIND, *Diagnostics & Intellectual Property*, November 2022, 3; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; Toole et al., “Diagnosing COVID-19,” October 2023.

⁹⁸ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 12 (covering the period from January 2020 through September 2022); Toole et al., “Diagnosing COVID-19,” October 2023, 9 (covering the period from December 2019 through March 2023).

⁹⁹ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023. WIPO’s 2023 report updates one published in 2022, WIPO, *COVID-19 Related Vaccines and Therapeutics: Preliminary Insights*, 2022; Toole et al., “Diagnosing COVID-19,” October 2023, 2.

¹⁰⁰ The USPTO’s methodology for identifying COVID-19-related published applications and patents is described in detail in the appendix to its report. The filing data reported here are for “COVID-19 specific” rather than “COVID-19 related” patent filings because this search strategy yielded more precise results. Toole et al., “Diagnosing COVID-19,” October 2023, 4–6.

¹⁰¹ Toole et al., “Diagnosing COVID-19,” October 2023, 7.

¹⁰² Toole et al., “Diagnosing COVID-19,” October 2023, 9.

¹⁰³ USPTO small entity criteria generally track Small Business Administration guidelines that require the number of an entity’s employees not exceed 500. Universities, research institutes, and nonprofit organizations in the United

Globally, the USPTO found that most COVID-19 diagnostic published patent filings were made in China, accounting for about 47 percent of “patent families.”¹⁰⁴ WIPO had the next highest share of COVID-19 diagnostic published patent families (about 35 percent). This likely reflects the value of the Patent Cooperation Treaty system, which enables applicants to begin pursuing patent protection in the 157 states that are members of the treaty, through a single filing at WIPO.¹⁰⁵ The USPTO was the location with the next highest share of patent filings, followed by the Indian Patent Office, and the regional European Patent Office.¹⁰⁶

COVID-19 diagnosis can be accomplished through a wide variety of scientific methods (and not just via the most common PCR and rapid antigen tests for which foundational patents reportedly have expired). The myriad of approaches is multiplied by the increasing role that digital, mechanical, or other technologies play in enhancing diagnostic approaches for physicians and patients, according to the USPTO.¹⁰⁷ As examples of these complex inventions, USPTO cites patents for a high throughput system designed to increase testing speed and reduce cost by testing many samples simultaneously, a patent for a digitally enabled at-home rapid testing device, and a patent for antibodies that may be used both to diagnose and treat COVID-19.¹⁰⁸

The patent activity reflected in the USPTO landscape report is consistent with the views of diagnostics industry representatives that IP protections are important. Industry representatives state that patents are important because of substantial investments in time and money needed to research and develop the technology, obtain regulatory approval, set up and maintain manufacturing, and implement distribution strategies. Some diagnostic companies rely on IP protections to protect these investments.¹⁰⁹

Most of the studies on the effects of patent protection covered in the literature review chapter focus on pharmaceuticals; less research has been done on medical instruments or diagnostics specifically.¹¹⁰ One study using U.S. firm-level data shows the medical equipment industry reports patents as being a more effective mechanism for appropriating gains from product and process innovations than for most

States and abroad qualify for small entity status regardless of size. Toole et al., “Diagnosing COVID-19,” October 2023, 9.

¹⁰⁴ For purposes of the USPTO landscape report, patent families are patent documents covering the same invention with the same applicant, assignee, or invention. Patent families are grouped together to avoid the overcounting of similar filings across multiple jurisdictions. Toole et al., “Diagnosing COVID-19,” October 2023, 18–19, 22.

¹⁰⁵ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 41; WIPO, “The PCT Now Has 157 Contracting States,” accessed July 20, 2023.

¹⁰⁶ Toole et al., “Diagnosing COVID-19,” October 2023, 18–19.

¹⁰⁷ Toole et al., “Diagnosing COVID-19,” October 2023, 14.

¹⁰⁸ Toole et al., “Diagnosing COVID-19,” October 2023, 16–17.

¹⁰⁹ AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representatives, interviews by USITC staff, March 7, March 21, June 1, and June 14, 2023; industry representative, email message to USITC staff, June 16, 2023.

¹¹⁰ See chapter 8 for academic literature on the effect of patent protection on innovation in the health sector and the effect of patent protection on access to medicine.

industries.¹¹¹ Another study using U.S. firm-level survey data estimates that, for medical instruments, the expected premium of patents is larger than patent application costs.¹¹²

One study using U.S. firm-level data shows the medical equipment industry reports patents as being a more effective mechanism for appropriating gains from product and process innovations than for most industries.¹¹³ Another study using U.S. firm-level survey data estimates that, for medical instruments, the expected premium of patents is larger than patent application costs.¹¹⁴

IP protections associated with COVID-19 diagnostic testing platforms reportedly have given rise to access challenges, see box 2.2.¹¹⁵

Box 2.2 IP Protections and Diagnostic Testing Platforms

Diagnostic testing platforms used in automated COVID-19 testing processes typically combine hardware, software, and chemistries and may involve numerous patents and trade secrets. One example is Cepheid's GeneXpert system. The GeneXpert platform can perform 20 different tests for diseases and conditions, including COVID-19.^a First brought to the clinical market in 2005, GeneXpert is a cartridge-based molecular diagnostics platform.^b Tests are performed inside a plastic cartridge, containing reagents and the patient's sample, and loaded into the GeneXpert device.^c More than 40,000 GeneXpert Systems are installed in 180 countries, including 10,000 procured by the Global Fund for COVID-19 polymerase chain reaction (PCR) testing in developing countries.^d These devices have been used by the World Health Organization to deploy PCR testing in relatively small machines, particularly in rural and remote areas.^e

Access to the devices themselves is not reported as a major constraint on testing capacity in developing countries, but access to the consumable cartridges has been an issue.^f Despite the existence of alternative platforms, such as the Abbott m2000 system and the Roche cobas 6800/8800 systems,^g the number of installed GeneXpert machines points to a substantial share of laboratory testing capacity in developing countries that rely on this particular platform for PCR testing. In 2021, GeneXpert accounted for 44 percent of the automatic PCR tests procured by the Diagnostics Supply Consortium.^h The cartridges needed to perform a GeneXpert test are reported to be under patent until 2037.ⁱ Patent and trade secret barriers to generic replication of cartridges are reported to have constrained testing capacity for laboratories dependent on GeneXpert devices for automated PCR testing.^j

^a See chapter 4 for more information on the difference between automated and manual PCR tests. Cepheid, "Tests," accessed April 13, 2023.

^b Cepheid, "A Higher Level of PCR Excellence," accessed April 12, 2023; Cepheid, "GeneXpert System," accessed April 13, 2023.

^c Cepheid, *Xpert Xpress SARS-CoV-2: Instructions for Use*, accessed April 13, 2023.

^d PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 7, 10.

^e PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; nonprofit organization representative, interview by USITC staff, Switzerland, June 8, 2023.

^f PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; nonprofit organization representative, interview by USITC staff, Switzerland, June 8, 2023; industry representative, interview by USITC staff, South Africa, June 29, 2023.

^g WHO, *WHO Emergency Use Listing for In Vitro Diagnostics (IVDs) Detecting SARS-CoV-2*, May 5, 2023; WHO, *Diagnostics - Technical Frequently Asked Questions*, 1, accessed April 17, 2023.

¹¹¹ Cohen, Nelson, and Walsh, "Protecting Their Intellectual Assets," February 2000.

¹¹² Arora, Ceccagnoli, and Cohen, "R&D and the Patent Premium," September 1, 2008.

¹¹³ Cohen, Nelson, and Walsh, "Protecting Their Intellectual Assets," February 2000.

¹¹⁴ Arora, Ceccagnoli, and Cohen, "R&D and the Patent Premium," September 1, 2008.

¹¹⁵ PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; FIND, *Diagnostics & Intellectual Property*, November 2022, 3; Médecins Sans Frontières, "Local Diagnostics to Meet Local Health Needs," July 2021, 7.

^h This figure represents only the share purchased through this one pooled procurement mechanism. PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 10.

ⁱ PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18.

^j Gotham et al., “Public Investments in the Development of GeneXpert Molecular Diagnostic Technology,” August 31, 2021; MSF, written submission to the USITC, May 23, 2023, 10; nonprofit organization representative, interview by USITC staff, Switzerland, June 8, 2023.

Patenting of COVID-19 Therapeutics: Landscape and Examples

According to WIPO’s patent landscape report, 4,787 patent applications for COVID-19 therapeutics were filed between January 2020 and the end of September 2022.¹¹⁶ Therapeutic patent applications were filed around the world. The top five filing offices were WIPO, China National Intellectual Property Administration, USPTO, European Patent Office, and Korean Intellectual Property Office.¹¹⁷ As with diagnostics, WIPO’s top ranking likely reflects applicants’ interest in leveraging the Patent Cooperation Treaty system to begin the protection of inventions across multiple jurisdictions.¹¹⁸ Published patent applications also illustrate collaborations in COVID-19 therapeutic inventions, particularly between universities and research institutes in the United States, Europe, and South Korea and, within China, between Chinese corporate entities and research institutions.¹¹⁹

Industry representatives consider patent protection to be essential to protect substantial investments in basic and applied research, clinical trials, manufacturing, regulatory review, and commercialization of new therapeutics. According to Pharmaceutical Research and Manufacturers of America (PhRMA), “The simplest rationale for protecting IP is that without it, copying would be more rational than innovating.”¹²⁰ Patent protections, which are time limited, may enable the innovator to recover costs and make profits on products that are expensive to bring to market and relatively easy to copy (e.g., small-molecule drugs).¹²¹ Another important function of patents and other IP protections is to provide a framework for collaboration among the different public and private actors who may work together as a product moves from R&D through commercialization.¹²² For small and medium-sized enterprises in particular, their patent portfolio may be their most valuable asset and one that enables them to access venture capital and other important funding sources.¹²³

¹¹⁶ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 12.

¹¹⁷ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 41–42.

¹¹⁸ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 41–42.

¹¹⁹ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 46.

¹²⁰ PhRMA, written submission to the USITC, March 17, 2023, 8–9.

¹²¹ See, e.g., Brant, Schultz, “Unprecedented,” November 2021, 9; PhRMA, written submission to the USITC, March 17, 2023, 8–9; Competere, written submission to the USITC, May 5, 2023, 18–19; INTERPAT, written submission to the USITC, May 4, 2023, 3; IFPMA, written submission to the USITC, May 5, 2023, 7–8.

¹²² See, e.g., Brant, Schultz, “Unprecedented,” November 2021, 8; Pfizer, written submission to the USITC, May 5, 2023, 3; Merck & Co., Inc. (“Merck”), written submission to the USITC, May 5, 2023, 14; Gilead, written submission to the USITC, May 5, 2023, 2; Lilly, prehearing brief submission to the USITC, March 17, 2023, 1; Novartis, written submission to the USITC, May 5, 2023, 1; BASF, written submission to the USITC, May 4, 2023, 2.

¹²³ See, e.g., BIO, written submission to the USITC, March 17, 2023, 2; Association of Women’s Business Centers, written submission to the USITC, May 5, 2023, 4; Business Council of New York State, written submission to the USITC, April 27, 2023, 1–2; California Life Sciences, written submission to the USITC, April 26, 2023, 2; MassBio, written submission to the USITC, May 1, 2023, 2; National Small Business Association, written submission to the USITC, May 4, 2023, 3–4.

Patents on a drug's active pharmaceutical ingredient (sometimes called "primary" patents) may be of particular value to the manufacturer because they are difficult to "invent around" (i.e., develop a competing product that does not infringe the patent).¹²⁴ Primary patents, however, are not the only type of patents important to producers. Pharmaceuticals may also be covered by patents covering modified forms of the base compound (e.g., salts or crystalline forms), medical uses of a known compound, combinations of known compounds, particular formulations (e.g., tablets and topical forms), dosage regimens, and processes used to make the product. These patents are sometimes called "secondary" because they come later in the sequence of innovation.¹²⁵ Virtually all COVID-19 therapeutics have many primary and secondary patent applications pending, as well as granted patents in multiple jurisdictions.¹²⁶ This substantial patenting is documented in the voluntary license agreements for ensitrelvir fumaric acid (originated by Shionogi), nirmatrelvir (+ ritonavir) (Pfizer), molnupiravir (Merck), and remdesivir (Gilead). In these agreements, the originator companies identify numerous product and process patents filed in multiple jurisdictions, including HICs, UMICs, and LMICs.¹²⁷ In addition, many drugs have related patent applications filed by entities other than the originator companies. These applications may involve new formulations, combinations, methods of manufacturing, or methods of use for the drugs.¹²⁸

Academic research has studied the effect of patent protections on the pharmaceutical industry.¹²⁹ Firm-level survey results for the United States on firms' views and use of patents generally imply that patent protection is more important for the pharmaceutical industry than for other industries.¹³⁰ Model-based analyses often find mixed results on the relationship between patent protection and innovation in the pharmaceutical industry. Some cross-country studies have provided evidence that patent protection supports innovation in the health sector in more developed countries but has little to

¹²⁴ Kyle, "Competition Law, Intellectual Property, and the Pharmaceutical Sector," 2016, 2.

¹²⁵ Kapczynski, Park, and Sampat, "Polymorphs and Prodrugs and Salts (Oh My!)," December 5, 2012, 1; Sampat and Shadlen, "Drug Patenting in India," August 2015, 519–520. See also INTERPAT, written submission to the USITC, May 4, 2023, 2.

¹²⁶ Dexamethasone is one of the few therapeutics recommended for use by WHO that is widely available off-patent. WHO, "Coronavirus Disease (COVID-19): Corticosteroids, Including Dexamethasone," March 28, 2023. See also Unitaid and WHO, "Improving Access to Novel COVID-19 Treatments," April 2023, 9–10 (identifying patents associated with therapeutics with a WHO recommendation as of December 2022).

¹²⁷ See MPP, "License Agreement between Pfizer and MPP," November 15, 2021, App. 2 (identifying 69 patent applications in 66 jurisdictions); Gilead, "2020 Original Covid-19 Voluntary License Agreement," accessed June 6, 2023 (identifying 512 patents and applications related to manufacturing and processes and 121 product patents and applications. Manufacturing and process patents were filed in 119 jurisdictions and product patents in 53 jurisdictions); MPP, "License Agreement between Merck and MPP," October 26, 2021, App. 2 (identifying 57 patent applications filed in 27 jurisdictions); MPP, "License Agreement between Shionogi and MPP," October 3, 2022, Ex. B (identifying 23 patent applications in seven jurisdictions). See table H.1, "Countries Covered by Voluntary Licenses by Treatment Type and Income Level."

¹²⁸ WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 47–48 (providing examples of secondary patent applications associated with remdesivir, nirmatrelvir (+ ritonavir), and molnupiravir).

¹²⁹ See chapter 8 for a review of the academic literature.

¹³⁰ Mansfield, "Patents and Innovation," 1986; Mansfield, Schwartz, and Wagner, "Imitation Costs and Patents," 1981; Levin et al., "Appropriating the Returns from Industrial Research and Development," 1987; Cohen, Nelson, and Walsh, "Protecting Their Intellectual Assets," February 2000.

no positive effect for innovation in developing countries and negative effects for access and affordability.¹³¹

Trade Secrets and COVID-19 Diagnostics and Therapeutics

Access to trade secrets and expertise is important to diagnostic producers, particularly those in developing countries. Some diagnostics technology has been transferred to COVID-19 diagnostic producers in Brazil, India, Kenya, Morocco, Senegal, South Africa, and Uganda, and technical information also has been placed in the public domain.¹³² As mentioned in chapter 5, agreements that involve only the transfer of trade secrets, data, knowledge, or other materials are sometimes referred to separately as technology transfer agreements. Many types of technology transfer agreements restrict further disclosure, and nonprofit organizations and others state there is a need for more sharing of trade secrets and expertise related to diagnostics technologies, particularly under Article 66.2 of the TRIPS Agreement.¹³³

A reported trade secret constraint related to diagnostics has been in the area of reagents—substances used in diagnostic tests to detect disease agents or antibodies (see box 2.3).¹³⁴

Box 2.3 Buffers, Shortages, and Trade Secrets

In early 2020, limited COVID-19 testing in the Netherlands was attributed in part to a shortage of the testing reagent produced by Roche Diagnostics, known as a lysis buffer. A lysis buffer is used in testing to break down a cell’s membrane and release its genetic information.^a The majority of Dutch laboratories depended on Roche test kits and machines, giving the company a reported 80 percent market share in the Netherlands.^b This dependency on one supplier meant that a shortage of Roche testing reagents was a severe constraint on the country’s testing capacity.^c At the time, Roche was able to cover only about 30 percent of its orders.^d

Roche’s lysis buffer was not under patent protection, and lysis buffers could be easily manufactured by laboratories.^e Roche’s specific recipe for the lysis buffer was not public, however, and reproduction without its recipe would require extensive testing to ensure reproductions functioned properly within Roche machines.^f This proprietary expertise is a type of trade secret, which in the case of diagnostics can range from chemistry recipes to proprietary manufacturing equipment and processes.^g Medical researchers and the Dutch House of Representatives issued public calls for Roche to disclose its recipe.^h

¹³¹ Qian, “Do National Patent Laws Stimulate Domestic Innovation,” August 1, 2007; Liu and La Croix, “The Impact of Stronger Property Rights in Pharmaceuticals,” March 14, 2014; Gamba, “The Effect of Intellectual Property Rights on Domestic Innovation,” November 1, 2017; Kyle and McGahan, “Investments in Pharmaceuticals Before and After TRIPS,” November 1, 2012; Borrell, “Pricing and Patents of HIV/AIDS Drugs,” March 1, 2007; Hellerstein, “What Do Drug Monopolies Cost Consumers in Developing Countries?,” July 1, 2012.

¹³² MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, Online Supplement 1.

¹³³ FIND, written submission to the USITC, May 16, 2023, 1; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 7; government representative, interview by USITC staff, Brazil, June 26, 2023; WIPO, “Technology Transfer Agreements,” accessed July 20, 2023.

¹³⁴ See chapter 4 for a detailed discussion of diagnostic tests.

Because of Roche’s substantial market position and the shortage of necessary testing reagents, the Netherlands Authority for Consumers and Markets (ACM) launched an investigation into Roche in collaboration with the European Commission’s competition authorities.ⁱ Roche could not confirm the existence of a lysis buffer shortage; however, it worked with the Dutch Ministry of Health, Welfare, and Sport to publicly share the recipe and help manufacturers and laboratories scale up production.^j The ACM expressed satisfaction with Roche’s commitments and declined to take further action.^k

^a Strop and Van Ark, “Test, Test, Test,” March 26, 2020.

^b DutchNews, “Roche Urged to Share Info,” March 26, 2020; Van Ark, Strop, “Roche Releases Recipe,” March 27, 2020; ML&P, written submission to the USITC, May 2, 2023, 6–7.

^c Strop and Van Ark, “Test, Test, Test,” March 26, 2020.

^d Van Ark and Strop, “Roche Releases Recipe after European Commission Considers Intervention,” March 27, 2020.

^e Roche Diagnostics, “Statement from Roche Diagnostics on Supply of the SARS-CoV-2 Test and Material,” March 27, 2020; Strop and Van Ark, “Test, Test, Test,” March 26, 2020.

^f Strop and Van Ark, “Test, Test, Test,” March 26, 2020; ML&P, written submission to the USITC, May 2, 2023, 6–7.

^g FIND, *Diagnostics & Intellectual Property*, November 2022, 3.

^h Strop and Van Ark, “Test, Test, Test,” March 26, 2020; Van Ark and Strop, “Roche Releases Recipe after European Commission Considers Intervention,” March 27, 2020.

ⁱ Netherlands ACM, “ACM Has Confidence in Commitments Made by Roche,” April 3, 2020; Strop and Van Ark, “Test, Test, Test,” March 26, 2020.

^j Roche Diagnostics, “Statement from Roche Diagnostics on Supply of the SARS-CoV-2 Test and Material,” March 27, 2020; Van Ark and Strop, “Roche Releases Recipe after European Commission Considers Intervention,” March 27, 2020.

^k Netherlands ACM, “ACM Has Confidence in Commitments Made by Roche,” April 3, 2020.

The biopharmaceutical industry relies on trade secret and patent protections to safeguard R&D, manufacturing processes, and regulatory approval requirements associated with small-molecule and biologic drugs.¹³⁵ The size and complexity of biologics generally prevent their exact replication as opposed to the simpler small molecule drugs.¹³⁶ Biologics, including the monoclonal antibodies (mAbs) used in some COVID-19 therapeutics, are produced from living organisms or extracted from biological materials.¹³⁷ Trade secrets—in the form of detailed information and expertise—generally are considered necessary to create and perfect the manufacturing processes for biologics and more complex small-molecule drugs.¹³⁸ Companies also protect clinical trial protocols and safety and efficacy data associated with small-molecule drugs and biologics through trade secret and patent protections.¹³⁹

¹³⁵ Schultz, *Trade Secrecy and Covid-19*, October 5, 2022, 8; Feldman, “Trade Secrets in Biologic Medicine,” January 2, 2023, 26; Levine and Sarnoff, “Compelling Trade Secret Sharing,” April 6, 2023, 993. The biopharmaceutical industry includes manufacturers of medical drugs produced using biotechnology, including biologics. Biologics are pharmaceutical products created by living cells or organisms, whereas small-molecule drugs are organic chemical compounds. See chapter 3 for additional information on biologics and small-molecule drugs.

¹³⁶ Generic small-molecule drugs must establish “bioequivalence” to originator drugs; generic biologics would not be equivalent but “biosimilar.” Biosimilar means a biological product that has no clinically meaningful differences in safety and effectiveness compared to a reference biological product. The standardization of biologic drugs is established through the manufacturing process. FDA, “Biosimilars Info Sheet,” accessed September 25, 2023; FDA, “Biological Product Definitions,” accessed August 21, 2023.

¹³⁷ Merck, *Making Biologics: Strategies and Policies for Enhancing Capacity*, May 2022, 4; Feldman, “Trade Secrets in Biologic Medicine,” January 2, 2023, 26; Levine and Sarnoff, “Compelling Trade Secret Sharing,” April 6, 2023, 993.

¹³⁸ Feldman, “Trade Secrets in Biologic Medicine,” January 2, 2023, 32; Levine and Sarnoff, “Compelling Trade Secret Sharing,” April 6, 2023, 993; Schultz, *Trade Secrecy and Covid-19*, October 5, 2022, 11.

¹³⁹ Industry representative, interview by USITC staff, June 22, 2023; industry representative, interview by USITC staff, Switzerland, June 8, 2023; PhRMA, written submission to the USITC, March 17, 2023, 28–29; INTERPAT,

Regulations to Bring Diagnostics and Therapeutics to Market

The regulatory ecosystem for COVID-19 diagnostics and therapeutics comprises a broad assortment of regulatory actors, including national regulatory authorities, the WHO Prequalification of Medicines Programme (PQP), procurement organizations, and WHO entities that publish WHO guidelines. In many high-income countries (HICs) and upper-middle-income countries (UMICs), domestic regulatory authorities provide approval and oversight for access to medicines and diagnostics.¹⁴⁰ As detailed below, in the case of low-income countries (LICs) and lower-middle-income countries (LMICs), national authorities, the WHO, and procurement organizations may all play roles in facilitating access.

National Regulatory Authorities

Every diagnostic and therapeutic must be approved for use by the national regulatory authority in each country in which it is sold.¹⁴¹ National regulatory authorities play a crucial role in the evaluation, approval, and oversight of medicines and diagnostics, including those used for the diagnosis and treatment of COVID-19. These regulatory bodies carefully assess data from preclinical studies, clinical trials, and other relevant research to ensure the safety, efficacy, and quality of drugs before they can be marketed and made available to the public. In situations like the COVID-19 pandemic, where there is an urgent need for diagnostics and treatments, regulatory authorities may grant Emergency Use Authorizations (EUAs). An EUA allows for expedited authorization of the use of drugs or vaccines based on preliminary evidence of safety and effectiveness. It enables the use of drugs before they receive full regulatory approval, ensuring access to potentially lifesaving treatments in a process separate from, and faster than, the drug approval process.¹⁴²

In the United States, all COVID-19 diagnostics and therapeutics generally must be submitted to and approved by the FDA before they can be used in patient care. However, the declaration of a public health emergency in early 2020 gave the FDA authority to grant EUAs for expedited access to diagnostics and medicines before the product or specific use was approved; under an EUA, or once approved, it can then be licensed or cleared for commercial distribution.¹⁴³ The FDA guidance for EUAs lists four main criteria required for issuance. First, the virus referred to in the public health emergency declaration must be capable of causing a serious or life-threatening disease. Second, only medical products that may

written submission to the USITC, May 4, 2023, 3; IFPMA, written submission to the USITC, May 5, 2023, 7–8; Feldman, “Trade Secrets in Biologic Medicine,” January 2, 2023, 32; Levine and Sarnoff, “Compelling Trade Secret Sharing,” April 6, 2023, 993.

¹⁴⁰ WHO, “National Regulatory Agencies,” accessed June 27, 2023; Macé, Rãgo, and Ravinetto, “How the Concept of WHO-Listed Authorities Will Change International Procurement Policies for Medicines,” February 10, 2022, 1–4.

¹⁴¹ WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

¹⁴² FDA, “Emergency Use Authorization,” April 25, 2023.

¹⁴³ The declaration issued by the Secretary of Health and Human Services (HHS) on February 4, 2020, was based on a public health emergency determination under the FDCA. 21 U.S.C. § 360bbb-3(b)(1)(C). USITC, *COVID-19 Related Goods*, December 2020, 151; FDA, *Policy for Coronavirus Disease-2019 Tests (Revised)*, January 12, 2023, 5. The COVID-19 public health emergency declaration expired on May 11, 2023. However, existing EUAs for products will remain in effect, and the agency may continue to issue new EUAs if the situation meets the criteria to do so. FDA, “Emergency Use Authorization,” April 25, 2023.

be effective to prevent, diagnose, or treat serious or life-threatening diseases or conditions are eligible for the EUA. Third, the product must undergo a risk-benefit analysis by the FDA. Finally, there must be no adequate, approved, and available alternative to the candidate product.¹⁴⁴

For COVID-19 diagnostics, EUAs were the primary form of regulatory clearance. However, there are other forms of clearance/approval within the FDA for diagnostics.¹⁴⁵ The 510(k) is a premarket submission made to FDA to demonstrate that the diagnostic is safe, effective, and substantially equivalent to an already cleared test that is on the market.¹⁴⁶ De novo classifications, by contrast, are for diagnostics for which there is no substantially equivalent test on the market.¹⁴⁷ While manufacturers largely utilized the EUA process for COVID-19 diagnostics, it is possible that both 510(k) and de novo clearances were submitted to the FDA during the course of the pandemic.¹⁴⁸

Full market approval of therapeutics by the FDA requires an extensive review process, including an analysis of the targeted condition and existing treatment landscape, an analysis of the data on the benefits and risks of the product from clinical studies, and a review of risk management strategies, including the approval of drug labeling.¹⁴⁹ Full approval for new therapeutics can take as little as 10 months or much longer.¹⁵⁰ However, there are ways to shorten the review process, including the agency's Fast Track approval process. Under Fast Track, a drug's review process is expedited if it will be used to treat serious conditions or fill an unmet medical need. Fast Track approval must be requested by the drug company.¹⁵¹

Some of the most stringent authorities (outside the United States) are located in Australia, Canada, the European Union (EU), Iceland, Japan, Liechtenstein, Norway, and Switzerland (box 2.4). In the EU, the EMA is responsible for approving medical products.¹⁵² For diagnostics, companies must comply with the EU Medical Device Regulation and the In Vitro Diagnostics Regulation.¹⁵³ Other stringent regulatory bodies include Health Canada and Japan's Pharmaceuticals and Medical Devices Agency.¹⁵⁴ While these

¹⁴⁴ FDA, *Emergency Use Authorization of Medical Products and Related Authorities*, January 2017.

¹⁴⁵ FDA, "FAQs on Testing for SARS-CoV-2," March 24, 2023.

¹⁴⁶ FDA, "Premarket Notification 510(k)," November 2, 2022.

¹⁴⁷ FDA, "De Novo Classification Request," October 3, 2022.

¹⁴⁸ Premarket approvals, another regulatory route for the clearance of diagnostics in general, typically apply only to Class III medical devices. For more, see FDA, "Premarket Approval (PMA)," October 3, 2022.

¹⁴⁹ FDA, "Development & Approval Process | Drugs," August 8, 2022.

¹⁵⁰ PharmaNewsIntelligence, "Understanding US Food and Drug Administration (FDA) Approval Processes," March 4, 2022.

¹⁵¹ 21 U.S.C. § 356(b)(1); FDA, "Fast Track," January 4, 2018. Shionogi has received FDA Fast Track designation for its oral antiviral ensitrelvir. Shionogi, "Shionogi Receives U.S. FDA Fast Track Designation for Ensitrelvir Fumaric Acid, an Investigational Oral Antiviral for COVID-19," accessed June 11, 2023.

¹⁵² Once a device passes a conformity assessment, demonstrating it is safe and performs as intended, the EMA grants manufacturers a Conformité Européenne mark. A Conformité Européenne mark allows commercialization of the device throughout the EU. Industry representative, email message to USITC staff, May 23, 2023, 2; EMA, "Medical Devices," accessed May 26, 2023; Emergo, "European CE Marking Strategy for Medical Devices," accessed May 26, 2023.

¹⁵³ The EU Medical Device Regulation is a set of regulations that governs the manufacturing and distribution of medical devices in the European market. European Union, "Regulation (EU) 2017/745 of the European Parliament," accessed May 11, 2023; Shah and Yvras, "The Medical Device Regulation ("MDR")," June 20, 2022.

¹⁵⁴ Other regulatory bodies, including the WHO, Brazil's Agência Nacional de Vigilância Sanitária Anvisa, and the UK's Medicines and Healthcare products Regulatory Agency (MHRA), have emergency use measures in place.

regulatory authorities are some of the most stringent, all countries either have their own national regulatory authorities or are part of regional regulatory bodies, albeit at various levels of maturity.¹⁵⁵ Indeed, of the 194 WHO member countries, only 30 percent have what are considered “mature” regulatory systems as defined by the WHO regulatory systems strengthening database. The remaining 70 percent are considered to have suboptimal regulatory systems, of which about half are at the lowest level of maturity.¹⁵⁶

Box 2.4 Stringent Regulatory Authorities and WHO-Listed Authority

All therapeutics and diagnostics must be approved for domestic use by a given country’s national regulatory agency. However, as noted above, not all regulatory authorities have the same maturity and stringency. On the most mature end of the regulatory spectrum are Stringent Regulatory Authorities (SRA). The SRA classification is based on whether an agency is affiliated with the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). According to the WHO, SRAs are regulatory authorities that have the expertise and resources to adequately evaluate both finished pharmaceutical products and active pharmaceutical ingredients (APIs).^a Specifically, this includes the ability to adequately assess a therapeutic’s quality, safety, and efficacy, as well as conduct regulatory inspections of both clinical trial and manufacturing sites.^b Procurement agencies, such as the Global Fund, rely on the stringent assessments conducted by the WHO Prequalification of Medicines Programme (PQP) and/or by an SRA for core medicines.^c Additionally, country health departments may also defer to market approvals by certain SRAs and/or WHO prequalification when rapidly qualifying products for domestic approval.^d

Authorities classified as SRAs include members of the ICH, ICH observers, and regulatory authorities associated with an ICH member through a legally binding mutual recognition agreement.^e Some of the countries and areas whose regulatory authorities have SRA classification include Australia, Canada, the EU, Iceland, Japan, Liechtenstein, Norway, Switzerland, and the United States.

However, the SRA designation, as tied to the ICH, is currently being replaced by the concept of WHO Listed Authority (WLA). The WLA initiative employs the WHO Global Benchmarking Tool, benchmarking national regulatory systems according to maturity level, as well as the WLA performance evaluation framework for evaluation along an extended set of measurements.^f Regulatory authorities that are evaluated (a country must request evaluation) will be classified in one of four maturity levels: at maturity level 1, only some elements of the regulatory system exist; at level 2, an evolving regulatory system partially performs essential regulatory functions; level 3 represents the minimum target, that is, a stable, well-functioning, and integrated regulatory system; and level 4 represents a regulatory system operating at an advanced level of performance and undergoing continuous improvement.^g A regulatory system at level 4 is considered a WLA.^h

^a WHO, “Regulatory Agencies,” accessed June 27, 2023. APIs are any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body. 21 C.F.R. § 270.2.

^b Macé, Rágo, and Ravinetto, “How the Concept of WHO-Listed Authorities Will Change International Procurement Policies for Medicines,” February 10, 2022, 1–4.

^c Global Fund, “Global Fund Quality Assurance Policy,” December 14, 2010.

¹⁵⁵ For more information on regulatory barriers due to sub-optimal regulatory authorities, see chapter 6.

¹⁵⁶ Multilateral organization representative, interview by USITC staff, Switzerland, June 5, 2023; Broojerdi et al., “The World Health Organization Global Benchmarking Tool: An Instrument to Strengthen Medical Products Regulation and Promote Universal Health Coverage,” August 2020, 1–7.

^d Government representative, interview by USITC staff, Zambia, June 21, 2023; government representative, interview by USITC staff, Bangladesh, July 17, 2023; government representative, interview by USITC staff, Malaysia, July 25, 2023; USITC, hearing transcript, March 30, 2023, 158–9 (testimony of Sanya Reid Smith, Social Watch).

^e WHO, “WHO Expert Committee on Specifications for Pharmaceutical Preparations,” 2017.

^f WHO, “WHO-Listed Authority (WLA),” accessed May 11, 2023.

^g Broojerdi et al., “The World Health Organization Global Benchmarking Tool: An Instrument to Strengthen Medical Products Regulation and Promote Universal Health Coverage,” August 2020, 1–7; Macé, Rågo, and Ravinetto, “How the Concept of WHO-Listed Authorities Will Change International Procurement Policies for Medicines,” February 10, 2022, 1–4.

^h WHO, “WHO-Listed Authority (WLA),” accessed May 11, 2023; Macé, Rågo, and Ravinetto, “How the Concept of WHO-Listed Authorities Will Change International Procurement Policies for Medicines,” February 10, 2022, 1–4.

World Health Organization

In addition to national regulatory authorities, the WHO plays a crucial role in ensuring access to COVID-19 diagnostics and medicines in LICs and LMICs. Its primary goal is to promote health, prevent diseases, and address global health challenges. For COVID-19, the WHO focuses on various areas to facilitate equitable distribution and availability of essential diagnostic and therapeutic products, including quality assurance and partnerships with procurement agencies to facilitate distribution. Specifically, it establishes guidelines and standards for good manufacturing practices, quality control, and regulation of products. Through its PQP and Emergency Use Listings (EULs) procedures, detailed below, the WHO assesses and approves medicines, vaccines, and diagnostics to be used in public health programs, particularly in resource-limited settings.

Therapeutics

The WHO PQP assesses the quality, safety, and efficacy of medicinal products purchased by international procurement agencies for distribution in LICs and LMICs.¹⁵⁷ According to the Global Fund, recipient countries are not authorized to procure medicines using grant funds unless those medicines appear in the current national, institutional, and/or WHO Standard Treatment Guidelines and/or Essential Medicines Lists.¹⁵⁸ In addition to national approval requirements, all antiretrovirals procured using Global Fund grants must be prequalified under the WHO PQP or authorized for use by an SRA.¹⁵⁹ Moreover, many LICs and LMICs now rely on WHO prequalification to facilitate rapid local registration, especially in those countries without a robust national regulatory authority.¹⁶⁰

The prequalification process begins when either the PQP, the Joint United Nations Program on HIV/AIDS (UNAIDS), the United Nations Children’s Fund (UNICEF), or Unitaid issue an invitation to a manufacturer to submit an expression of interest for product evaluation.¹⁶¹ Next, the manufacturer must provide data on the quality, safety, and efficacy of the product being evaluated. The data are then assessed by evaluators from the WHO and national regulatory authority experts. Afterwards, manufacturing sites for

¹⁵⁷ WHO, “Prequalification of Medicines by WHO,” January 31, 2013.

¹⁵⁸ The Global Fund, “Interim Quality Assurance Requirements,” June 25, 2021.

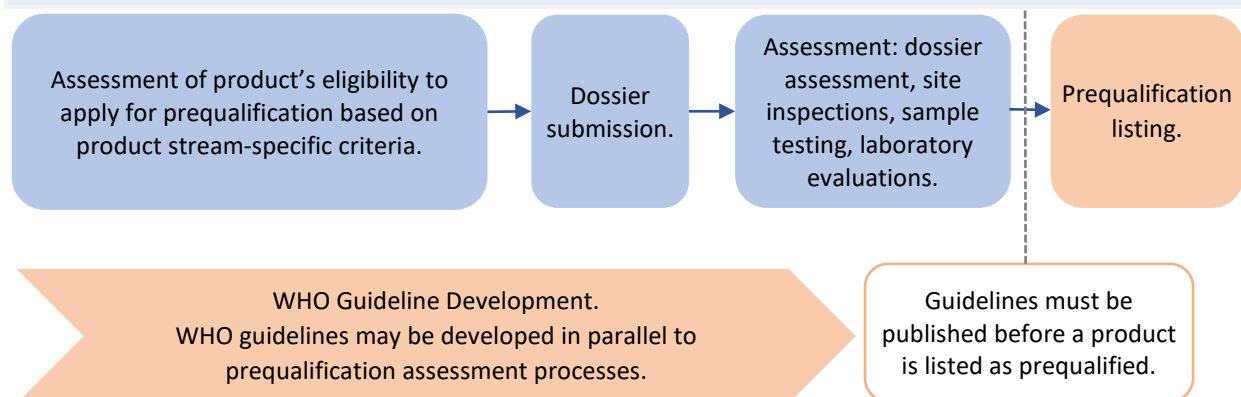
¹⁵⁹ Approval by an SRA appears to mean market (full) approval, not authorization for use under an EUA.

¹⁶⁰ Blaschke, Lumpkin, and Hartman, “The World Health Organization Prequalification Program,” January 2020, 68–71.

¹⁶¹ Manufacturers can submit their products for prequalification under four categories: innovator products, generic products with bioequivalence data, innovator biotherapeutics, and biosimilar products. Because the PQP is open only to companies invited by the WHO, there is no possibility for manufacturers to independently pursue access for their products. EFPIA, written submission to the USITC, May 4, 2023, 3.

the finished product and its API(s) are inspected for compliance with WHO good manufacturing practice. Lastly, a decision is made as to whether the product will be added to the WHO list of prequalified medicinal products (figure 2.1).¹⁶² The standard timeline for the prequalification process is 270 days, which does not include the time it takes for manufacturers to respond to evaluators' questions.¹⁶³ Additionally, there are fees for a full prequalification assessment of finished pharmaceutical products: a USD\$25,000 application fee and an additional annual fee of USD\$20,000.¹⁶⁴

Figure 2.1 WHO prequalification process



Source: Adapted by the USITC from Hodges, et al., *Navigating Complexity to Improve Global Access*, August 20, 2022, 1–39.

To date, five COVID-19 therapeutics from 10 companies have received WHO prequalification: tocilizumab, dexamethasone, molnupiravir, remdesivir, and nirmatrelvir (+ ritonavir) (table 2.1). Currently, there are 12 finished product applications under assessment for WHO prequalification, including 7 for molnupiravir and 5 for nirmatrelvir (+ ritonavir).¹⁶⁵ Information is not available on the generic manufacturers currently under assessment, including country of production.¹⁶⁶ It is also worth noting that the WHO puts out a number of training modules, which include recommended or endorsed drugs that may not be prequalified. Examples of therapeutics discussed in a WHO training module include, but are not limited to, corticosteroids, antivirals, interleukin inhibitors, and monoclonal antibodies.¹⁶⁷

¹⁶² Hodges, et al., *Navigating Complexity to Improve Global Access*, August 20, 2022, 1–39.

¹⁶³ Multilateral organization representative, interview by USITC staff, Switzerland, June 5, 2023. Product assessment can be accelerated, however, if prequalification coordinates with certain stringent regulatory authorities, such as the FDA, to conduct joint dossier reviews. The average time from application submission to prequalification for products undergoing an accelerated assessment was 6 months, compared to 17 months for a full assessment. Hodges, et al., *Navigating Complexity to Improve Global Access*, August 20, 2022, 1–39.

¹⁶⁴ WHO, “Prequalification Procedures and Fees,” September 12, 2016.

¹⁶⁵ A finished product application is an application for WHO prequalification for finished pharmaceutical products, as opposed to applications for active pharmaceutical ingredients. The WHO prequalifies the medicinal products submitted by applicants (manufacturers) and thus may receive multiple applications for the same therapeutic.

¹⁶⁶ WHO, “FPFs Under Assessment,” accessed June 29, 2023.

¹⁶⁷ See, e.g., Diaz, Relan, and Checkett, “Clinical Management of COVID-19: Introduction to Therapeutics and COVID-19,” WHO Learning Module, Health Emergencies Programme, November 15, 2021, 2, 15, 16.

Table 2.1 Applicants that have received WHO prequalification for therapeutics

Therapeutic	Applicant	Date of prequalification
Tocilizumab (3)	Roche, Germany	February 10, 2022
Dexamethasone	Farmak, Ukraine	November 5, 2020
Dexamethasone	Noridem Enterprises Ltd., Cyprus	December 17, 2021
Dexamethasone	Demo S.A., Greece	September 29, 2021
Nirmatrelvir (+ ritonavir)	Pfizer Limited, United Kingdom (UK)	April 22, 2022
Molnupiravir	Hetero Labs Ltd., India	September 21, 2022
Molnupiravir	Dr Reddy's Laboratories Limited, India	April 17, 2023
Molnupiravir	Emcure Pharmaceuticals Ltd., India	December 26, 2022
Remdesivir	Gilead Sciences, Ireland	April 25, 2022
Nirmatrelvir (+ ritonavir)	Hetero Labs Ltd., India	December 25, 2022

Source: WHO, "Status of COVID-19 Medicines and Active Pharmaceutical Ingredients," August 10, 2023; Lamontagne et al., "A Living WHO Guideline on Drugs," updated January 12, 2023.

Notes: Sotrovimab was prequalified on November 25, 2021, but has not been recommended by WHO for patients with non-severe COVID-19 since January 13, 2023, and it is not included in this table. There are three prequalifications for tocilizumab, each submitted by Roche, but for various dosage forms and strengths, so these entries were consolidated in the table.

Diagnostics

COVID-19 diagnostics can be approved for use under the WHO Emergency Use Listing (EUL). The EUL is a process by which the WHO assesses the quality, safety, and efficacy of unlicensed vaccines and in vitro diagnostics for use in a public health emergency.¹⁶⁸ Like WHO prequalification for medicines, the EUL process assists interested UN procurement agencies and recipient countries in determining the acceptability of using specific products.¹⁶⁹ However, the assessment process differs from prequalification, and because it is used only during public health emergencies, the assessment timeframe is shorter.¹⁷⁰ Each WHO member state has sole discretion to use the EUL as the basis to authorize an unlicensed vaccine or diagnostic for use. To qualify for an EUL, the product being evaluated must meet several criteria, including:

- The disease for which the product is intended is serious or immediately life threatening and has the potential of causing an outbreak, epidemic, or pandemic, and it is reasonable to consider the product for an EUL assessment;
- Existing products have not been successful in eradicating the disease or preventing outbreaks;
- The product is manufactured in compliance with current good manufacturing practice in the case of medicines and vaccines, and under a functional Quality Management System in the case of in vitro diagnostics; and
- The applicant undertakes to complete the development of the product (validation and verification of the product in the case of in vitro diagnostics) and apply for WHO prequalification

¹⁶⁸ Multilateral organization representative, interview by USITC staff, Switzerland, June 5, 2023; WHO, "Emergency Use Listing Procedure for In Vitro Diagnostics," accessed May 24, 2023. There are no EULs for therapeutics. With the end of the public health emergency, the WHO is transitioning to only prequalifications and will no longer use EULs for COVID-19 diagnostics. Multilateral organization representative, interview by USITC staff, Switzerland, June 6, 2023.

¹⁶⁹ WHO, "Diagnostics Laboratory Emergency Use Listing," accessed May 30, 2023.

¹⁷⁰ Multilateral organization representative, interview by USITC staff, Switzerland, June 5, 2023.

once the product is licensed.¹⁷¹ Currently, COVID-19 diagnostics are not eligible for WHO prequalification.¹⁷²

At this time, 37 in vitro diagnostic products have been granted EULs by the WHO.¹⁷³ Of these, 4 are rapid antigen self-tests, 12 are rapid antigen tests for professional use, and 21 are PCR tests.

Guidance (WHO Recommendation)

WHO guidance refers to recommendations or statements designed to inform decisions on whether and how to undertake public health measures, including the use of diagnostics and therapeutics.¹⁷⁴ Typically, for a product to receive prequalification, it must first be included in WHO guidelines.¹⁷⁵ During the public health emergency, the guidance process was parallel with prequalification or an EUL.¹⁷⁶ However, guidance can be issued after the product receives prequalification or an EUL, which can lead to delays in in-country distribution.¹⁷⁷ While all prequalified and EUL products receive WHO guidance documentation, not all products for which guidelines are generated are prequalified.¹⁷⁸

Status of U.S. COVID-19 Diagnostics and Therapeutic Approvals and EUAs

One antiviral therapeutic was under an EUA as of July 2023, but had not yet been approved by the FDA—molnupiravir (table 2.2). Four COVID-19 therapeutics were issued EUAs and have subsequently received full market approval. The therapeutic nirmatrelvir (+ ritonavir), after the EUA was issued, had the quickest approval (figure 2.2).¹⁷⁹

¹⁷¹ WHO, “Diagnostics Laboratory Emergency Use Listing,” accessed May 30, 2023.

¹⁷² Current diagnostics eligible for WHO prequalification include diagnostics for HIV/AIDS, malaria, cholera, HPV, and hepatitis. WHO, “In Vitro Diagnostics Eligible for WHO Prequalification,” January 28, 2020.

¹⁷³ WHO, *WHO Emergency Use Listing for In Vitro Diagnostics*, May 5, 2023.

¹⁷⁴ WHO, “WHO Guidelines,” accessed April 6, 2023.

¹⁷⁵ Hodges et al., *Navigating Complexity to Improve Global Access*, August 20, 2022.

¹⁷⁶ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

¹⁷⁷ For more information on delays related to guidance issuance and prequalification, see chapter 6.

¹⁷⁸ Prequalification is invitation only and aligns with the needs of procurement agencies.

¹⁷⁹ Several monoclonal antibodies (mAbs) were given EUAs, including REGEN-COV (casirivimab and imdevimab), sotrovimab, bamlanivimab, bamlanivimab and etesevimab, bebtelovimab, and Evusheld (tixagevimab and cilgavimab). Because of the high frequency of COVID-19 variants circulating within the United States that are not susceptible to these mAbs, these therapeutics are no longer authorized by the FDA and are not currently prescribed for the treatment of COVID-19. FDA, “Coronavirus (COVID-19): Drugs,” March 10, 2023.

Table 2.2 FDA EUA and full approval dates for authorized COVID-19 therapeutics

— = not applicable

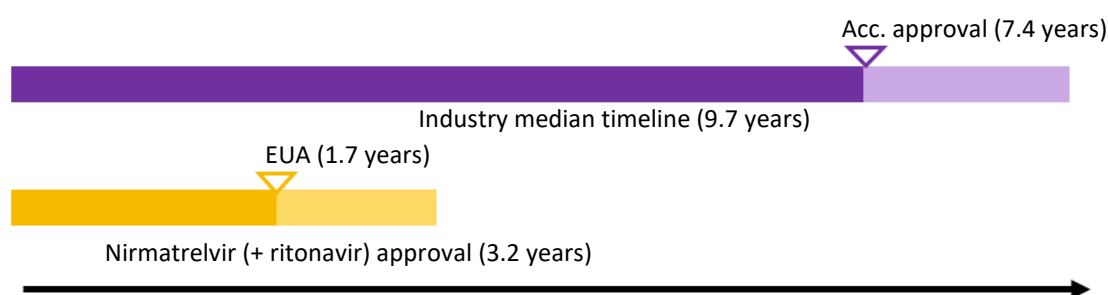
Therapeutic	Date EUA issued	Date of full approval	Time between EUA and full approval (days)
Molnupiravir	February 4, 2022	—	—
Nirmatrelvir (+ ritonavir)	February 4, 2022	May 25, 2023	475
Tocilizumab	August 5, 2021	December 21, 2022	503
Baricitinib	February 19, 2021	May 10, 2022	445
Remdesivir	May 1, 2020	October 22, 2020	174

Source: Airfinity, “COVID-19,” Therapeutics, Approvals, by Country, accessed July 14, 2023.

Note: Baricitinib and tocilizumab are host-directed therapeutics, prescribed for the clinical management of COVID-19.

Figure 2.2 Average timelines for drug approvals, normal and pandemic, United States

Acc. = accelerated approval; EUA = Emergency Use Authorization.



Source: Adapted by the USITC based on Allais et al., “Development of the Commercial Manufacturing Process for Nirmatrelvir,” March 29, 2023, 849–857; Brown et al., “Clinical Development Times for Innovative Drugs,” November 2022, 793–94.

Notes: The industry timeline begins with the submission of investigational new drug application and follows it to approval. A clinical trial can begin 30 days after submission of the application to the FDA. The timeline for nirmatrelvir begins from the first synthesis of the compound. This compressed development and commercialization of drugs is being called “lightspeed” development in the literature.

For diagnostics, the FDA had authorized 278 molecular diagnostic tests and 64 antigen tests under EUAs as of July 2023.¹⁸⁰ The EUA for the Centers for Disease Control and Prevention’s (CDC’s) COVID-19 test was issued on February 4, 2020, while the first EUA for a rapid antigen self-test was issued December 15, 2020 (figure 2.3). To assist the review process, the FDA provides a series of templates containing validation recommendations and suggestions on the types of data and information to include in a COVID-19 diagnostics EUA submission.¹⁸¹ Additional guidance and recommendations to accelerate test development and deployment for diagnostics manufacturers are contained in the FDA’s *Policy for Diagnostic Tests for Coronavirus Disease* (Revised), issued in January 2023.¹⁸²

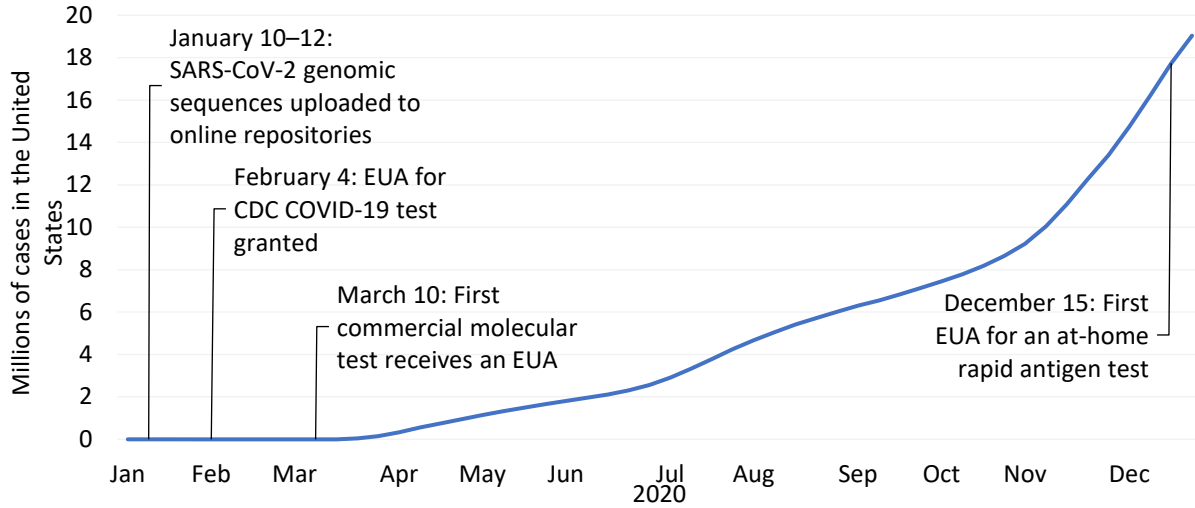
¹⁸⁰ FDA, “In Vitro Diagnostics EUAs - Molecular Diagnostic Tests for SARS-CoV-2,” July 21, 2023.

¹⁸¹ Validation recommendations include metrics on sensitivity and specificity using measures of positive and negative percent agreement. Sensitivity describes how often a positive case is correctly identified, while specificity describes how often a negative case is correctly identified. Positive agreement is the percentage of positive results the new test and the CDC reference test agree on, while negative agreement is the percentage of negative results the new test and CDC reference test agree on. FDA, *Policy for Coronavirus Disease-2019 Tests (Revised)*, January 12, 2023, 14–15; FDA, “Statistical Guidance on Reporting Results,” March 13, 2007, 21–25; USITC, *COVID-19 Related Goods*, December 2020, 148.

¹⁸² Industry representative, email message to USITC staff, May 23, 2023; FDA, *Policy for Coronavirus Disease-2019 Tests (Revised)*, January 12, 2023, 1–15. South Korea instituted a similar EUA program in 2016 after its experience with the MERS outbreak. It designed its program using the U.S. system as a model. Shuren and Stenzel, “South Korea’s Implementation of A COVID-19 National Testing Strategy,” May 25, 2021.

Figure 2.3 Number of reported cases of COVID-19 in 2020, with key dates in the United States for development and approval of COVID-19 diagnostic tests, by month

Millions of COVID-19 cases, U.S. cumulative. Underlying data for this figure can be found in appendix J, [table J.7](#).



Source: WHO, “WHO Coronavirus (COVID-19) Dashboard,” accessed May 13, 2023; CDC, “CDC Museum COVID-19 Timeline,” accessed April 7, 2023.

Note: WHO listed the first quality-assured SARS-CoV-2 self-test for emergency use 19 months after the EUA by FDA.

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COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

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Chapter 3

Definitions and the Universe of COVID-19 Diagnostics and Therapeutics

Introduction

This chapter addresses the elements of the U.S. Trade Representative’s (Trade Representative’s) request letter related to identifying and defining COVID-19 diagnostics and therapeutics. In particular, this chapter (1) identifies the range of definitions for diagnostics and therapeutics in the medical field; (2) identifies and defines the universe of existing COVID-19 diagnostics and therapeutics covered by patents, as well as diagnostics and therapeutics in development; and (3) provides a broad overview of relevant COVID-19 diagnostics and therapeutics.¹⁸³ Unlike COVID-19 vaccines, which are comparatively easy to identify (i.e., a COVID-19 vaccine is one administered to prevent an infection of COVID-19), defining the universe of COVID-19 diagnostics and therapeutics is more complicated, and what may or may not be encompassed by the terms can be subject to interpretation. Therefore, the information provided highlights various considerations and possible approaches that can be followed when attempting to define and identify the universe of COVID-19 diagnostics and therapeutics. Similarly, identifying “relevant” COVID-19 diagnostics and therapeutics among the universe of COVID-19 diagnostics and therapeutics can also be subjective, and depends on a number of factors.

In providing a broad overview of relevant COVID-19 diagnostics and therapeutics, this chapter identifies parameters that can be employed to identify relevant diagnostics and therapeutics among the broader universe of those products. In the chapters that follow, these parameters are applied to identify relevant COVID-19 diagnostics and therapeutics for purposes of reporting on the information, data, and views requested in the Trade Representative’s letter. The parameters applied to identify relevant COVID-19 products differ somewhat among chapters or within chapters, due to data availability issues and to focus the discussion, but also because in some instances, application of a particular parameter would exclude important COVID-19 diagnostics and therapeutics products from the information provided in this report. For example, because the foundational technologies for polymerase chain reaction (PCR) and antigen tests are generally no longer subject to patents, applying a parameter that the product must be covered by patents would largely exclude PCR and antigen tests from the report’s discussion of relevant COVID-19 diagnostics and therapeutics.

¹⁸³ The request letter does not ask USITC to explicitly define relevant COVID-19 diagnostics and therapeutics, but rather asks for a broad overview and description of relevant COVID-19 diagnostics and therapeutics.

Identifying the Range of Definitions for Diagnostics and Therapeutics

Broadly, pharmaceuticals can be placed into three different categories: prophylactic (prevention), diagnostic (identification), and therapeutic (treatment).¹⁸⁴ While all three categories are recognized as being key to the pharmacological needs associated with a disease, the Trade Representative's request focused on defining and identifying diagnostics and therapeutics, not prophylactics (which include vaccines). In general, the definitions of these terms, and the types of goods covered by such definitions, vary slightly by source. Nonetheless, among the multitude of sources consulted, the range of definitions for diagnostics and therapeutics were largely synonymous, and generally coalesce around diagnostics as a tool or means to diagnose or identify an illness or disease or evaluate the body's response to treatment and therapeutics as a treatment for an illness or disease. Identifying the specific goods that qualify under each definition, however, is more challenging.

Diagnostics

To identify the range of definitions for the term "diagnostics" a variety of sources were consulted, including medical dictionaries, international health organizations, and regulatory agencies.¹⁸⁵ Key sources include *Taber's Cyclopedic Medical Dictionary*, which defines "diagnostics" as the science, art, or practice of diagnosis of a disease. It is the use of scientific or medical technologies to identify the cause, nature, and severity of a patient's illness. It defines the term "diagnostic" as an instrument, tool, or method in identifying a diagnosis, to determine the nature of a specific disease, and to distinguish one disease from another.¹⁸⁶ Similarly, *Dorland's Illustrated Medical Dictionary* defines "diagnostics" as a good that pertains to or subserves diagnosis and "diagnosis" as the determination of the nature of a disease or the art of distinguishing one disease from another.¹⁸⁷

Entities such as the U.S. Food and Drug Administration (FDA) and the World Health Organization (WHO) have preferred definitions, some specific to in vitro or in vivo diagnostics.¹⁸⁸ According to the WHO, in

¹⁸⁴ Fed. Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(g)(1); Abraha et al., "Diagnostic, Preventive and Therapeutic Evidence," October 2018, 1.

¹⁸⁵ Aside from the references mentioned in this paragraph, the USITC consulted myriad sources in the medical field with respect to the definition of diagnostics. Most reported similar information.

¹⁸⁶ *Taber's Cyclopedic Medical Dictionary*, 22nd ed. (2013).

¹⁸⁷ *Dorland's Illustrated Medical Dictionary*, 33rd ed. (2020); Roche, "What Are Diagnostic Tests?," October 3, 2022. The *Oxford English Dictionary*, a source outside the medical field, defines diagnostics simply as "[o]f or pertaining to diagnosis." Brown, "Diagnostic," *Shorter Oxf. Engl. Dict. Hist. Princ.*, 1993, 660. Additionally, *Law Insider*, a legal subscription service outside the medical field, defines diagnostic to also include any biological molecule or diagnostic test that may be used to see how the body responds to a treatment for a disease or condition. *Law Insider*, "Diagnostic Product Definition," accessed July 20, 2023.

¹⁸⁸ WHO, "In Vitro Diagnostics – Global," accessed July 20, 2023; FDA, "In Vitro Diagnostics EUAs," January 12, 2023. Diagnostic tests may be in vitro or in vivo. In vitro diagnostics are tests conducted within test tubes and similar equipment in laboratories, healthcare facilities, or even in the home, while in vivo tests are conducted in the body itself. Zhou et al., "Gold Nanoparticles for In Vitro Diagnostics," October 14, 2015, 10575–10636.

vitro diagnostics are tests that can detect disease, conditions, and infections.¹⁸⁹ The WHO provides a long list of prequalified in vitro diagnostics and optical tools for in vivo diagnostics.¹⁹⁰ The FDA defines in vitro diagnostic devices as tests performed on samples taken from the human body. In addition to detecting diseases and other conditions, the FDA states in vitro diagnostics can be used to monitor a person's overall health to help cure, treat, or prevent diseases.¹⁹¹ The Medical Subject Heading "Ontology" from the U.S. National Library of Medicine, a component of the National Institutes of Health, states that diagnosis is "the determination of the nature of a disease or condition, or the distinguishing of one disease or condition from another."¹⁹²

Thus, while there is some slight variation, combining the range of definitions of "diagnostics" discussed above in aggregate, the term "diagnostics" could refer to any means or tool used to identify or diagnose a disease or health condition, including how the body is responding to treatment.¹⁹³

Therapeutics

Similar to diagnostics, there are varying but largely compatible definitions for the term "therapeutics."¹⁹⁴ *Taber's Cyclopedic Medical Dictionary* and *Dorland's Illustrated Medical Dictionary*, two of the medical dictionaries commonly used by healthcare professionals, define therapeutics as an agent "having medicinal or healing properties...[a] healing agent" and the "branch of medicine concerned with the application of remedies and the treatment of disease" (*Taber's*) and "1. The branch of medical science concerned with the treatment of disease. 2. Therapy" (*Dorland's*).¹⁹⁵ Echoing these definitions, one infectious disease expert defined a therapeutic as "something that you administer as a treatment."¹⁹⁶

The U.S. Federal Food, Drug, and Cosmetic Act (FDCA),¹⁹⁷ which establishes the legal framework for the FDA, does not define therapeutics,¹⁹⁸ nor is the term defined in the relevant sections of the U.S. Code of

¹⁸⁹ Many health organizations, such as the WHO, as well as regulators have dedicated definitions specifically for in vitro diagnostics, but have limited information on "diagnostics" more broadly. WHO, "In Vitro Diagnostics – Global," accessed July 20, 2023.

¹⁹⁰ WHO, "Prequalified In Vitro Diagnostics," January 27, 2020; WHO, "COVID-19 Case Management Capacities: Diagnostics, Therapeutics, Vaccine Readiness," July 7, 2021.

¹⁹¹ FDA, "In Vitro Diagnostics EUAs," January 12, 2023.

¹⁹² Toole et al., "Diagnosing COVID-19," October 2023, 4.

¹⁹³ A previously issued report by the USITC indicated that "diagnostic product" can refer to the assemblage of reagents, including but not limited to reagents packaged in the form of laboratory test kits (test kits). USITC, *COVID-19 Related Goods*, December 2020, 354.

¹⁹⁴ Aside from the references mentioned in this paragraph, the USITC consulted a myriad sources in the medical field with respect to the definition of therapeutics. Most reported similar definitions, but information varied with respect to the products falling under the scope of the term therapeutics.

¹⁹⁵ See Venes, "Therapeutics," *Taber's Cyclopedic Med. Dict.*, 2013, 2305–06, and Newman, "Therapeutics," *Dorland's Illus. Med. Dict.*, 2020, 1882.

¹⁹⁶ Government representative, interview by USITC staff, April 24, 2023. See also FDA, "Drugs@FDA Glossary of Terms," accessed September 4, 2023. The scope of the term "therapeutics" is also defined by sources outside of the medical profession; for example, the *Oxford English Dictionary* defines therapeutics as "curative agent[s]" within "[t]he branch of medicine that deals with the treatment and cure of disease and ill health; the art of healing." Brown, "Therapeutics," *Shorter Oxf. Engl. Dict. Hist. Princ.*, 1993, 3274.

¹⁹⁷ 21 U.S.C. §§ 301–99i.

¹⁹⁸ See, e.g., 21 U.S.C. § 321.

Federal Regulations that pertain to the FDCA.¹⁹⁹ However, the FDCA and the pertinent portions of the U.S. Code of Federal Regulations do define “drugs” as “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals”²⁰⁰ and “therapeutic action or effect” as an “action or effect [that] includes any effect or action of the combination product intended to diagnose, cure, mitigate, treat, or prevent disease, or affect the structure or any function of the body,”²⁰¹ respectively. The term “therapeutics” is not explicitly defined in the founding directives and regulations of the European Union’s European Medicines Agency (EMA);²⁰² however, the EMA categorizes medicines, human medicines, and medicinal products as therapeutics.²⁰³ Combining the range of definitions and uses of the term discussed above in aggregate, the term “therapeutics” could refer to any product or remedy used or applied to treat or cure a disease.

Identifying the Universe of COVID-19 Diagnostics and Therapeutics

As discussed above, the definitions of diagnostics and therapeutics generally coalesce around the explanation that diagnostics are tools used to identify or diagnose a disease or health condition, including how the body is responding to a treatment, and therapeutics are products or remedies used to treat or cure a disease. By that rationale, a COVID-19 diagnostic is a good used to diagnose COVID-19 or identify how patients respond to a treatment for COVID-19, and a COVID-19 therapeutic is a good used to treat COVID-19.²⁰⁴ The Trade Representative’s request letter specifically requested that the Commission identify the universe of COVID-19 diagnostics and therapeutics covered by patents as well

¹⁹⁹ See, e.g., FDA, Product Jurisdiction, 21 C.F.R. § 3.2.

²⁰⁰ 21 U.S.C. § 321(g)(1). See also FDA, Product Jurisdiction, 21 C.F.R. § 3.2(g).

²⁰¹ FDA, Product Jurisdiction, 21 C.F.R., § 3.2(k). Section 3.2(k) also defines the more general term “mode of action,” which is defined as “the means by which a product achieves an intended therapeutic effect or action.” *Id.* The definition of therapeutic mode of action refers to a “combination product,” which is generally defined as “[t]wo or more . . . products” that are combined or mixed or packaged as a unit. FDA, Product Jurisdiction, 21 C.F.R., § 3.2(e)(1), (2). Combination products may be composed of drugs, devices, or biological products. FDA, Product Jurisdiction, 21 C.F.R., § 3.2(e)(3). The definitions of “mode of action” and “therapeutic action or effect” appear in a part of the Code of Federal Regulations; its purpose, among others, is to specify how FDA will determine which of its organizational components is designated to have primary jurisdiction for premarket review and regulation of combination products. FDA, Product Jurisdiction, 21 C.F.R., §§ 3.1–3.5.

²⁰² See generally European Parliament and the Council of the European Union, Directive 2001/83/EC, “Relating to Medicinal Products for Human Use,” November 6, 2001. See also European Parliament and the Council of the European Union, Regulation (EC) No. 726/2004, March 31, 2004.

²⁰³ “Medicinal products” are defined as “[a]ny substance or combination of substances presented for treating or preventing disease in human beings”; additionally, “[a]ny substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting, or modifying physiological functions in human beings is likewise considered a medicinal product.” European Parliament and the Council of the European Union, Directive 2001/83/EC, Title I, Art. 1, par. 2.

²⁰⁴ Diagnostic products are also included in the WTO’s scope of pharmaceutical products. The 1994 Agreement on Trade in Pharmaceutical Products includes products classified in HS chapter 30, which contains many diagnostic products. Under advisement from the WTO, Malaysia included test kits in their legal code’s definition of pharmaceutical product to better align with the TRIPS agreement. See the diagnostics trade section of this chapter for more information on diagnostics HS codes. General Agreement on Tariffs and Trade: Trade in Pharmaceutical Products, L/7430, March 25, 1994; Foreign government official, interview by USITC staff, Malaysia, July 21, 2023.

as those in development. The universe of products that fall within these expansive definitions is broad and varied.²⁰⁵

It is difficult to catalogue in its entirety the full scope of products that fall within the vast universe of COVID-19 diagnostics and therapeutics, both for existing products under patent and those in development. Public awareness of the SARS-CoV-2 virus has only existed for a short time, and the virus regularly mutates to a new variant. Therefore, the full epidemiology of COVID-19 in humans is still being discovered and understood, as are the means that can be used to treat it. Further, as the virus mutates, the efficacy of a given diagnostic or therapeutic for COVID-19 can also change. However, there are available data and information sources to aid in understanding the universe of products covered by patents or in development, as described below.

Box 3.1 Scope of Diagnostics and Therapeutics in World Trade Organization Members’ Proposals

The World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) does not define diagnostics or therapeutics.^a In communications suggesting the possible modification of TRIPS Agreement obligations in the context of COVID-19, WTO members proposed different scopes of product coverage. The October 2020 proposal to the TRIPS Council from India and South Africa sought a waiver of TRIPS Agreement obligations in relation to the “prevention, containment, or treatment of COVID-19”^b and indicated that an effective response to the COVID-19 pandemic required access to affordable “medical products,” including “diagnostic kits, medical masks, other personal protective equipment and ventilators, as well as vaccines and medicines for the prevention and treatment of patients in dire need.”^c

In May 2021, proponents of India and South Africa’s original proposal submitted to the TRIPS Council a revision intended to add more specificity to the product coverage. The revised proposal stated that certain TRIPS Agreement obligations “shall be waived in relation to health products and technologies, including diagnostics, therapeutics, vaccines, medical devices, personal protective equipment, their

²⁰⁵ The vast majority of individuals interviewed by USITC staff did not provide a clear definition of the term “diagnostics” or “therapeutics” or “COVID-19 diagnostics and therapeutics,” and often individuals only addressed information that pertained to their sphere of expertise (e.g., law, trade, or manufacturing). Several associations and manufacturers highlighted what they thought should not be considered a COVID-19 diagnostic (e.g., X-ray or computed tomography scans) or a COVID-19 therapeutic (e.g., ventilators). Disparate organizations also gave overlapping examples of products that are used as COVID-19 therapeutics. For example, although Pfizer noted “the difficulty in defining ‘COVID-19 therapeutics’ as a distinct category of product,” the biopharmaceutical company also stated that there are several “medicines relevant to the treatment of COVID-19,” including “COVID-19 therapeutics like Paxlovid.” Médecins Sans Frontières also provided similar examples of products that are examples of therapeutics. For instance, it listed “antiviral . . . monoclonal antibodies such as casirivimab [and] imdevimab and sotrovimab” and “antivirals . . . (for example nirmatrelvir/ritonavir)” as “therapeutics for the treatment of COVID-19 and COVID-19 symptoms.” Much of the information provided by interested parties and persons interviewed by the Commission reflect opinions or point to the definitions provided by public health and regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and World Health Organization (WHO) or international organizations, such as the World Intellectual Property Organization (WIPO). AdvaMed, written submission to the USITC, March 17, 2023, 3. Industry representative, interview by USITC staff, July 11, 2023. Innovators Legal, written submission to the USITC, May 1, 2023, 1–2. Pfizer, written submission to the USITC, May 5, 2023, 13, 28. See also Merck & Co., Inc., written submission to the USITC, May 5, 2023, 15 (stating that “there is no agreed definition of what constitutes a ‘COVID-19 therapeutic’”). MSF, written submission to the USITC, May 17, 2023, 1–2. Nirmatrelvir (+ ritonavir) are the APIs of the brand name drug Paxlovid, which was developed by Pfizer. See, e.g., Pfizer, written submission to the USITC, May 5, 2023, 1, 13–15.

materials or components, and their methods and means of manufacture for the prevention, treatment, or containment of COVID-19.”^d In September 2021, these same proponents added information on their proposed scope of product coverage. They explained that the term “health products and technologies” refers to the whole range of products critical for the prevention, treatment, and containment of COVID-19, such as those listed in the World Health Organization’s list of priority medical devices for COVID-19.^e The discussion of “diagnostics” focused on diagnostic tests to support treatment and public health actions in low-income countries.^f For therapeutics, these proponents cited a rapidly evolving medical landscape, including antivirals, monoclonal antibodies, immunomodulators, and antithrombotic therapies.^g The proponents included other products, such as ventilators and oxygen delivery devices, in a separate category for “medical devices and personal protective equipment.”^h

Discussions related to these and other proposals in the TRIPS Council reached an impasse, and in December 2021, the European Union, India, South Africa, and the United States (the Quad), with the support of the WTO Secretariat, launched informal consultations on the various proposals. In May 2022, the WTO Director-General announced that an “outcome document” had emerged from the Quad that could be the basis for further discussions among WTO members.ⁱ Instead of broadly covering health products and technologies, the Quad document was limited to vaccines.^j

On June 12, 2022, at the 12th Ministerial Conference, WTO members adopted the Ministerial Decision on the TRIPS Agreement (the 2022 Ministerial Decision).^k Like the Quad document, the 2022 Ministerial Decision focuses on COVID-19 vaccines, including the ingredients and processes necessary for their manufacture.^l It does not extend to health products and technologies more broadly, contrary to the initial and revised proposals of the waiver proponents. WTO members continue to discuss whether to extend the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics.^m

^a TRIPS Agreement, Annex and Appendix, par. 1(a), as amended December 6, 2005, entered into force January 23, 2017.

^b WTO TRIPS Council, “Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19,” IP/C/W/669, October 2, 2020 (“original proposal”), annex, par. 1.

^c Original Proposal, October 2, 2020, recital par. 5.

^d WTO TRIPS Council, “Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19: Revised Decision Text,” IP/C/W/669/Rev.1, May 25, 2021 (revised proposal), annex, par. 1. This communication was from the African Group (African members (and Observers) of the WTO), Bolivia, Egypt, Eswatini, Fiji, India, Indonesia, Kenya, the least-developed countries (LDC) Group (LDCs are the world’s poorest countries per the UN), Maldives, Mozambique, Mongolia, Namibia, Pakistan, South Africa, Vanuatu, Venezuela, and Zimbabwe.

^e WTO TRIPS Council, “Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19,” IP/C/W/684, September 30, 2021 (September 2021 explanation), par. 11.

^f September 2021 explanation, par. 15.

^g September 2021 explanation, par. 17 (citing National Institutes of Health (NIH) and WHO sources).

^h September 2021 explanation, pars. 23–24.

ⁱ WTO TRIPS Council, “Communication from the Chairperson,” May 3, 2022, 1–4; WTO, “Quad’s Outcome Document,” May 3, 2022.

^j WTO TRIPS Council, “Communication from the Chairperson,” May 3, 2022, pars. 1 and 8.

^k WTO, “Ministerial Decision on the TRIPS Agreement,” WT/MIN(22)/30, June 22, 2022, 1–2.

^l WTO, “Ministerial Decision on the TRIPS Agreement,” WT/MIN(22)/30, June 22, 2022, 2.

^m WTO, “Members to Stretch Deadline on Extending TRIPS Decision,” December 16, 2022; WTO, “Members Continue Discussion on TRIPS Decision Extension,” March 17, 2023.

Existing COVID-19 Diagnostics

For COVID-19 diagnostics, the universe includes both in vitro diagnostics (e.g., rapid antigen tests) and in vivo diagnostics (e.g., MRIs).²⁰⁶ It includes those that are deployed to identify whether SARs-CoV-2 has

²⁰⁶ Arias-Londoño, Moure-Prado, and Godino-Llorente, “Automatic Identification of Lung Opacities,” April 10, 2023; FDA, “In Vitro Diagnostics EUAs,” January 12, 2023, 1–22.

infected the host as well as those used to diagnose symptoms prevalent to COVID-19 infections (e.g., decreased lung function). The universe of products can also include articles intended for use in performing the diagnostic test such as swabs, platforms (i.e., machines), and plastic consumables (e.g., cartridges).

Although it is difficult to definitively identify the full scope of existing products that fall within the universe of COVID-19 diagnostics, it is possible to outline the types of goods that currently exist within the universe. The range of COVID-19 diagnostics generally comprises three broad categories: (1) tests used to diagnose an active infection of the SARS-CoV-2 virus, (2) tests that measure an adaptive immune response to the virus, and (3) tests used in the management of patients with COVID-19.²⁰⁷ The most prominent COVID-19 tests used to diagnose an active SARS-CoV-2 infection are PCR tests²⁰⁸ and rapid antigen tests.²⁰⁹ Serology (blood) tests are used to detect antibodies or T cells to measure the immune response to the virus.²¹⁰ Management tests, such as those used to detect biomarkers related to inflammation, are used to inform decisions for the management of patients with COVID-19.²¹¹ All categories of COVID-19 diagnostic tests require a number of ancillary products depending on the requirements of a test's specific protocol, which can include analyzers, cartridges, swabs, and plastic consumables (such as those to hold specimens and/or reagents).

To identify the universe of COVID-19 diagnostics and therapeutics under patent, this report uses the patent landscape reports prepared by the U.S. Patent and Trademark Office (USPTO) for diagnostics and World Intellectual Property Organization (WIPO) for therapeutics (see chapter 2), which describe patent activity since the emergence of COVID-19.²¹² The USPTO patent landscape report identifies 824 COVID-19 diagnostic-specific published patent filings at the USPTO between December 2019 and the end of March 2023.²¹³ Published patent filings for COVID-19 diagnostics represented a small share of overall diagnostic patent filings during the same period—2.6 percent at its peak in the fourth quarter of

²⁰⁷ FDA, "In Vitro Diagnostics EUAs," January 12, 2023.

²⁰⁸ PCR is a standard laboratory technique used to amplify or copy small segments of genetic material. PCR tests are also referred to as "molecular" tests. National Human Genome Research Institute, "Understanding COVID-19 PCR Testing," accessed April 11, 2023. See chapter 4 of this report for a more detailed description of PCR testing.

²⁰⁹ Antigen tests are used to detect the presence of viral proteins in a patient's sample. See chapter 4 of this report for a more detailed description of rapid antigen testing. Other tests, such as those that analyze breath samples, have been developed for the detection of a COVID-19 infection, but they are not commonly used. FDA, "In Vitro Diagnostics EUAs," January 12, 2023; FDA, "In Vitro Diagnostics EUAs—Other Tests for SARS-CoV-2," February 16, 2023.

²¹⁰ FDA, "In Vitro Diagnostics EUAs," January 12, 2023.

²¹¹ FDA, "In Vitro Diagnostics EUAs," January 12, 2023.

²¹² Searches of patent databases for COVID-19-related patent filings return a significant number of results. See, e.g., Toole et al., "Diagnosing COVID-19," October 2023, 4-6 (a search for COVID-19-related filings returned over 18,000 results from across the globe). For purposes of this report, the Commission relies upon reports from USPTO and WIPO whose searches were targeted to patents for diagnostics and therapeutics used to diagnosis or treat COVID-19. WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 12 (covering the period from January 2020 through September 2022); Toole et al., "Diagnosing COVID-19," October 2023, 5, 9 (covering the period from December 2019 through March 2023).

²¹³ The USPTO's methodology for identifying COVID-19-related published applications and patents is described in detail in the appendix to its report. The filing data reported here are for "COVID-19 specific" rather than "COVID-19 related" patent filings because this search strategy yielded more precise results. Toole et al., "Diagnosing COVID-19," October 2023, 4-6.

2021 and tapering to 1.4 percent in the most recent data (2023 Q1).²¹⁴ While the patenting of new diagnostic innovations has occurred, these patents primarily serve to enhance or augment existing diagnostic technologies, rather than supplant them.²¹⁵ As discussed in chapter 2, the foundational patents for PCR and rapid antigen tests have expired.

Existing COVID-19 Therapeutics

The universe of COVID-19 therapeutics includes medical devices (e.g., ventilators) and medicines that treat COVID-19. It includes therapies prescribed to treat or manage symptoms of COVID-19 (e.g., ECMO and/or ventilation) or secondary infections or symptoms (e.g., baricitinib, tocilizumab, vilobelimab) that result from complications of a SARS-CoV-2 viral infection (e.g., inflammation, blood clots, poor pulse oxygen levels) as well as drugs that were either developed or redesigned from a drug used to treat another disease (i.e., repurposed) into a drug that can also treat COVID-19 (e.g., favipiravir).²¹⁶

In general, therapeutics to treat COVID-19 can be classified by molecule size (category), drug target (class), and/or mechanism of action (mode of action); these classifications are not necessarily mutually exclusive.²¹⁷ When defined by the size of the molecule, there are two predominant categories—small molecule drugs and biologics (biological molecules). Small molecule drugs are typically molecules that have a low molecular weight and are simpler to characterize than biological molecules. By contrast, biologics are typically large complex molecules, which makes them difficult to characterize or replicate. Both biologics and small molecules can also be further distinguished by source of derivation.²¹⁸ Small molecule drugs are usually described as organic molecules, which means that they are chemically synthesized or extracted from natural sources (e.g., willow bark). Biologics are isolated from a variety of natural sources (e.g., human, animal, or microorganism), and can be produced by biotechnology methods or other related technologies.²¹⁹

Broadly speaking, COVID-19 therapeutics are largely small molecule drugs or biologics that can be broken down into three classes—virus-directed therapies, host-directed therapies, and adjunctive therapies (table 3.1).²²⁰ Virus-directed therapeutics target the SARS-CoV-2 virus itself and include virus-directed antivirals, which target virus sites and inhibit viral replication (e.g., remdesivir). Host-directed therapeutics, by comparison, either target components of the host cell to hinder virus replication or aim

²¹⁴ Toole et al., “Diagnosing COVID-19,” October 2023, 7.

²¹⁵ See chapter 2 for more information on the patented technologies included in the USPTO report.

²¹⁶ NIH, “Clinical Spectrum of SARS-CoV-2 Infection,” March 6, 2023. Drug repurposing is generally used to describe the identification of potential novel uses of existing drugs. Several existing pharmaceuticals have been “repurposed” for use in treating COVID-19 infections. FDA, “Capturing Clinician’s Experiences Repurposing Drugs,” June 9, 2020; FDA, “Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products,” September 19, 2023.

²¹⁷ For example, an anti-inflammatory can be a small molecule or large molecule, while monoclonal antibodies can be virus-directed or host-directed. Antivirals could be small molecule drugs or biologics.

²¹⁸ NIH, “Clinical Spectrum of SARS-CoV-2 Infection,” March 6, 2023.

²¹⁹ FDA, “What are ‘Biologics,’” February 6, 2018.

²²⁰ Ho et al., “Perspective Adjunctive Therapies for COVID-19,” 2021, 314–24; Singh and de Wit, “Antiviral Agents for the Treatment of COVID-19,” February 11, 2022, 1–5.

to reduce the inflammatory response to infection (e.g., baricitinib).²²¹ Adjunctive therapies are therapeutics given in addition to a primary treatment (virus-directed or host-directed) to maximize the effectiveness of the primary treatment.²²²

Table 3.1 Examples of COVID-19 therapeutics, category, class, and mode of action

mAb = monoclonal antibody; IL-6 = Interleukin-6; JAK = Janus kinase

Therapeutic	Category	Therapeutic class	Mode of action
Molnupiravir	Small molecule	Virus-directed antiviral	Nucleoside analogue
Remdesivir	Small molecule	Virus-directed antiviral	Nucleotide analogue
Ensitrelvir	Small molecule	Virus-directed antiviral	Protease inhibitor
Casirivimab and imdevimab	Biologic	Virus-directed antiviral	Neutralizing mAbs
Sotrovimab	Biologic	Virus-directed antiviral	Neutralizing mAb
Bamlanivimab and etesevimab	Biologic	Virus-directed antiviral	Neutralizing mAbs
Dexamethasone	Small molecule	Host-directed therapy	Immune suppression (corticosteroids)
Baricitinib	Small molecule	Host-directed therapy	JAK inhibitor
Tocilizumab	Biologic	Host-directed therapy	IL-6 inhibitor mAb
Nirmatrelvir (+ ritonavir)	Small molecule	Virus-directed antiviral	Protease inhibitor
Vitamin C	Small molecule	Adjunctive therapy	Secondary (immunomodulatory)
Heparin	Small molecule	Adjunctive therapy	Secondary (anticoagulant)
Acetaminophen	Small molecule	Host-directed or adjunctive therapy	Secondary (analgesic and antipyretic)

Source: Adapted by the USITC from Ho et al., “Perspective Adjunctive Therapies for COVID-19,” 2021, 314–24; Singh and de Wit, “Antiviral Agents for the Treatment of COVID-19,” February 11, 2022, 1–5; Kushner et al., “The Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs),” September 21, 2022, 1–10.

Notes: Adjunctive therapies are given in addition to the primary or initial therapy to maximize its effectiveness but are not solely prescribed for the treatment of COVID-19. For the purposes of our analysis, the mode of action for these types are denoted as secondary, even though they all have different modes of action, which are denoted in the parentheses as they are prescribed in addition to virus-directed and host-directed therapies. Trade names and respective international nonproprietary names are as follows: Paxlovid (nirmatrelvir (+ ritonavir)), Veklury (remdesivir), Lagevrio (molnupiravir), Xocova (ensitrelvir), Xevudy (sotrovimab), REGEN-COV (casirivimab and imdevimab), Tylenol (acetaminophen). Not all the therapeutics listed had commonly referred to trade names as of July 2023 (i.e., bamlanivimab and etesevimab, baricitinib, tocilizumab, vitamin C, heparin).

Mechanism of action or mode of action of the drug refers to how a drug or other substance produces an effect in the body. For example, as described above, antivirals inhibit viral replication in a host. In the case of COVID-19, there are several sites in the SARS-CoV-2 virus that antivirals can target to provide the antiviral effect in a host. For example, ensitrelvir and molnupiravir target different virus sites—conserved viral main protease for the former and RNA-dependent RNA polymerase for the latter.²²³ Ultimately, differences in the mode of action contribute to the efficacy of a therapeutic.²²⁴ Table 3.1 provides examples of COVID-19 therapeutics and their respective molecule size (category), drug target (class), and mechanism of action (mode of action). In terms of patents, some products’ (e.g., acetaminophen, dexamethasone, and vitamin C) foundational patents have been expired for decades; however, it is impossible to know if some of these therapies are in new patent filings for COVID-19 treatment as part of a therapeutic protocol or formulation.

²²¹ In the case of COVID-19, the majority of host-directed therapies that are currently available are those intended to dampen the dysregulated inflammatory response to infection. Airfinity, “COVID-19,” accessed July 14, 2023; Singh and de Wit, “Antiviral Agents for the Treatment of COVID-19,” February 11, 2022, 1–5.

²²² UK, NHS Data Model and Dictionary, s.v. “Adjunctive Therapy,” accessed June 28, 2023.

²²³ See, e.g., Vangeel et al., “Remdesivir, Molnupiravir and Nirmatrelvir,” February 2022.

²²⁴ See, e.g., Vangeel et al., “Remdesivir, Molnupiravir and Nirmatrelvir,” February 2022.

In seeking to identify the universe of COVID-19 therapeutics and diagnostics, the Trade Representative requested inclusion of both products under patent and those still in development. Looking at emerging COVID-19 therapeutics and diagnostics is important, owing to the dynamic nature of the virus, the changing efficacy of drugs, and uncertainty over the eradication of SARS-CoV-2. Since the early days of the pandemic, the push to develop new, effective COVID-19 diagnostics and therapeutics has been ongoing. As of 2023, there have been hundreds of tests produced and hundreds of therapeutics studied, all specific to COVID-19, and there are new clinical trials for therapeutics being added to the pipeline every week around the world.²²⁵ This section describes COVID-19 diagnostics and therapeutics in development based on data available from the NLM database of clinical trials and other studies conducted in all U.S. states and 220 additional countries.²²⁶

Unlike therapeutics, *in vitro* diagnostics do not typically go through a clinical trial.²²⁷ A search in the NLM database for COVID-19 diagnostics yielded only 10 clinical trials involving COVID-19 diagnostics, most of which involved diagnostics to assess the efficacy of a drug to treat COVID-19.²²⁸ The process for authorization of a new diagnostic may involve a premarket notification to the FDA to demonstrate that the new diagnostic is “substantially equivalent” to a legally marketed device.²²⁹ A search of the NLM database for studies outside clinical trials for COVID-19 diagnostics yielded 202 results;²³⁰ these results are not exhaustive of the research and development occurring with respect to COVID-19 diagnostics

²²⁵ Clinical trials for therapeutics are conducted in four phases. Phase I tests a drug in a small group of healthy people, primarily to evaluate safety and side effects. Phase II trials are larger and aim to estimate the effectiveness of the drug. Phase III trials involve even more patients, often from different populations and tested with different dosages or combinations. Positive results from phase III trials form a key element in meeting requirements to obtain regulatory approval. Following approval, phase IV trials are conducted to monitor safety and efficacy. Some studies are directed to more than one clinical trial phase. Kyle, “Covid-19 and Clinical Trials,” 2022, 176.

²²⁶ The NLM database can be queried for characteristics of the study such as the subject matter (e.g., those related to COVID-19 and synonymous terms) and the type of intervention (e.g., vaccines, drugs, or diagnostics). If the study involves a drug, queries can identify the clinical trial phase(s) to which the study is directed.

²²⁷ The clinical trial and approval pathway for diagnostics differs from that of therapeutics. This was especially apparent during the COVID-19 pandemic, when diagnostic tests were commercially available, but the data packages for the tests were not studied until a later date. BIO, BIO COVID-19 Therapeutic Development Tracker, “Development Start Date (for COVID-19) Demonstrates Unprecedented Industry Response,” accessed August 10, 2023; FDA, “In Vitro Diagnostics EUAs—Molecular Diagnostic Tests,” accessed on April 11, 2023; FDA, “In Vitro Diagnostics EUAs Antigen Diagnostic Tests for SARS-CoV-2,” accessed on April 11, 2023.

²²⁸ In the NLM database, the search was run for all clinical trial phases (e.g., early phase I, phase I, phase II, etc.). NIH, NLM, ClinicalTrials.gov database, accessed July 10, 2023 (sorting by interventions with the “Diagnostic” tag).

²²⁹ One of these premarket authorizations can be a 510(k) premarket notification. 21 U.S.C. § 360(k); FDA, “Premarket Notification 510(k),” October 3, 2022. Additionally, there are also *de novo* classifications for diagnostics, which are for diagnostics for which there is no substantially equivalent test on the market. FDA, “De Novo Classification Request,” October 3, 2022. See chapter 2 for more information on diagnostics regulatory clearance.

²³⁰ In the NLM database, these diagnostics can be located by selecting the category “phase not applicable” and filtering out nondiagnostic submissions. The category “phase not applicable” includes studies that compare the diagnostic to a predicate device as required for a 510(k) submission. Additionally, interventions listed only as “device” or “diagnostic test” were selected and the conditions column was filtered to only include those that contained “COVID” or “SARS.” NIH, NLM, ClinicalTrials.gov database, accessed July 10, 2023 (sorting by interventions with the “Diagnostic” tag).

around the world.²³¹ Rather, they provide a snapshot of research and innovation that are occurring for COVID-19 diagnostics.

Conversely, the NLM database yields far more information about COVID-19 therapeutics in development. As of July 2023, the database includes a total of 1,762 clinical trials of COVID-19 drugs in all phases worldwide, with 30 percent (530) of them occurring in the United States.²³² During that same period, of the total number of clinical trials in phase III status (407), more than one quarter were occurring in the United States (103).²³³

The geographic locations, by region, of the clinical trials of drugs in phase III are set forth in table 3.2, as well as the share of those trials that are designated as phase III (i.e., late-stage trials). These phases are likely a good indicator of drugs that are in more advanced stages of development, but unlike those in phase IV, have not yet been approved by regulators. Focusing on the late-stage trials allows for a narrower focus on the drugs that have a higher probability of making it to market. Due to the compressed timeline that became the norm during the pandemic, the traditional separation of the phases for the clinical development for drugs has been blurred.²³⁴ However, even for drugs that reach late-stage trials or drugs and diagnostics that obtain Emergency Use Authorizations (EUAs), there is no guarantee of final approval, especially with the continuing mutations of the virus.²³⁵

²³¹ The results of this search encompass a wide range of studies on COVID-19 diagnostics, including studies on the performance or efficacy of tests; studies related to general purpose testing techniques and strategies for COVID-19; and studies on COVID-19 clinical management diagnostics. For example, some general-purpose studies may look at FDA Product Classifications Product Code NCT: the sensitivity of the “lollipop” sample collection method (NCT05801341), the optimal length for nasal swabs (NCT04840082), or the uptake of take-home testing for schools (NCT05060510). COVID-19 diagnostic product studies include marketed tests like the Lucira COVID-19 All-in-One test kit (NCT04720235) and the Abbott BinaxNow COVID-19 rapid antigen test (NCT04959760). An example of a clinical management study is one on the implementation of lung ultrasounds in management of patients hospitalized with COVID-19 (NCT04542421). NIH, NLM, ClinicalTrials.gov database, accessed July 12, 2023.

²³² The FDA describes clinical trial phases as clinical research designed to evaluate and test new interventions. Each phase serves a different purpose providing answers to researchers to properly evaluate the intervention. The 1,762 research studies for COVID-19 therapeutics fall into the following phases: early phase I = 37; phase I = 238; phase I/phase II = 142; phase II = 613; phase II/III = 192; phase III = 407; phase IV = 133. The count excludes studies with terminated, suspended, unknown, or withdrawn statuses. It also excludes those that are about vaccines. The 530 studies identified as taking place in the United States may also have study locations outside the United States. NIH, NLM, ClinicalTrials.gov database, accessed July 12, 2023; FDA, “What Are the Different Types of Clinical Research?,” January 4, 2018.

²³³ NIH, NLM, ClinicalTrials.gov database, accessed July 12, 2023; FDA, “What Are the Different Types of Clinical Research?,” January 4, 2018.

²³⁴ See, for example, the “lightning” development of nirmatrelvir by Pfizer. Allais et al., “Development of the Commercial Manufacturing Process for Nirmatrelvir,” March 29, 2023, 849–857.

²³⁵ See, for example, the rescinding of EUAs for several monoclonal antibodies that target the SARS-CoV-2 virus: FDA, “Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products,” accessed July 19, 2023. The FDA has written guidance on the topic of transitioning from EUA to full approval. See FDA, “Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs),” March 2023.

Table 3.2 Phase III clinical trials for COVID-19 therapeutics, as of July 2023

In count and percentages.

Region Name	Number of trials (count)	Share of total number of trials in phase III (%)
Africa	170	50
Central America	32	47
East Asia	226	31
Europe	480	34
Middle East	148	26
North America	700	25
North Asia	118	44
Pacifica	35	34
South America	237	40
South Asia	110	45
Southeast Asia	108	50

Source: NLM, ClinicalTrials.gov database, accessed July 10, 2023.

Notes: The values provided in the “number of trials” column represent the number of trials in that region from “early phase I” to “phase IV.” The number excludes clinical trials with terminated, suspended, unknown, or withdrawn statuses. Items tagged as “Biological,” “Drug,” and “Combination product” were included, and selective inclusion/exclusion was conducted of the “Other,” “Procedure,” and “Radiation” tags. The values in the “number of trials” column in this table are not additive and will not yield the total of 1,762 clinical trials of COVID-19 drugs that have been conducted worldwide as reported above.

Hearing testimony and the literature described several key characteristics related to COVID-19 therapeutics in development.²³⁶ First, witnesses and academic researchers highlighted the importance of repurposed drugs in the COVID-19 development pipeline.²³⁷ To illustrate, the Biotechnology Innovation Organization (BIO) indicated that more than 60 percent of COVID-19 therapeutics in development have other previously approved indications—for example, as anti-inflammatory or oncology drugs.²³⁸ Second, U.S.-based biotech firms that are SMEs are conducting most COVID-19 therapeutic development in the United States.²³⁹ Third, when looking at patents filed, COVID-19 drugs in development are largely small molecule or biologic, and range from antivirals, including viral-neutralizing mAbs; immune modulators; and others that function via various mechanisms without direct effects on viral invasion.²⁴⁰

Relevant COVID-19 Diagnostics and Therapeutics

Building on the information provided above on definitions and the universe of existing COVID-19 diagnostics and therapeutics, this section addresses several aspects related to identifying relevant diagnostics and therapeutics covered in this report based on the best available information. Compared

²³⁶ Information on the development pipeline for diagnostics is much more limited, as they do not go through the same defined clinical trial phases as therapeutics.

²³⁷ Repurposed drugs constituted 69 percent of U.S. registered clinical trials in the first quarter of 2020, although de novo drug research became more important as the pandemic progressed. Geneva Network, written submission to the USITC, April 25, 2023, 5; Greenblatt, Gupta, and Kao, “Drug Repurposing During The COVID-19 Pandemic,” March 2023, 424–432.

²³⁸ BIO, prehearing brief submission to the USITC, March 17, 2023, 2.

²³⁹ BIO, prehearing brief submission to the USITC, March 17, 2023, 2; BIO, BIO COVID-19 Therapeutic Development Tracker: “Therapies in Development by Originating Company Headquarters,” accessed July 8, 2023.

²⁴⁰ WIPO, “COVID-19-Related Vaccines and Therapeutics,” 2022, 47.

to the thousands of diagnostics and therapeutics on the market or under development for COVID-19, the scope of products that are relevant could be narrowed on the basis of a number of factors. As indicated above, COVID-19 diagnostics or therapeutics are products used to diagnose or treat COVID-19. In order to identify relevant COVID-19 diagnostics and therapeutics, a number of specific parameters and criteria can be used to construct a more focused group of products.²⁴¹ For example, as the discussion about the extension of the 2022 Ministerial Decision to diagnostics and therapeutics involves IP protection, a relevant COVID-19 therapeutic could be one that is covered by patent protections (now or in the future).²⁴² However, as the WIPO and USPTO reports illustrate, the number of COVID-19 diagnostics and therapeutics potentially covered by patents is vast, and as noted above the most common COVID-19 diagnostics, PCR and antigen tests, are reportedly no longer covered by patents, yet information on those products may nonetheless inform the discussion.

Another parameter to identify relevant therapeutics could be to refine the selection of products according to the therapeutic class, type of medicine (traditional or modern), or mode of action, for example.²⁴³ Therapeutic class could be used to narrow the number of relevant COVID-19 therapeutic products to only those that are virus-directed and thus specific to the SARS-CoV-2 virus.²⁴⁴ For diagnostics, a virus-directed parameter could be used to narrow the number of relevant COVID-19 diagnostics to only those that detect an active SARS-CoV-2 infection by identifying the molecular presence of the virus or associated antibodies. A virus-directed parameter would exclude tests or treatments for a secondary infection or complications stemming from a COVID-19 infection. It would also exclude host-directed therapies, including those referenced in table 3.1 above,²⁴⁵ and would also exclude general-purpose equipment and platform instruments used in the administration of COVID-19 diagnostics and therapeutics.²⁴⁶

A virus-directed parameter would eliminate some of the more prominent therapeutics and platform technologies used in the diagnosis and treatment of COVID-19. At the same time, the metric “virus-

²⁴¹ See appendix E.

²⁴² Pfizer, written submission to the USITC, May 5, 2023, 22–28; Merck, written submission to the USITC, May 5, 2023, iii. The COVID-19 diagnostics and therapeutics covered by patents are discussed earlier in this chapter and in chapter 2. See also appendix E, table E.1.

²⁴³ See WIPO, COVID-19 Vaccines and Therapeutics, April 2023 and Toole et al., “Diagnosing COVID-19,” October 2023, 4.

²⁴⁴ Although the class is “virus-directed,” the mode of actions (i.e., the nature of the attack on the virus) can differ. See, e.g., Ho et al., “Perspective Adjunctive Therapies for COVID-19,” 2021; Singh and de Wit, “Antiviral Agents for the Treatment of COVID-19,” February 11, 2022.; Kushner et al., “The Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs),” September 21, 2022; Vangeel et al., “Remdesivir, Molnupiravir and Nirmatrelvir,” February 2022.

²⁴⁵ Some host-directed therapies target components of the host cell to hinder virus replication, and in theory, such therapies could be developed that specifically hinder replication of the COVID-19 virus. Existing host-directed COVID-19 therapeutics identified in this investigation, however, appear to target the inflammatory response to the infection rather than specifically hinder replication of the COVID-19 virus. Tripathi et al., “Host Directed Therapies,” 2021.

²⁴⁶ For example, in the case of diagnostics, this would exclude PCR equipment and platform instruments that were developed for uses that were not specific to the detection of a SARS-CoV-2 infection but could include the COVID-19 specific test kits used in these machines. By extension, depending on how the parameter is defined for purposes of diagnostics, this could also include any ancillary supplies packaged in these test kits, such as cassettes, cartridges, and reagents. For more information on diagnostics instruments and platform technologies, see chapters 2 and 4.

directed” focuses on tests and drugs that were specifically and successfully (to some extent) deployed for COVID-19 rather than for other conditions. This would narrow the scope of products, but certain medicines that have been prescribed for the treatment of COVID-19 would be excluded using this parameter (e.g., dexamethasone and baricitinib).²⁴⁷ Table 3.3 lists examples of virus-directed COVID-19 therapeutics.

Table 3.3 Examples of virus-directed therapeutics for the treatment of COVID-19

INN = International Nonproprietary Name; Lilly = Eli Lilly and Company; Vir = Vir Biotechnology; GSK= GlaxoSmithKline; mAb = monoclonal antibody.

Trade name (manufacturer)	INN	Category	Therapeutic class (mode of action)
Paxlovid (Pfizer)	Nirmatrelvir (+ ritonavir)	Small molecule	Antiviral (protease inhibitor)
Veklury (Gilead)	Remdesivir	Small molecule	Antiviral (nucleotide analogue)
Lagevrio (Merck)	Molnupiravir	Small molecule	Antiviral (nucleoside analogue)
Xocova (Shionogi)	Ensitrelvir	Small molecule	Antiviral (protease inhibitor)
Bebtelovimab (Lilly)	Bebtelovimab	Biologic	SARS-CoV-2 targeting mAb
Xevudy (GSK, Vir)	Sotrovimab	Biologic	SARS-CoV-2 targeting mAb
Bamlanivimab and etesevimab (Lilly)	Bamlanivimab and etesevimab	Biologic	SARS-CoV-2 targeting mAbs
REGEN-COV (Regeneron, Roche)	Casirivimab and imdevimab	Biologic	SARS-CoV-2 targeting mAbs

Sources: Shionogi, “Shionogi Receives U.S. FDA Fast Track Designation for Ensitrelvir Fumaric Acid, an Investigational Oral Antiviral for COVID-19,” accessed June 11, 2023; Shionogi, “Xocova (Ensitrelvir Fumaric Acid) Tablets 125mg Approved in Japan,” accessed August 27, 2023; Lamontagne et al., “A Living WHO Guideline on Drugs,” updated January 12, 2023; FDA, “Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products,” July 19, 2023; FDA, “Coronavirus (COVID-19): Drugs,” March 10, 2023.

Another parameter in scoping relevant COVID-19 diagnostics or therapeutics could be whether the products have gained authorization—or equivalent thereof—or approval of a national or international health regulatory body (and thus do not include medicines that are only indicated for research settings).²⁴⁸ This parameter would allow for the inclusion of goods in late-stage clinical trials that have gained some form of authorization to enter the market to test or treat COVID-19 but have not received full regulatory approval and may not be widely available during the period covered by this report.²⁴⁹

Compiling a list of COVID-19 diagnostics and therapeutics that have been approved by a regulatory body is challenging. One element of this challenge is that lists of products approved to diagnose or treat COVID-19 change over time, meaning the lists are different depending on when during the pandemic the list was created or updated. Since 2020, some authorizations of certain COVID-19 diagnostics and therapeutics have been rescinded because they lacked sensitivity, specificity, or efficacy. Even if

²⁴⁷ Dexamethasone and baricitnib are host-directed therapies. “Host-directed” therapies may be used to treat innumerable infections or disease (e.g., cancers) and in a variety of patient settings (e.g., in an intensive care unit on a ventilator).

²⁴⁸ Not all regulatory authorities use the same terminology to indicate when a product may be put on the market for general use. For example, in the United States, the FDA authorized nirmatrelvir (+ ritonavir) and molnupiravir under emergency use authorization in December 2021 but did not grant full market approval to nirmatrelvir (+ ritonavir) until May 2023, and molnupiravir has not received full market approval as of October 2023. The WHO, for example, may recommend or endorse products prior to approval through the prequalification process.

²⁴⁹ For example, ensitrelvir is still under review by the WHO and many regulatory regimes, including the FDA, although it is authorized to be on the market in Japan. For the FDA review, ensitrelvir did receive fast-track designation. Shionogi, “Shionogi Receives U.S. FDA Fast Track Designation for Ensitrelvir Fumaric Acid,” accessed June 11, 2023.

regulatory authorization, or the equivalent thereof, of a COVID-19 diagnostic or therapeutic is rescinded, it may later be reauthorized for COVID-19 diagnosis or treatment.²⁵⁰ Another complication is that many lists of authorized COVID-19 diagnostics and therapeutics are no longer updated frequently or at all.²⁵¹ Adding to the difficulty in developing a list of diagnostics or therapeutics that have been authorized or approved is that the list of products authorized or approved to diagnose or treat COVID-19 may differ among regulatory authorities in different countries or between national and international regulatory authorities. A diagnostic or therapeutic that is approved in one country may not be approved in another or may not be included on the WHO prequalified medicinal products list.²⁵²

Further, therapeutics are prescribed according to disease severity and patient setting (i.e., inpatient or outpatient). Thus, a therapeutic could be approved or authorized for use with patients with a certain level of severity of COVID-19 or for use in particular settings, further complicating the compilation of a list of approved or authorized COVID-19 diagnostics and therapeutics. Several therapeutic options are available for patients with mild COVID-19, and for those with severe or critical COVID-19.²⁵³

Table 3.4 shows the number of COVID-19 diagnostic tests authorized by region. The vast majority of diagnostic authorizations are in Europe, the Americas, and the Western Pacific, while Africa has the lowest number of authorizations.²⁵⁴

Table 3.4 Number of authorized COVID-19 diagnostic tests by region

In number of test approvals

Region	Authorized
Africa	192
Americas	579
Europe	792
Southeast Asia	211
Western Pacific	416

Source: PATH, "Global availability of COVID-19 diagnostic tests," accessed June 2, 2023.

Note: The total reported for each region represents the number of diagnostic tests authorized by at least one regulatory body in the associated region. The "authorized" column is not additive across regions because one diagnostic test could be authorized in multiple regions.

In aggregate, based on publicly available information, national regulatory authorities in 85 countries have granted approval for therapeutics for the treatment of COVID-19 under EUA, full approval, or

²⁵⁰ Additionally, a pause in authorization in one country or region may not occur in every market. For example, in the case of hydroxychloroquine (HCQ), in the United States the EUA was revoked in June 2020, but in Brazil, HCQ was a key drug in the COVID-19 kits distributed starting in 2020 and continuing through 2021. FDA, "Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization," June 15, 2020; Furlan and Caramelli, "The Regrettable Story of the 'Covid Kit,'" December 2021.

²⁵¹ The lists published by the Regulatory Affairs Professionals Society had a COVID-19 therapeutics tracker that has not been updated since July 2022, but BIO has a tracker that is currently updated monthly. BIO, "BIO COVID-19 Therapeutic Development Tracker," accessed August 10, 2023; Craven, "COVID-19 Therapeutics Tracker," July 1, 2022.

²⁵² See table 3.6. Airfinity, Science 360, Regulatory, by treatment, July 15, 2023. See also chapters 2 and 6 for a discussion of the WHO prequalification program and its relationship to availability of COVID-19 diagnostics and therapeutics in some countries.

²⁵³ Severity of COVID-19 is defined based on symptoms. NIH, "Clinical Spectrum of SARS-CoV-2 Infection," March 6, 2023.

²⁵⁴ PATH, "Global Availability of COVID-19 Diagnostic Tests," accessed June 2, 2023.

recommendation (for use or approval),²⁵⁵ amounting to at least 220 EUAs and 46 full approvals, and 8 recommended for use for 37 discrete therapeutics (table 3.5).²⁵⁶ Molnupiravir has the largest number of EUAs (39), followed by nirmatrelvir (+ ritonavir), 34, and remdesivir (33). Nirmatrelvir (+ ritonavir) also has the largest number of approvals (30), with remdesivir having the second largest (5).²⁵⁷

Table 3.5 Therapeutics for treatment of COVID-19 that are approved, recommended, or have an EUA as of July 2023, by drug

In number of countries: EUA = Emergency Use Authorization; — = not applicable

Therapeutic	EUA	Approved	Recommended
2-deoxy-D-glucose	1	—	—
Hexapeptide succinate	—	1	—
Anakinra	1	—	—
Aviptadil	1	—	—
Azvudine	1	—	—
Baricitinib	6	2	—
Amubarvimab and romlusevimab	1	—	—
Colchicine	1	—	—
Convalescent plasma	3	—	—
Regdanvimab	7	—	—
Dexamethasone	11	1	—
Enoxaparin	3	—	—
Ensitrelvir	1	—	—
Tixagevimab and cilgavimab	5	2	—
Favipiravir	1	—	—
Hydrocortisone	1	—	—
Hydroxychloroquine	8	—	—
Linosine acedoben dimepranol	—	1	—
Lopinavir (+ ritonavir)	1	—	—
Bebtelovimab	1	—	—
Bamlanivimab and etesevimab	4	—	—
Bamlanivimab	12	—	—
Methylprednisolone	2	—	—
SiCoV/KK46	1	—	—
Molnupiravir	39	—	8
Nirmatrelvir (+ ritonavir)	34	30	—
Proxalutamide	1	—	—
Leritrelvir	1	—	—
Casirivimab and imdevimab	11	—	—
Remdesivir	33	5	—
Sarilumab	1	—	—
Simnotrelvir (+ ritonavir)	1	—	—
Tocilizumab	12	4	—

²⁵⁵ These numbers do not include authorization or approval by the European Commission for marketing in the European Economic Area; to the extent authorization or approval was granted by an EU member state, it is included. Airfinity, Science 360, Regulatory, by treatment, July 15, 2023.

²⁵⁶ See appendix E for virus-directed COVID-19 therapeutics that are approved, recommended, or have an EUA.

²⁵⁷ Tixagevimab and cilgavimab, commonly referred to as Evusheld, had been predominantly prescribed during the pandemic as a prophylactic for immunocompromised patients. Although Evusheld used solely as a prophylactic was excluded from the data, table 3.5 shows there have been authorizations or approvals for the drug as a therapeutic as of July 2023.

Therapeutic	EUA	Approved	Recommended
Vilobelimab	1	—	—
Sotrovimab	10	—	—
Renmindevir	2	—	—
Zofin	1	—	—
Total	220	46	8

Source: Airfinity, Science 360, Regulatory, by treatment, July 15, 2023.

Notes: In some instances, a therapeutic included in this table does not have an INN or generic name, so the reported name or the investigational name is used. Drugs that are solely approved as prophylactics for COVID-19 are excluded. These numbers do not include authorization or approval by the European Commission for marketing in the European Economic Area; to the extent authorization or approval has been granted by an EU member state, it is included. The table reflects information available from Airfinity as of July 15, 2023.

With respect to countries in the EU and the European Economic Area (EEA), the EMA makes recommendations to the European Commission for the marketing approval of drugs across the EEA (table 3.6).²⁵⁸ Examples of therapeutic medicinal products authorized for use by the EMA for the treatment of COVID-19 include both small-molecule antivirals and certain monoclonal antibodies.²⁵⁹ In response to the COVID-19 pandemic, the EMA “established an ad hoc EMA Emergency Task Force to identify and support the development of promising medicinal products in the fight against COVID-19.”²⁶⁰ Broader classes of COVID-19 therapeutics identified by the task force include, but are not limited to, “small molecules and monoclonal antibodies, antivirals and immunomodulators.”²⁶¹

On a global scale, as noted in chapter 2, WHO prequalification of medicines is a service provided by the WHO to assess the quality, safety, and efficacy of medicinal products and is the only international medicines quality assurance program.²⁶² A number of countries and international procurement agencies rely on the WHO list of prequalified medicinal products to guide purchasing decisions. However, these lists are limited in scope, are updated infrequently, and/or are not updated on a set schedule.²⁶³

²⁵⁸ EEA extends the EU’s single market to Iceland, Norway, and Liechtenstein. EMA, “National Competent Authorities (Human),” accessed August 24, 2023.

²⁵⁹ EMA, “COVID-19 Treatments,” accessed April 19, 2023. See also chapter 4.

²⁶⁰ European Commission (EC), “Communication from the Commission,” COM(2021) 355 Final/2, May 6, 2021, 5.

²⁶¹ EC, “Communication from the European Commission,” COM(2021) 355 Final/2, May 6, 2021, 5.

²⁶² WHO, “World Health Organization Prequalification,” accessed August 28, 2023.

²⁶³ As an example, on the diagnostics side, the EUL was last updated May 5, 2023, but it is a much smaller list than its FDA equivalent. For therapeutics, 15 months passed before the WHO’s “Status of COVID-19 Medicines and Active APIs” was updated (April 2022 to June 2023), then was updated again August 2023. WHO, *WHO Emergency Use Listing for In Vitro Diagnostics*, May 5, 2023. WHO, “Status of COVID-19 Medicines and Active Pharmaceutical Ingredients (APIs),” April 28, 2022.

Table 3.6 Therapeutics for treatment of COVID-19 that are approved, recommended, or have an EUA by the WHO or the EEA, July 2023

In number of regulatory signoffs. EEA = European Economic Area (European Medicines Agency (EMA) and/or European Commission (EC)); WHO = World Health Organization; EUA = Emergency Use Authorization; PQ = prequalification; — = not applicable

Therapeutic	EUA	Endorsed	Approved	PQ	Recommended
Anakinra	EEA	EEA	—	—	—
Regdanvimab	EEA	EEA	EEA	—	—
Tixagevimab and cilgavimab	—	—	EEA	—	EEA
Bamlanivimab and etesevimab	—	EEA	—	—	—
Bamlanivimab	—	EEA	—	—	—
Molnupiravir	—	EEA	—	—	—
Nirmatrelvir (+ ritonavir)	EEA	EEA, WHO	EEA	—	EEA
Casirivimab and imdevimab	—	EEA, WHO	EEA	—	—
Remdesivir	EEA	—	EEA	—	WHO
Tocilizumab	EEA	EEA, WHO	—	WHO	—
Sarilumab	—	WHO	—	—	—
Sotrovimab	EEA	EEA	EEA	—	—
Dexamethasone	—	EEA	—	WHO	—

Source: Airfinity, Science 360, Regulatory, by treatment, July 15, 2023.

Notes: Drugs solely approved as prophylactics for COVID-19 are excluded. This table reflects information that was publicly available as of July 15, 2023. See chapter 6 for more information on regulatory approvals and availability.

For diagnostics, as of May 2023, the WHO lists 21 molecular tests and 15 rapid antigen tests that are approved under emergency use listing.²⁶⁴ As of July 2023, there are six COVID-19 therapeutics included in the WHO COVID-19 Medicine and Active Pharmaceutical Ingredients (APIs) list (also sometimes known as the prequalification list): dexamethasone, molnupiravir, nirmatrelvir or nirmatrelvir (+ ritonavir), remdesivir, tocilizumab, and sotrovimab (see chapter 2).²⁶⁵ Conversely, 10 therapeutics have received WHO recommendation/approval for treatment of COVID-19: three antivirals, four corticosteroids, two Interleukin-6 (IL-6) receptor blockers, and one Janus kinase (JAK) inhibitor.²⁶⁶

As discussed above, various parameters could be applied, individually or in combination, to identify relevant COVID-19 diagnostics and therapeutics. The chapters that follow in this report provide information as requested in the Trade Representative’s letter on relevant COVID-19 diagnostics and therapeutics. Chapters 4, 5, and 6 answer different portions of the request letter pertaining, respectively, to supply chains, production, and trade (chapter 4); compulsory licensing and the medicines patent pool (MPP) (chapter 5); and market segmentation, demand, consumption, pricing, and availability (chapter 6). As noted, the parameters applied to identify relevant COVID-19 products to report on in these chapters differ somewhat among chapters or within chapters—because of data availability issues and to focus the discussion—but also to ensure inclusion of information that

²⁶⁴ See chapter 2 for more on the differences in regulatory pathways with respect to both national and international granting authorities. WHO, *WHO Emergency Use Listing for In Vitro Diagnostics*, May 5, 2023.

²⁶⁵ Dexamethasone and tocilizumab are host-directed treatments, while molnupiravir, nirmatrelvir or nirmatrelvir (+ ritonavir), remdesivir, and sotrovimab are virus-directed treatments for COVID-19. “Status of COVID-19 Medicines and Active Pharmaceutical Ingredients (APIs),” March 7, 2023.

²⁶⁶ Remdesivir is one of the three antivirals that have received a WHO recommendation, including molnupiravir and nirmatrelvir (+ ritonavir). Remdesivir received full U.S. approval October 22, 2020. In November, the WHO recommended against using remdesivir for the treatment of COVID-19, but reversed course with a conditional recommendation on April 22, 2022, after new clinical testing data were available. Lamontagne et al., “A Living WHO Guideline on Drugs,” updated January 12, 2023.

otherwise would be excluded (e.g., if a covered-by-patent parameter were applied to COVID-19 antigen or PCR tests).

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Chapter 4

COVID-19 Diagnostics and Therapeutics Manufacturing Supply Chain and Trade

Introduction

In pharmacology, diagnostics and therapeutics are two related but distinct fields.²⁶⁷ Discovery and production of efficacious diagnostics and therapeutics have been critical to the continued fight against SARS-CoV-2.²⁶⁸ Through key examples, this chapter responds to several elements of the request letter by describing the development, production, and trade of COVID-19 diagnostics and therapeutics; discussing the regulations needed to bring these goods to the global market; and providing an overview of the key producing countries and firms operating in the supply chain.²⁶⁹ The scope of diagnostics discussed in this chapter is limited to the two primary methods used for identifying an active COVID-19 infection: polymerase chain reaction (PCR) tests and rapid antigen tests. For therapeutics, the COVID-19 drugs highlighted in the discussion are those that are virus-directed (i.e., SARS-CoV-2 directed therapeutics) and on the market at any time between January 2020 and July 2023.²⁷⁰ To the extent practicable, the chapter discusses the location of the manufacturing of COVID-19 diagnostics and therapeutics, grouped by country income level: high-income countries (HICs), upper-middle-income countries (UMICs), lower-middle-income countries (LMICs), and low-income countries (LICs).

Information Sources and Data Gaps

The scope of information available on global supply chains for COVID-19 diagnostics and therapeutics varies greatly from country to country and from region to region, resulting in various information gaps. Data, as they relate to trade of COVID-19 diagnostics and therapeutics, are largely not COVID-19 specific; therefore, the trade data reported encompass a wider range of goods as reported in Global Trade Atlas. Moreover, when examining information by product (i.e., diagnostic or therapeutic), specific pieces of

²⁶⁷ As previously noted, this report does not address COVID-19 prophylactics (e.g., vaccines), but prophylactics are another important field in the fight against COVID-19. See chapter 3 for more on diagnostics and therapeutics terminology and scoping.

²⁶⁸ SARS-CoV-2 is the virus that causes the infectious disease that we refer to as COVID-19.

²⁶⁹ The examples discussed in this chapter largely exclude immune modulators, such as Kineret (anakinra), Olumiant (baricitinib), and Actemra (tocilizumab). Immune modulators are a category of drugs that help activate, boost, or suppress the immune function. In cases of COVID-19 infection, the immune system can become hyperactive and immune modulators may help suppress hyperinflammation. The modulators, however, are not virus-directed therapeutics. FDA, "Coronavirus (COVID-19): Drugs," March 10, 2023.

information regarding manufacturing are difficult to ascertain.²⁷¹ For example, the announcement that a therapeutic would be produced does not mean that commercial production occurred or is actively occurring at the time of this writing.

Data on production volumes of COVID-19 diagnostics are limited; however, the identification of known manufacturers allows for a useful mapping of production and industry reach.²⁷² Similarly, data on production status and capacity for COVID-19 therapeutics are limited; however, the identification of manufacturers through announced production arrangements allows for a mapping of potential production.²⁷³ Further complicating matters is the multinational reach of pharmaceutical companies. If a firm has a manufacturing footprint in multiple countries or several locations in any one country, it is difficult to know if COVID-19 diagnostics or therapeutics are being manufactured at every site. Data are particularly limited with respect to production costs. Although major factors impacting overall production costs are known, the cost of manufacturing a specific input or finished product often is not. These costs can vary substantially, depending on the inputs and the supply chains of each producer, and are often not publicly disclosed.

Overview of Manufacturing Supply Chains for COVID-19 Diagnostics and Therapeutics

Although COVID-19 diagnostics and therapeutics differ across many factors, they are both part of the pharmaceutical value chain. Generally, within the value chain, the supply chain involves a network of researchers, regulators, and producers and can be divided into two stages: (1) manufacturing and (2) distribution. The manufacturing and distribution supply chain for pharmaceuticals can be complex, ranging from obtaining inputs to marketing the final products to customers.

The specific components of the supply chain can vary by product and by the country or region in which the diagnostic or therapeutic is being deployed (e.g., because of infrastructure or regulatory constraints). In the context of the COVID-19 pandemic, parts of the manufacturing supply chain for diagnostics and therapeutics were developed in tandem, as opposed to sequentially, in response to the public health emergency.²⁷⁴ For the purposes of this discussion, the manufacturing portion of the supply chain is separated into two parts: (1) development and (2) production. The distribution and deployment portion of the value chain, including pricing, procurement agreements, donations, and various access programs for relevant COVID-19 diagnostics and therapeutics, is covered in chapter 6.

²⁷¹ Manufacturers of COVID-19 diagnostics and therapeutics in this section refer to firms that have produced, announced their intention to produce, or are actively producing either COVID-19 diagnostics or therapeutics.

²⁷² Diagnostics manufacturers were identified using the FIND “COVID-19 Test Directory.” FIND, “COVID-19 Test Directory,” June 25, 2023.

²⁷³ Therapeutics manufacturers were primarily identified through studying production arrangements in the Airfinity database where manufacturing was part of the arrangement (i.e., API/excipient manufacturing, finished drug product, and fill/finish). Companies with production arrangement solely for distribution or commercialization, or those with arrangements that have been noted as inactive (with no production, not “launched”) were excluded. Information is not available to determine how many production facilities in each country were covered under these arrangements. This methodology and the comprehensiveness of the database are limited by what information can be gleaned from publicly available production arrangements.

²⁷⁴ Industry representative, interview by USITC staff, March 7, 2023; Gilead Sciences, prehearing brief submission to the USITC, March 17, 2023, 3–4.

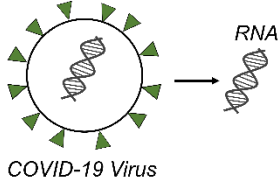
Diagnostics

As mentioned previously, the primary types of in vitro diagnostics currently in use for the detection of an active COVID-19 infection fall into two categories: PCR tests²⁷⁵ and rapid antigen tests.²⁷⁶ PCR tests assay²⁷⁷ a patient's sample for the presence of the virus's genetic material (figure 4.1).²⁷⁸ Antigen tests detect the presence of viral proteins in a patient's sample.²⁷⁹ The two types of tests largely feed separate market channels: PCR tests require a medical laboratory and are analyzed in clinical settings, while antigen tests are used in point-of-care and at-home testing kits.²⁸⁰

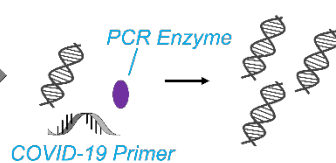
Figure 4.1 Categories of COVID-19 tests in use

PCR Test

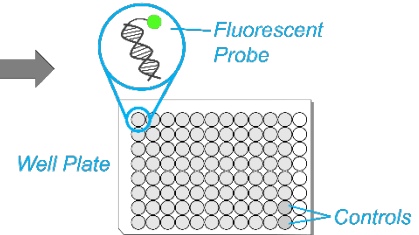
(1) The virus is broken up to release RNA using an *RNA extraction kit*.



(2) The quantity of RNA is amplified using polymerase chain reaction (PCR).

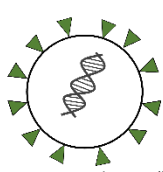


(3) A collection of samples is loaded into an *instrument*, delivering the diagnosis.

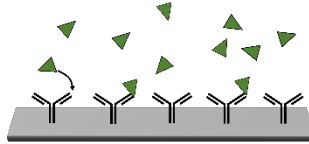


Antigen Test

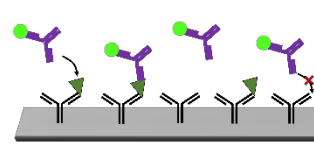
(1) The virus is broken to release the antigens.



(2) The antigens are added to a surface and bind to attached *antibodies*.



(3) *Fluorescent antibodies* are added that can be detected by an instrument.



Source: Goodman, "COVID-19 Testing Supplies One Year into the Pandemic," 2021; Abingdon Health, "What Is a Lateral Flow Test?," accessed June 8, 2023; Maynooth University, "Science Week: How Covid Lateral Flow Tests Work," accessed June 8, 2023; Sartorius, "German-Engineered Nitrocellulose Membranes," April 26, 2023.

Notes: The source refers to "PCR test" as "Nucleic Acid Test." In an antigen test, the antibodies are attached to the surface of a paper-like material, known as a nitrocellulose sheet or membrane. A patient's liquid sample interacts with the antibodies as it flows along the surface of the sheet through a process known as capillary action. This common diagnostic technique is known as a "lateral flow test."

²⁷⁵ PCR tests are sometimes referred to as "molecular tests" or "nucleic acid tests."

²⁷⁶ Rapid antigen tests are sometimes referred to as "rapid tests," "rapid diagnostic tests," "rapid antigen self-tests," or "RDTs." Blood (serological) tests were a component of testing capabilities in previous stages of the pandemic but are no longer routine for diagnosis because they do not detect an active SARS-CoV-2 infection.

²⁷⁷ Assays are scientific experiments performed to detect the presence of a specific item. In the case of COVID-19, an assay is often synonymous with "test" in that it is an experiment to detect the presence of SARS-CoV-2 cells. An assay also means to conduct such an experiment. Montgomery, "Defining COVID-19 Terms: Assay," April 9, 2022.

²⁷⁸ For more information on how this type of test functions, see USITC, *COVID-19 Related Goods*, December 2020, 148; Goodman, *COVID-19 Testing Supplies*, May 2021, 4–5.

²⁷⁹ For more information on how this type of test functions, see Goodman, *COVID-19 Testing Supplies*, May 2021, 6.

²⁸⁰ For the purposes of this report, a test kit refers to a kit that consists of a variety of protocol-specific reagents to test for COVID-19, often including sample collection materials, primer-probes mixes, and positive controls. USITC, *COVID-19 Related Goods*, December 2020, 147.

In general, PCR tests are considered to have greater sensitivity and specificity but require more robust medical infrastructure and capital.²⁸¹ Antigen tests are considered to be faster and usable in any environment but are less reliable, i.e., have a greater probability of false negative or false positive results. Regardless of manufacturer, all tests within the two categories function in the same fundamental way and provide the same information (table 4.1). Globally, more than 700 PCR tests and 1,000 antigen tests for detecting COVID-19 are currently on the market.²⁸²

Table 4.1 Available COVID-19 tests in the United States

EUA = Emergency Use Authorization

Type of test	Collection method	Active EUAs (number)	Manufacturers (number)	Example manufacturers
PCR	Swab	278	206	Abbott, BD, Qiagen, Roche
Antigen	Swab	64	45	Abbott, BD, Qiagen
Serology	Blood draw	83	58	Abbott, Qiagen, Roche
Other	Other	1	1	InspectIR Systems

Sources: FDA, “In Vitro Diagnostics EUAs - Molecular Diagnostic Tests for SARS-CoV-2,” updated May 31, 2023; FDA, “In Vitro Diagnostics EUAs - Antigen Diagnostic Tests for SARS-CoV-2,” updated May 31, 2023; FDA, “In Vitro Diagnostics EUAs - Serology and Other Adaptive Immune Response Tests for SARS-CoV-2,” updated May 8, 2023; FDA, “In Vitro Diagnostics EUAs - Other Tests for SARS-CoV-2,” February 16, 2023.

Both types of tests require materials and services to deliver results.²⁸³ Collecting a sample from a patient for either a PCR test or a rapid antigen test typically involves a nasopharyngeal swab to gather material and a plastic tube containing viral transport medium²⁸⁴ in which to deposit it.²⁸⁵ PCR tests require additional RNA extraction kits²⁸⁶ and consumable reagents once the sample arrives at a laboratory, as well as diagnostic instruments operated by a trained technician.²⁸⁷ In contrast, antigen tests are processed immediately using a cassette preloaded with the necessary reagents so that users need only add their samples and await the results.

The instruments used in conducting a PCR test depend on whether the test is automated or manual. Automated tests are typically performed on platform devices, which are complex instruments combining hardware, software, and chemistries.²⁸⁸ These devices integrate and automate time-intensive steps such as sample preparation, DNA amplification, and detection, therefore requiring limited hands-on skill and technician time.²⁸⁹ These tests operate in closed systems, meaning they are platform specific and not

²⁸¹ USITC, *COVID-19 Related Goods*, December 2020, 148.

²⁸² PCR test counts can be found within the FIND test directory data by selecting “assay target” = “RNA,” and antigen test counts can be found by selecting “assay target” = “antigen.” FIND, “COVID-19 Test Directory,” June 25, 2023.

²⁸³ NAM, *Emerging Stronger*, 2022, 340.

²⁸⁴ Viral transport medium is a buffered salt solution with preservatives to prevent bacterial or fungal growth. Goodman, *COVID-19 Testing Supplies*, May 2021, 11.

²⁸⁵ USITC, *COVID-19 Related Goods*, December 2020, 157–59; Goodman, *COVID-19 Testing Supplies*, May 2021, 7–13, 21–24.

²⁸⁶ An RNA extraction kit is used in the majority of PCR tests to isolate and purify the COVID-19 genetic material. These kits are not a single, unique product, but are sets of consumable plastic laboratory materials (small centrifuge tubes, filters, and collection vials) and chemical reagents (solutions for breaking the virus apart and purification) assembled by a manufacturer. Goodman, *COVID-19 Testing Supplies*, May 2021, 15.

²⁸⁷ Goodman, *COVID-19 Testing Supplies*, May 2021, 15–21, 24–26.

²⁸⁸ AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5.

²⁸⁹ Danaher Corporation, *Form 10-K 2022*, December 31, 2022, 16; WHO, “Diagnostics - Technical Frequently Asked Questions,” 1, accessed April 17, 2023.

interoperable with devices from other manufacturers.²⁹⁰ As the name suggests, manual test kits require more manual steps and the technician performing the procedure must be more hands-on. Manual tests are typically performed on open systems, however, which are interoperable with a variety of testing devices.²⁹¹

Therapeutics

The search for effective therapeutics to treat SARS-CoV-2 is ongoing. Broadly speaking, relevant COVID-19 therapeutics may be classified into two distinct categories: (1) small-molecule drugs and (2) biological products (biologics).²⁹² Traditionally, small-molecule drugs have been the cornerstone of modern medicine and account for a large share of pharmaceuticals currently marketed.²⁹³ Small-molecule drugs generally have more predictable action, involve simpler manufacturing processes, and are often administered as oral formulations.²⁹⁴ Biologics, a comparatively newer field of drugs and therapies, currently represent a small share of pharmaceuticals on the market. In 2019, it was estimated that small-molecule drugs constituted as much as 90 percent of drug sales.²⁹⁵

The share of biologics on the market, however, is growing as new therapeutics reach the market.²⁹⁶ Biologics are typically more expensive because of more complex manufacturing processes, are more fragile to store and transport, and are available solely as intravenous injections.²⁹⁷ Small-molecule drugs can be novel (also referred to as innovative) or generic, and biologics are generally classified as novel or biosimilar.²⁹⁸ Both small-molecule and biologic therapeutics have been studied for the treatment of

²⁹⁰ Examples of automated test kits include the Abbott Realtime SARS-CoV-2 tests, the Cepheid Xpert Xpress SARS-CoV-2 test, and the Roche cobas SARS-CoV-2 Qualitative assay. Their associated platforms are the Abbott m2000, the Cepheid GeneXpert, and the Roche cobas 6800/8800, respectively. WHO, *Diagnostics - Technical Frequently Asked Questions*, 2, accessed April 17, 2023.

²⁹¹ Examples of manual test kits are the BGI Real-time fluorescent RT-PCR kit for detecting 2019-nCoV and the Thermo Fisher TaqPath COVID-19 kit. The BGI kit, for instance, is interoperable with software and devices from Applied Biosystems, ABI, Roche, and QuantStudio, and also requires standard lab equipment such as a vortex mixer and a microcentrifuge. BGI Genomics Co. Ltd., *Real-Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2 Instructions for Use*, April 2022, 7.

²⁹² Traditional Medicines represents another category of treatments that can and have been patented and used to treat COVID-19. USITC, *COVID-19 Related Goods*, December 2020, 135; WIPO, *COVID-19-Related Vaccines and Therapeutics: Preliminary Insights*, 2022, 37.

²⁹³ USITC, *COVID-19 Related Goods*, December 2020, 135–36; Makurvet, “Biologics vs. Small Molecules,” March 2021.

²⁹⁴ Oral formulations in this case refer to pills or tablets. USITC, *COVID-19 Related Goods*, December 2020, 135–36.

²⁹⁵ USITC, *COVID-19 Related Goods*, December 2020, 135–36; Makurvet, “Biologics vs. Small Molecules,” March 2021, 4.

²⁹⁶ USITC, *COVID-19 Related Goods*, December 2020, 135–36; Makurvet, “Biologics vs. Small Molecules,” March 2021.

²⁹⁷ USITC, *COVID-19 Related Goods*, December 2020, 135–36; Makurvet, “Biologics vs. Small Molecules,” March 2021.

²⁹⁸ Although generic drugs and biosimilars are approved through abbreviated pathways, the approval requirements are different. A generic drug must have the same characteristics as an existing approved brand-name drug (i.e., dosage, administration, safety, strength, quality, and performance). A biosimilar is a biological product that must be “highly similar” to an existing, already approved reference product and must have no meaningful differences from the existing product. USITC, *COVID-19 Related Goods*, December 2020, 136–137; Makurvet, “Biologics vs. Small Molecules,” March 2021.

COVID-19.²⁹⁹ Despite differences between small-molecule drugs and biologics, all drugs (novel, generic, and biosimilar) have an active pharmaceutical ingredient (API) that is the basis of the finished dosage product.³⁰⁰

The therapeutics discussed in this chapter are directed at the SARS-CoV-2 virus (i.e., virus-directed), have been prescribed as treatment for patients infected with COVID-19, and experienced demand (either for the finished product or for licensure to manufacturing) during the COVID-19 pandemic.³⁰¹ They are also all subject to patents or pending patent applications. It should be noted that specific discussion of virus-directed monoclonal antibodies (mAbs), a type of biologic that was initially used to treat COVID-19, is more limited because as of early 2023, the Omicron stage of the pandemic, virus-directed mAbs were generally no longer prescribed for, in part, because of waning efficacy.³⁰² Table 4.2 highlights the COVID-19 therapeutics discussed in this chapter.³⁰³ These virus-directed drugs target different parts of the virus structure, which helps explain the differences in efficacy and why some drugs are no longer recommended as therapeutics for COVID-19.³⁰⁴

Table 4.2 Virus-directed COVID-19 therapeutics by trade name, international nonproprietary name, form of administration, and category

Lilly = Eli Lilly and Company; Vir = Vir Biotechnology; GSK = GlaxoSmithKline; ensitrelvir = ensitrelvir fumaric acid.

Trade name (manufacturer)	International nonproprietary name (INN)	Form of administration	Category
Paxlovid (Pfizer)	nirmatrelvir (+ ritonavir)	Pill	Small molecule
Veklury (Gilead)	remdesivir	Infusion	Small molecule
Lagevrio (Merck)	molnupiravir	Pill	Small molecule
Xocova (Shionogi)	ensitrelvir	Pill	Small molecule
Bebtelovimab (Lilly)	bebtelovimab	Infusion	Biologic
Xevudy (GSK, Vir)	sotrovimab	Infusion	Biologic
Bamlanivimab and etesevimab (Lilly)	bamlanivimab and etesevimab	Infusion	Biologic
REGEN-COV (Regeneron, Roche)	casirivimab and imdevimab	Infusion	Biologic

Sources: Shionogi, “Shionogi Receives U.S. FDA Fast Track Designation for Ensitrelvir Fumaric Acid, an Investigational Oral Antiviral for COVID-19,” accessed June 11, 2023; Shionogi, “Xocova (Ensitrelvir Fumaric Acid) Tablets 125mg Approved in Japan,” accessed August 27, 2023; Lamontagne et al., “A Living WHO Guideline on Drugs,” updated January 12, 2023; FDA, “Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products,” July 19, 2023; FDA, “Coronavirus (COVID-19): Drugs,” March 10, 2023.

Notes: For more information on the categories of therapeutics see chapter 3.

²⁹⁹ Despite the general distinction between small-molecule drugs and biologics, when reviewing patents, some therapeutics under development are designated as both. WIPO, *COVID-19-Related Vaccines and Therapeutics: Preliminary Insights*, 2022, 11, 47.

³⁰⁰ USITC, *COVID-19 Related Goods*, December 2020, 136; WHO, “Glossary,” accessed September 29, 2023.

³⁰¹ The analysis in this chapter will not focus on drugs that were or are prescribed as part of clinical management of a COVID-19 infection (e.g., immune modulators). The parameters for therapeutics were chosen largely because of data availability and include the most commonly demanded COVID-19 therapeutics.

³⁰² Vangeel et al., “Remdesivir, Molnupiravir and Nirmatrelvir Remain Active,” January 24, 2022.

³⁰³ These example therapeutics are also highlighted in chapters 3 and 5.

³⁰⁴ For more on modes of actions of the COVID-19 antivirals and mAbs, see chapter 3.

Production, Market Segmentation, and Trade

The pharmaceutical industry, including manufacturers producing diagnostics and therapeutics, tends to be multinational in its operations, from research and development (R&D) to commercial production. Manufacturers tend to rely on complex global supply chains, spanning multiple countries and continents. This multinational aspect is driven by several factors, including the need for large-scale production at multiple locations and in multiple countries to optimize production efficiency, be close to key markets, and provide security of supply; and for tax and regulatory reasons.

Additionally, the differences between individual countries and regions, expertise, resources, and regulatory frameworks in turn contribute to the segmentation of production that then dictates trade flows (i.e., where the product is coming from and where the orders are going) (box 4.1).³⁰⁵ Furthermore, the pharmaceutical industry commonly has collaborations and partnerships across borders that facilitate knowledge sharing, the pooling of resources, and innovation.

Box 4.1 Pharmaceutical Manufacturing in the United States

Pharmaceutical manufacturing in the United States varies significantly in the extent of vertical integration at each plant: some perform operations ranging from research and development to formulation, but others fulfill only one or more of the specific steps in the production process.^a The industry also includes establishments that engage in contract manufacturing for other firms.^b Production facilities take an average of five years to begin operations, although the amount of time varies depending on the final drug formulation and form of administration (e.g., oral versus intravenous).^c Once facilities are established, capacity is not necessarily dedicated to a specific drug, and capacity (as well as production level) depends on the product (e.g., small-molecule versus biological products, generic versus novel).^d Pharmaceuticals described in this section include the products of four industry groups, as classified by the North American Industry Classification System (NAICS). The NAICS industries selected for inclusion are the primary NAICS classification codes for pharmaceuticals identified by the Commission in its June 2020 and December 2020 reports on COVID-19-related goods (box table 4.3).

According to data from the U.S. Bureau of Labor Statistics, the U.S. pharmaceutical industry comprises nearly 5,000 establishments, with manufacturing concentrated in areas with significant production of upstream chemicals (e.g., Texas and New Jersey) or with significant biotechnology/biomedical clusters (e.g., California, Florida, Massachusetts, New York, and Texas).^e U.S. facilities generally include production sites engaged in various steps of pharmaceutical production, including API (also known as drug substance), production, formulation, and fill and finish.^f Also, in some instances, biotechnology small- and medium-sized enterprises (SMEs) have teamed up with larger firms in strategic alliances to develop and market their products.^g These consolidations and agreements are intended to help ensure a pipeline of new products, extend product portfolios, reduce risk for the developing company, diversify geographic reach, and mitigate losses from patent expirations.^h

³⁰⁵ Box 4.1 only addresses manufacturing in the United States and does not address the extent to which global pharmaceutical manufacturing is based in the United States or in other countries. As discussed later in this chapter, the top three countries with the highest number of manufacturers as enumerated through production agreements are India, Bangladesh, and China.

Box Table 4.3 Pharmaceutical industry coverage, by NAICS code

NAICS	Description	Examples
325411	Medicinals and botanicals	Uncompounded medicinal and botanical chemicals and their derivatives (i.e., generally for use by pharmaceutical preparation manufacturers). These are typically bulk active pharmaceutical ingredients (APIs).
325412	Pharmaceutical preparations	In vivo diagnostic substances and pharmaceutical preparations (except biological) intended for internal and external consumption in dose forms (e.g., ampoules, tablets, capsules, vials, ointments, powders, solutions, and suspensions).
325413	In vitro diagnostic substances	In vitro (i.e., not taken internally) diagnostic substances (e.g., chemical, biological, or radioactive substances) used for diagnostic tests that are performed in test tubes, petri dishes, machines, etc.
325414	Biological products (except diagnostic)	Vaccines, toxoids, blood fractions, and culture media of plant or animal origin (except diagnostic).

Source: NAICS Association, <https://www.naics.com/>; SICCODE Business Data, <https://siccode.com/>.

^a In general, in vitro diagnostic establishments are concentrated in advanced biotechnology R&D sectors, for access to skilled labor and IP.

^b USITC, *COVID-19 Related Goods*, December 2020, 136.

^c USITC, *COVID-19 Related Goods*, December 2020, 137.

^d Traditionally, small-molecule drugs are manufactured via batch processing, but some manufacturers have adopted continuous processing, reducing time from API production to final formulation from months to days. By comparison, going from API production to formulation for a batch of monoclonal antibodies (biologic) can take anywhere from 30 to 90 days. USITC, *COVID-19 Related Goods*, December 2020, 137.

^e An establishment is defined as a single physical location at which business is conducted or services or industrial operations are performed. The U.S. in vitro diagnostics industry is heavily concentrated (27 percent) in California. BLS, “Quarterly Census of Employment and Wages,” preliminary annual estimate 2022; USITC, *COVID-19 Related Goods*, December 2020, 137.

^f Companies routinely evaluate the economics and location of existing production capacity, assessing factors such as market access; location(s) of drug approvals; employee skills, availability, and labor costs; financial incentives; and duty rates, among others. Many firms have several production facilities within the United States. USITC, *COVID-19 Related Goods*, December 2020, 137.

^g USITC, *COVID-19 Related Goods*, December 2020, 138.

^h USITC, *COVID-19 Related Goods*, December 2020, 138.

Diagnostics

Development

The process for pharmaceutical production involves several stages, starting with R&D. Although the pandemic was not declared until March 2020, the virus had been identified and sequenced in mid-January 2020. As soon as a genomic structure was sequenced and verified, the development of a diagnostic test for infection of SARS-CoV-2 started worldwide. The first diagnostic test was developed by a group of researchers in Germany; the protocol was published on January 22, 2020, and was soon adopted by the World Health Organization (WHO) to serve as a guideline for diagnostic laboratories around the world.³⁰⁶

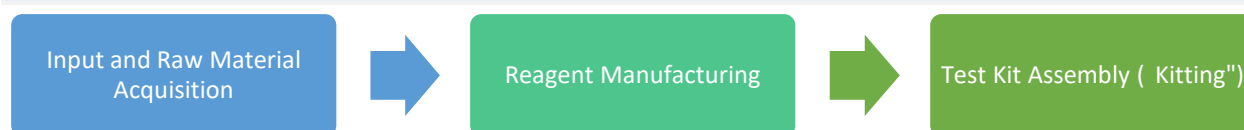
³⁰⁶ The work was done at the Deutsche Zentren Der Gesundheitsforschung (DZIF) working under the leadership of Christian Drosten (Director of the Institute of Virology on Campus Charité Mitte). Drosten helped develop the novel Zika virus tests and the standard test for the MERS (Middle East Respiratory Syndrome) pathogen, which are now used worldwide. He is also credited as one of the codiscoverers of the SARS (severe acute respiratory syndrome) virus in 2003. Corman et al., “Detection of 2019 Novel Coronavirus (2019-NCoV) by Real-Time RT-PCR,” January 22, 2020; DZIF, “Researchers Develop First Diagnostic Test for Novel Coronavirus in China,” January 16, 2020; FDA, *South Korea’s Response to COVID-19*, March 3, 2020, 8.

Generally, the R&D process for the private diagnostics industry consists of four phases: conceptualization, feasibility and design, validation, and regulatory approval.³⁰⁷ Conceptualization focuses on identifying a product to address the unmet diagnostic need, which may involve detecting a new disease, measuring biomarkers, and gathering relevant research. During feasibility and design, companies evaluate the materials and manufacturing processes involved in production of the new product.³⁰⁸ Validation requires comparing the performance of a new test to an existing one.³⁰⁹ Regulatory approval requires submitting the newly developed test to the relevant regulatory bodies for approval. Afterward, the product enters the manufacturing and distribution stage, which involves the scaling up of production and establishment of supply chains. Except for during national and global health emergencies, this process typically takes three to five years for a new test and five to seven years for a new testing platform.³¹⁰

Manufacturing

The manufacturing supply chain for both polymerase chain reaction (PCR) and antigen test kits has three main components: acquisition of inputs and raw materials, reagent manufacturing, and assembly of the final test kit (figure 4.2). Some companies engage in activities across the entire supply chain. Reagent manufacturing, however, involves more complex processes and is typically done by specialized companies.³¹¹ This leads many manufacturers, particularly in LMICs, to focus on the largely manual stage of test kit assembly (“kitting”) (box 4.2).³¹²

Figure 4.2 Overview of COVID-19 test kit manufacturing stages



Source: Compiled by the USITC.

³⁰⁷ Industry representative, email message to USITC staff, May 23, 2023; Abbott, *Form 10-K 2022*, December 31, 2022, 32.

³⁰⁸ A company may develop two tests for different markets, using established manufacturing capacity and supply chains. For example, Abbott’s BINAXNOW is the company’s U.S. rapid antigen test, but its Panbio is used internationally, especially in lower- and middle-income countries. The underlying technology in the tests is the same, but BINAXNOW uses a paper card and Panbio uses a traditional plastic cassette. Internationally, established manufacturing facilities produce cassette HIV tests, and those facilities had the ability to pivot and scale up production more quickly for COVID-19. Industry representative, interview by USITC staff, June 1, 2023; Abbott, “BinaxNOW COVID-19 Antigen Self-Test,” accessed June 11, 2023; Abbott, “Panbio COVID-19 Ag Rapid Test Device,” accessed June 11, 2023.

³⁰⁹ Typically, run against a CDC standard test.

³¹⁰ Incremental changes, which improve upon foundational technologies, are said to occur every 2–3 years. AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representative, interview by USITC staff, June 28, 2023.

³¹¹ Heil, “What’s a ‘Reagent,’” April 18, 2020; industry representative, email message to USITC staff, May 23, 2023.

³¹² MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 2.

Quality control assessments are performed throughout the manufacturing process. Calibration and validation, through repeated testing, ensure safety and efficacy of reagents and the final test kits.³¹³ Because of the number of components involved in the manufacturing process for both types of tests, quality control standards and regulations make transferring technology and ensuring consistency difficult.³¹⁴

Inputs

The inputs required for a COVID-19 test can be divided into three categories: sample collection materials, reagents, and equipment. For PCR tests, the sample collection requires a swab, typically made of synthetic fibers or flocked materials, and a viral transport medium.³¹⁵ Reagents needed for PCR tests include primers, probes, nucleotides, enzymes, and buffers.³¹⁶ The primers and probes, often included in an RNA extraction kit, are designed to specifically isolate and purify the genetic material of SARS-CoV-2. Equipment required to perform PCR tests includes PCR machines or thermal cyclers and associated lab equipment for the amplification and detection process (box 4.2).

Rapid antigen tests require similar inputs to PCR tests, with slight variation. The sample collection materials also include a swab and may require a transport medium or extraction buffer. The reagents needed for an antigen test are antibodies conjugated to a reporter molecule, typically a dye or fluorescent molecule.³¹⁷ An antigen test requires a lateral flow assay device, typically a plastic cassette containing a nitrocellulose sheet.³¹⁸

³¹³ Additionally, monitoring software keeps track of operational efficiency. Industry representative, email message to USITC staff, May 23, 2023; industry representative, interview by USITC staff, May 31, 2023.

³¹⁴ Moving a facility only a number of miles took one U.S. manufacturer 2.5 years in order for the facility to be fully operational and compliant with regulatory requirements. Industry representative, interview by USITC staff, May 31, 2023.

³¹⁵ Sample collection kits typically also contain plastic consumables, such as disposable plastic vials and pipettes. For more information on the market for swabs, viral transport media, and plastic consumables, see Goodman, *COVID-19 Testing Supplies*, May 2021, 7–24; industry representative, email message to USITC staff, May 23, 2023.

³¹⁶ One reagent commonly used in PCR tests is taq polymerase. This heat-stable DNA polymerase automates the step of amplifying DNA sequences during the PCR process referred to in figure 4. The patent for taq polymerase expired in 2005. Industry representative, email message to USITC staff, May 23, 2023; Aliouche, “What Is Taq Polymerase?,” January 24, 2022; Economist, “Patent Ending,” April 7, 2005.

³¹⁷ These “antibodies” can be mAbs, which is a slight overlap in terms of input material between diagnostics and therapeutics. Mark et al., “Expression of Mammalian Proteins for Diagnostics and Therapeutics,” November 2022; Schardt et al., “Discovery and Characterization of High-Affinity,” October 20, 2021; Siddiqui, “Monoclonal Antibodies as Diagnostics,” 2010; industry representative, email message to USITC staff, May 23, 2023.

³¹⁸ The lateral flow assay device is typically included in an antigen test kit. Industry representative, email message to USITC staff, May 23, 2023; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 8.

Box 4.2 Instrumentation and Related Supplies for Diagnostics

The instruments and platform devices used for polymerase chain reaction (PCR) testing are typically sold separately from the test kits themselves. These devices contain a wide range of components such as metals, plastics, semiconductors, and software.^a Each of these components is highly specialized and has its own supply chains and market for production.

The devices for manual PCR testing typically use the sample collection materials, RNA extraction kits, and the primers and probes contained in a PCR test kit, but automated PCR machines require more specialized inputs.^b Often, automated PCR tests, such as Cepheid's GeneXpert platform, use a cartridge-based system.^c Each test, such as the Xpert Xpress SARS-CoV-2 test, requires a single-use disposable cartridge containing the necessary reagents to host the testing process.^d The plastic cartridges are typically manufactured using precision injection molding.^e The cartridges are then sent to a second facility where liquid and dry reagents are deposited using an automated filling line.^f

^a Industry representative, email message to USITC staff, May 23, 2023.

^b USITC, *COVID-19 Related Goods*, December 2020, 147–150.

^c See chapter 2 for more information on the GeneXpert platform.

^d Cepheid, *Xpert Xpress SARS-CoV-2: Instructions for Use*, accessed April 13, 2023, 4. These cartridges could be considered analogous to the pods or K-Cups used in single-serve coffee machines or the ink cartridges used in ink jet printers.

^e Cepheid, "Learn How Cepheid's Xpert(R) Xpress SARS-CoV-2 Test Cartridge Is Made & How It Works," accessed May 8, 2023.

^f The mixing of these reagents within the cartridge initiates the amplification process of the test.

Reagent Manufacturing

The reagents required in COVID-19 test kits are produced through a combination of biological, chemical, and manufacturing processes.³¹⁹ Primers and probes are designed using bioinformatics tools³²⁰ and are chemically synthesized by specialized companies. The enzymes are produced through recombinant DNA technology.³²¹ The buffers and other chemicals used are produced by chemical synthesis or extracted from biological sources.³²²

The antibodies used in antigen tests are produced using a three-stage process.³²³ First, animals (typically mice) are immunized with the target viral protein in order for their immune systems to produce antibodies. Second, the antibody-producing cells are extracted and fused with immortalized cells³²⁴ yielding hybridoma cells.³²⁵ Lastly, the hybridoma cells are cultured in bioreactors where they secrete

³¹⁹ Industry representative, email message to USITC staff, May 23, 2023.

³²⁰ Bioinformatics is the application of computation and analysis tools to biological data. These tools are typically computer software, which perform sequence analysis of DNA and proteins. Bayat, "Science, Medicine, and the Future: Bioinformatics," April 27, 2002, 1018–19.

³²¹ Recombinant DNA technology uses enzymes and laboratory techniques to manipulate and isolate segments of DNA. National Human Genome Research Institute, "Recombinant DNA Technology," May 16, 2023.

³²² Domestic producers of reagents used in PCR tests include Roche, Promega, IDT, Becton Dickinson (BD), and Qiagen. Qiagen is a European-headquartered company with manufacturing facilities in the United States. USITC, *COVID-19 Related Goods*, December 2020, 153.

³²³ Industry representative, email message to USITC staff, May 23, 2023.

³²⁴ Immortalized cells are cells that can survive and continue to produce proteins outside the human body. Pfizer, "The 'Immortalized' Cells That Sparked an International Incident," accessed June 8, 2023.

³²⁵ Hybridoma cells can produce large amounts of antibodies. Industry representative, email message to USITC staff, May 23, 2023.

the antibodies, which are purified via chromatography techniques.³²⁶ The purified antibodies are then sprayed onto the nitrocellulose sheet contained in the rapid test cassette or card.³²⁷

The Finished Test Kit

The manufacture of reagents is a combination of manual and automated processing. Packaging of the final COVID-19 test kit is a largely labor-intensive process, even when automation is involved.³²⁸ The process of kitting is typically done in either a moving assembly line or in a station-type setup, whereby workers at each station perform an assigned step on multiple test kits at a time.³²⁹ Some manufacturers produce most, if not all, of the necessary inputs for their test kits, but others focus on kitting inputs procured from external suppliers.³³⁰ The lifecycle of production from raw materials to a final test kit is estimated to be about three to six months.³³¹

Manufacturing Costs and Regulations

The exact cost to manufacture COVID-19 test kits is not publicly known or available to the Commission.³³² The supply chains and production processes vary by both manufacturer and product. One estimate by British manufacturer Mologic, however, places the cost of producing a rapid antigen test kit around \$2.³³³ In general, the primary contributors to production costs are raw materials, capital investments, labor, transportation, and regulatory compliance.

Diagnostics manufacturers must comply with regulations and standards from a variety of domestic and international regulatory bodies. Domestically, some of the most fundamental regulations include the Food and Drug Administration's (FDA's) Current Good Manufacturing Practice (CGMP), Medical Device Reporting, and Quality System regulation.³³⁴ The CGMP contains minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packaging a drug product.³³⁵ Under the Medical Device Reporting regulation, medical device manufacturers are required to report to the FDA when they learn that any of their devices may have contributed to a serious death or injury.³³⁶ Quality System regulation provides requirements for the establishment and maintenance of a quality management system.³³⁷

³²⁶ Chromatography is a method by which a mixture is separated by distributing its components between a stationary phase and a mobile phase. Chemistry LibreTexts, "Chromatography," accessed May 24, 2023.

³²⁷ Industry representative, interview by USITC staff, May 31, 2023.

³²⁸ Industry representatives, interviews by USITC staff, May 31, and June 1, 2023.

³²⁹ Industry representative, interview by USITC staff, May 31, 2023.

³³⁰ Industry representative, interview by USITC staff, May 31, 2023; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 8.

³³¹ Industry representative, interview by USITC staff, May 31, 2023.

³³² Cerullo, "COVID-19 Test Providers Reap Profits," accessed June 11, 2023.

³³³ O'Donnell, "Rapid COVID-19 Tests Increasingly Scarce," October 5, 2021.

³³⁴ Danaher Corporation, *Form 10-K 2022*, December 31, 2022, 28; Hologic, Inc., *Form 10-K 2022*, September 24, 2022, 15; Quidel, *Form 10-K 2022*, January 1, 2023, 22–24.

³³⁵ FDA, "Current Good Manufacturing Practice (CGMP) Regulations," November 16, 2022.

³³⁶ FDA, "Mandatory Reporting Requirements: Manufacturers, Importers and Device User Facilities," May 22, 2020.

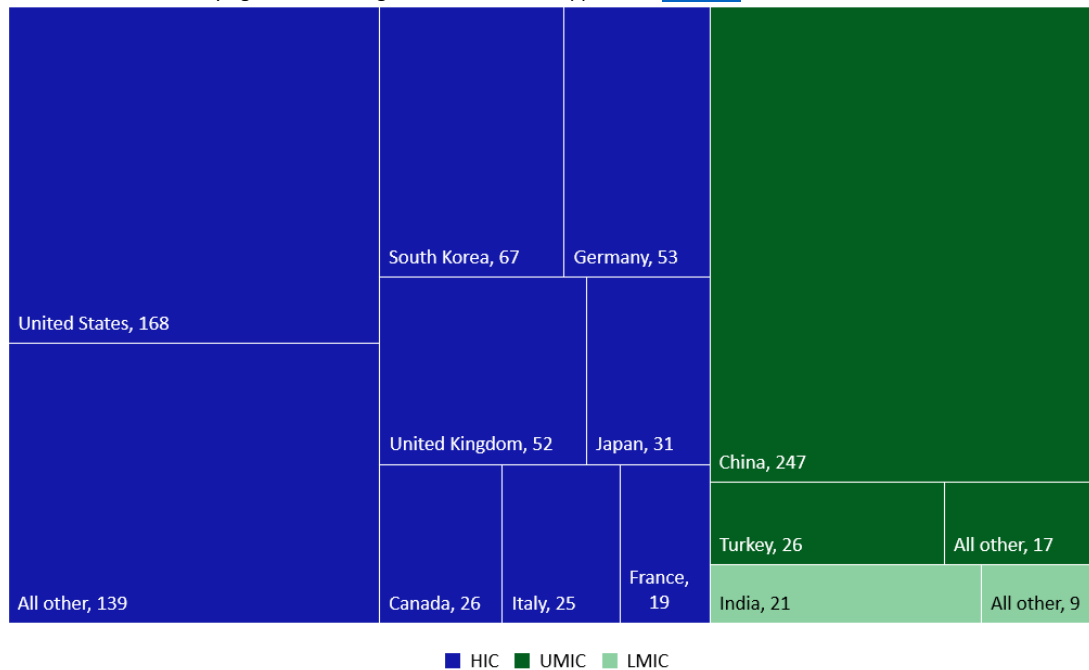
³³⁷ FDA, "Quality System (QS) Regulation/Medical Device Good Manufacturing Practices," February 23, 2022.

Global Production

COVID-19 diagnostics manufacturing, ranging from reagent manufacturing to kitting, occurs worldwide. As of June 2023, according to the Foundation for Innovative Diagnostics (FIND), 900 COVID-19 diagnostics manufacturers were operating in 53 countries (figure 4.3).³³⁸ The majority of manufacturers have headquarters in HICs, such as Roche (Switzerland), Abbott (United States), Cepheid (United States), Hologic (United States), and Thermo Fisher (United States) (box 4.3).³³⁹ UMIC-headquartered manufacturers are concentrated in China, which also has the highest number of manufacturers worldwide, and India is home to the largest number of manufacturers headquartered in LMICs. No manufacturing was reported in LICs, according to source data.³⁴⁰

Figure 4.3 Number of COVID-19 diagnostics manufacturers by country income class and country as of June 30, 2022

Shaded area represents number of manufacturers. HIC = high-income countries, UMIC = upper-middle-income countries, LMIC = lower-middle-income countries. Underlying data for this figure can be found in appendix J, [figure J.8](#).



Source: FIND, “COVID-19 Test Directory,” June 25, 2023.

Notes: Manufacturers are classified by headquarters location; countries’ income classes are based on World Bank classifications.

³³⁸ The FIND database does not indicate whether these manufacturers are separate companies or also include multiple manufacturing facilities of single companies. FIND identified more than 2,000 COVID-19 test kit products from these manufacturers. FIND, “COVID-19 Test Directory,” June 25, 2023.

³³⁹ Cepheid, Hologic, Roche, and Abbott are the largest suppliers of automated PCR tests to the ACT-Accelerator, and Thermo Fisher was one of the two largest suppliers of manual PCR tests in 2021. Abbott is also a major producer of rapid antigen self-tests authorized by both the WHO and the FDA. PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 11; WHO, *Diagnostics - Technical Frequently Asked Questions*, 1, accessed April 17, 2023; WHO, *WHO Emergency Use Listing for In Vitro Diagnostics (IVDs) Detecting SARS-CoV-2*, May 5, 2023, 1; FDA, “In Vitro Diagnostics EUAs - Antigen Diagnostic Tests for SARS-CoV-2,” accessed April 11, 2023.

³⁴⁰ FIND, “COVID-19 Test Directory,” June 25, 2023.

Box 4.3 U.S. Manufacturing and Employment

COVID-19 diagnostic manufacturing occurs worldwide, and the United States accounts for more than 40 percent of the global \$57 billion in vitro diagnostics market and is home to the second-largest number (after China) of COVID-19 diagnostics manufacturers.^a According to AdvaMed, the wider medical devices industry directly supports more than 400,000 jobs in the United States across all 50 states and indirectly supports about 2 million jobs.^b Diagnostics producers are generally unable to distinguish between COVID-19-specific jobs and jobs in their industry more broadly.^c U.S. employment in the in vitro diagnostics sector, however, expanded by 14 percent between 2019 and 2021.^d The vast majority of these newly created jobs were likely attributable to COVID-19. Box table 4.4 lists a few of the largest diagnostics manufacturers in the United States by location. U.S. production reportedly peaked in February 2022 with 900 million test kits being produced that month.^e

Box Table 4.4 Six diagnostics manufacturers by U.S. manufacturing locations

Manufacturer	Headquarters location	Example(s) of U.S. facility location
Abbott	U.S.	Des Plaines/Lake Forest, IL
Cepheid	U.S.	Lodi/Sunnyvale, CA
Roche	Switzerland	Branchburg, NJ
Thermo Fisher	U.S.	Lenexa, KS
Qiagen	Germany	Germantown, MD
Quidel	U.S.	Athens, OH

Sources: Abbott, “Locations and Contacts,” accessed August 29, 2023; Cepheid, “Learn How Cepheid’s Xpert(R) Xpress SARS-CoV-2 Test Cartridge is Made & How it Works,” accessed May 8, 2023; Hale, “Thermo Fisher Builds \$40M Coronavirus Test Tube Manufacturing Facility,” August 31, 2020; Roche, “Welcome to Branchburg,” accessed August 29, 2023; Qiagen, “Qiagen Divisions,” accessed June 14, 2023; Quidel, “Locations,” accessed August 29, 2023.

Notes: Many of these manufacturers have multiple facilities across both the United States and globally. Qiagen also has headquarters in the Netherlands and the United States.

^a AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 6; FIND, “COVID-19 Test Directory,” June 25, 2023.

^b AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 1.

^c Industry representative, interview by USITC staff, February 7, 2023.

^d AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 6.

^e Perrone, “Free COVID Testing Will Fade with US Health Emergency in May,” April 11, 2023; Abbott, “Locations and Contacts,” accessed August 29, 2023; Cepheid, “Learn How Cepheid’s Xpert(R) Xpress SARS-CoV-2 Test Cartridge Is Made & How It Works,” accessed May 8, 2023; Hale, “Thermo Fisher Builds \$40M Coronavirus Test Tube Manufacturing Facility,” August 31, 2020; Roche, “Welcome to Branchburg,” accessed August 29, 2023; Qiagen, “Qiagen Divisions,” accessed June 14, 2023; Quidel, “Locations,” accessed August 29, 2023.

Upper-Middle-Income Country (UMIC) Production

China is home to the largest number of COVID-19 diagnostics manufacturers and accounts for the vast majority of manufacturers headquartered in UMICs. China’s BGI Genomics Co. is a leading global producer of PCR tests, accounting for the largest share of manual PCR tests procured by the Supply Consortium in 2021.³⁴¹ One Chinese manufacturer, Andon Health, received multibillion-dollar U.S. Department of Defense contracts to produce rapid antigen self-tests through its California-based

³⁴¹ Specifically, the COVID-19 Diagnostics Consortium, led by the WHO, included the Global Fund to Fight AIDS, Tuberculosis and Malaria; Stop TB Partnership’s Global Drug Facility; PAHO; UNDP; UNICEF; and Unitaid/CHAI. PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 10; WHO, “Procurement Considerations for COVID-19 Diagnostics,” January 2021.

subsidiary iHealth Labs.³⁴² These contracts were part of the U.S. effort to deliver 500 million free COVID-19 self-tests. Chinese manufacturing hubs containing multiple supply chain elements, and strong logistical capabilities allowed Chinese manufacturers like Andon to ramp up production quickly.³⁴³

Outside China, manufacturing in UMICs is more limited and has been supported by international organizations. One such organization, the Access to COVID-19 Tools Accelerator (ACT-A), has provided support to bolster manufacturing capacity in UMICs such as Brazil and South Africa.³⁴⁴ For example, through ACT-A, FIND and Unitaid are supporting a technology transfer from DCN Dx, a diagnostic center the United States, to WAMA Diagnóstica in Brazil.³⁴⁵ Although WAMA Diagnóstica was already an established manufacturer of diagnostics, it could not perform upstream manufacturing processes and relied on imports of semifinished products.³⁴⁶ With equipment, infrastructure, and training from the technology transfer, WAMA Diagnóstica is now able to perform end-to-end manufacture of rapid antigen tests and supply them to Latin America and the Caribbean region.³⁴⁷ Public-private partnerships in Brazil were instrumental in enabling local production. In another case, Abbott, in partnership with Fiocruz, a federal government laboratory, was able to manufacture about 70 million tests.³⁴⁸

Many African countries are reliant on diagnostics imports from China, which over the course of the pandemic led to governments prioritizing local manufacturing.³⁴⁹ In South Africa, an industry representative reported that it costs \$1–2 million to set up a diagnostic manufacturing facility and takes six to nine months to bring the facility online. An additional \$6–7 million was said to be needed to set up protein farms, which are necessary for reagent production. The costs of bringing a diagnostic manufacturing facility online reportedly are much lower than that of a therapeutics or vaccines facility.³⁵⁰

Lower-Middle-Income Country (LMIC) Production

In LMICs, COVID-19 diagnostics manufacturing is largely concentrated in India. The country accounts for 21 of the 30 manufacturers in LMICs, as shown in figure 4.3. Two major local manufacturers of rapid in vitro diagnostics are J. Mitra & Co. and Meril Diagnostics.³⁵¹ In addition to Meril's rapid antigen test, a third firm, 3B BlackBio Biotech, produces a nucleic antigen test that is eligible for procurement by the Global Fund.³⁵² Indian diagnostics manufacturers are also looking to compete in more advanced testing platforms as well. Another Indian manufacturer, Molbio Diagnostics, produces a micro-PCR testing

³⁴² Nathan-Kazis, Brown, "Why the U.S. Contracted with a Chinese Covid Test-Kit Maker You've Never Heard of," March 3, 2022; USDOD, "DOD Awards Contracts to Purchase COVID-19 Antigen Over-the-Counter Test Kits," January 13, 2022.

³⁴³ Nathan-Kazis, Brown, "Why the U.S. Contracted with a Chinese Covid Test-Kit Maker You've Never Heard of," March 3, 2022.

³⁴⁴ ACT Accelerator, *ACT-Accelerator Outcomes Report*, December 14, 2022, 5.

³⁴⁵ Unitaid, "FIND and Unitaid Invest to Support Technology Transfer," July 15, 2021.

³⁴⁶ Nonprofit organization representative, interview by USITC staff, Switzerland, June 8, 2023.

³⁴⁷ Nonprofit organization representative, interview by USITC staff, Switzerland, June 8, 2023.

³⁴⁸ Industry representative, interview by USITC staff, Brazil, June 28, 2023.

³⁴⁹ Industry representative, interview by USITC staff, South Africa, June 28, 2023.

³⁵⁰ Industry representative, interview by USITC staff, South Africa, June 29, 2023.

³⁵¹ Research and Markets, "India Rapid IVD Kits Market Outlook 2022–2027," September 20, 2022.

³⁵² Global Fund, "List of SARS-CoV-2 Diagnostic Test Kits and Equipments Eligible for Procurement," March 28, 2023.

platform called Truelab, which is similar to Cepheid’s GeneXpert. Instead of using cartridges, a typical component, Molbio’s platform modified the process by using microchips preloaded with the necessary ingredients from its Truenat test line. Molbio has been supported by the government through policies favoring the procurement of locally produced products.³⁵³

Outside India, LMICs often rely on imported diagnostic tests from the United States, Europe, and Asia because of limited local manufacturing.³⁵⁴ Manufacturers in LMICs outside Asia often focus on assembly of imported semifinished products and do not produce any raw materials or conduct original test development.³⁵⁵ In many African countries, for example, the manufacture of rapid tests tends to be limited to assembling the test strip within the cassette.³⁵⁶

One major hurdle to local production is the large investments required to support infrastructure, procurement of raw materials, manufacturing setup, and R&D.³⁵⁷ Because of their small production volumes, local manufacturers often fail to attract private investors interested in larger operations with profit-generating products.³⁵⁸ Therefore, funding is typically only available to large companies with existing operations, making market entry difficult for new firms. Additionally, most public and philanthropic grants are too small and short term to scale up and sustain commercial manufacturing sites.³⁵⁹

ACT-A is also providing support to bolster manufacturing capacity in LMICs. Through their support, FIND and Unitaid provided \$40 million to support technology transfer, local production, scaling, and lower prices for COVID-19 rapid antigen tests for two existing manufacturers.³⁶⁰ One example is an agreement to transfer know-how from Bionote (South Korea) and Mologic (United Kingdom) to DiaTROPIX (Senegal) for the manufacture of rapid antigen tests.³⁶¹ Additionally, the Pasteur Institute of Dakar, a nonprofit public health organization, provided DiaTROPIX access to clinical samples, clinical know-how, and clinical support.³⁶² The goal of this technology transfer was to enable DiaTROPIX to perform all stages of the manufacturing process for rapid antigen tests and boost manufacturing capacity in Africa.³⁶³

Trade

Trade in COVID-19 diagnostics is difficult to measure due to the number of inputs that are critical to COVID-19 diagnostic testing, the number of products/goods that are involved in a COVID-19 test kit, and the lack of global harmonization of trade data at a level that is specific to COVID-19. Six Harmonized

³⁵³ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 6; Molbio Diagnostics Pvt. Ltd., “Molbio,” accessed May 31, 2023.

³⁵⁴ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 1.

³⁵⁵ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 2.

³⁵⁶ Public health organization representative, interview by USITC staff, Switzerland, June 6, 2023.

³⁵⁷ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 5.

³⁵⁸ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 5.

³⁵⁹ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 5.

³⁶⁰ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 5.

³⁶¹ Unitaid, “FIND and Unitaid Invest to Support Technology Transfer,” July 15, 2021.

³⁶² Pasteur Network, “Institut Pasteur de Dakar,” accessed May 31, 2023; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 10.

³⁶³ Nonprofit organization representative, interview by USITC staff, June 8, 2023.

System (HS) subheadings could include COVID-19 diagnostics.³⁶⁴ These six HS subheadings cover diagnostics for a range of diseases, and it is difficult to know the extent to which the data reflect mainly COVID-19 diagnostics or other types of diagnostics. The data largely exclude non-kitted ancillary materials (e.g., plastic vials). The primary HS subheading for trade related to COVID-19 diagnostics test kits is 3822.19, which covers certain diagnostic or laboratory reagents.³⁶⁵

HICs contributed 95 percent of world exports of diagnostics, including COVID-19 diagnostics, in 2022 and accounted for 86 percent of world imports (figure 4.4). These data include trade in mAbs and test kits. Although certain mAbs are therapeutics, mAbs can also be used in antigen tests, where they are typically tagged with a dye or fluorescent molecule.³⁶⁶ More specifically, HICs accounted for 78 percent of world exports of test kits and 80 percent of world imports in 2022.³⁶⁷ These countries also provided almost all mAb exports (99 percent) and imports (88 percent).³⁶⁸

Switzerland was the top overall exporter of diagnostics, and it is likely that the majority of its exports for diagnostics were related to mAbs, used in kits (table 4.5).³⁶⁹ Switzerland is home to Roche, which is a major manufacturer of both diagnostics and therapeutics. The top exporters of test kits in 2022 were China (\$11.0 billion), the United States (\$10.6 billion), and Germany (\$7.0 billion).³⁷⁰ The top exporters of trade that included COVID-19 diagnostics in 2022 were Switzerland (\$43.7 billion), Ireland (\$33.4 billion), and Germany (\$35.3 billion).³⁷¹

³⁶⁴ For U.S. trade data of pharmaceuticals by North American Industry Classification System (NAICS), see appendix I. The six HS subheadings are 3821.00, 3822.00, 3822.19, 3002.13, 3002.14, 3002.15.

³⁶⁵ Specifically, 3822.19 covers diagnostic or laboratory reagents (other than those for malaria, zika, or blood grouping) on a backing, prepared diagnostic or laboratory reagents, whether or not on a backing, whether or not put up in the form of kits. For more information on the classification of the subheadings related to COVID-19 diagnostics, see appendix F.

³⁶⁶ Mark et al., “Expression of Mammalian Proteins for Diagnostics and Therapeutics,” November 2022; Schardt et al., “Discovery and Characterization of High-Affinity,” October 20, 2021; Siddiqui, “Monoclonal Antibodies as Diagnostics,” 2010; industry representative, email message to USITC staff, May 23, 2023.

³⁶⁷ S&P Global, Global Trade Atlas, HS subheadings include 3821.00 and 3822.19, accessed June 6, 2023.

³⁶⁸ S&P Global, Global Trade Atlas, HS subheadings include 3002.13, 3002.14, 3002.15, accessed June 6, 2023.

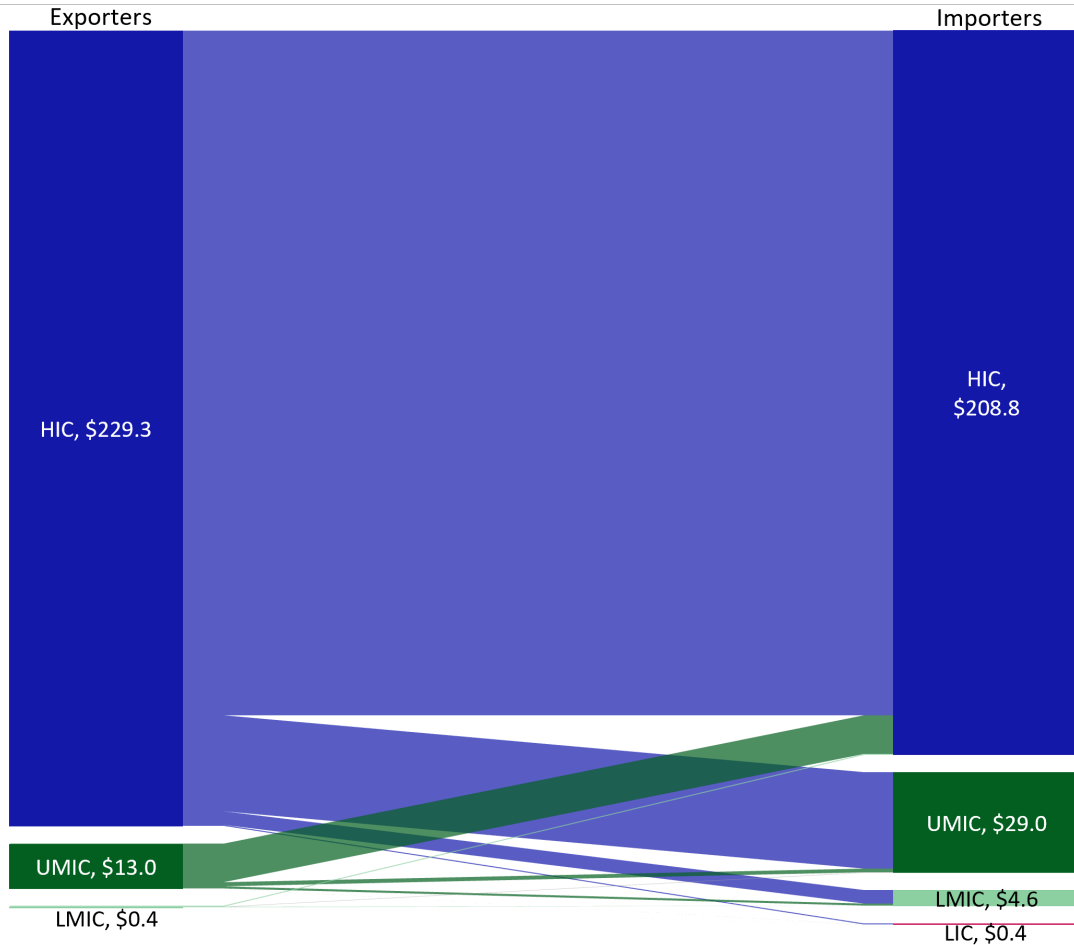
³⁶⁹ Specifically exports under 3002.15 (immunological products, put up in measured doses or in forms or packings for retail sale) amounted to over \$41.7 billion. Trade under HS subheadings 3002.13, 3002.14, 3002.15 are also included in the COVID-19 therapeutics trade estimates since mAbs for therapeutics are also under these subheadings. S&P Global, Global Trade Atlas, HS subheadings 3821.00, 3822.00, 3822.19, 3002.13, 3002.14, 3002.15, accessed September 7, 2023.

³⁷⁰ S&P Global, Global Trade Atlas, HS subheadings include 3821.00 and 3822.19, accessed June 6, 2023.

³⁷¹ S&P Global, Global Trade Atlas, HS subheadings include 3002.13, 3002.14, 3002.15, 3821.00, 3822.00, 3822.19, accessed September 7, 2023.

Figure 4.4 Diagnostics, including COVID-19 diagnostics: exports and imports by income level of exporter (left) and importer (right), 2022

In billions of dollars. HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries. Underlying data for this figure can be found in appendix J, [table J.9](#).



Source: S&P Global, Global Trade Atlas, Harmonized System (HS) subheadings 3821.00, 3822.00, 3822.19, 3002.13, 3002.14, 3002.15, accessed September 7, 2023.

Notes: This figure uses 2022 data because the HS divided and reclassified diagnostics-related codes in 2022, enabling a more detailed analysis of COVID-19-related-diagnostics than in previous years, specifically kits. Although as of 2022, subheading 3822.00 is no longer an active HS subheading, trade was still reported under that subheading due to how data is collected and reported. Data reported are export data by exporters and trade partners (importers).

Table 4.5 Global exports of diagnostics, including COVID-19 diagnostics, by major exporting country, 2018–22

In billions of dollars.

Exporters	2018	2019	2020	2021	2022
Switzerland	26.6	31.7	36.8	40.9	43.7
Ireland	19.7	22.7	30.6	33.7	33.4
Germany	27.1	25.5	30.1	34.5	35.3
United States	19.6	21.4	24.3	29.8	32.6
Netherlands	13.2	12.0	14.5	20.1	18.5
Top 5 exporters	106.2	113.3	136.3	158.9	163.5
All other exporters	42.1	47.6	67.9	84.4	79.3
Total	148.4	160.9	204.2	243.3	242.8

Source: S&P Global, Global Trade Atlas. HS subheadings include 3002.13, 3002.14, 3002.15, 3821.00, 3822.00, 3822.19, accessed September 7, 2023.

Notes: HS subheading 3822.19 was established in 2022, and data for the subheading is only included for the year 2022. Global exports of goods classified under 3822.19 totaled \$47.3 billion in 2022. HS subheading 3822.19 was partially formed in 2022 from four existing subheadings (3002.13, 3002.14, 3002.15, and 3822.00). Trade under 3002.13, 3002.14, and 3002.15 are also included in the COVID-19 therapeutics trade estimates, since mAbs for therapeutics are also under the subheadings.

Therapeutics

Development

In early 2020, as hospitals and healthcare centers around the world became overrun with cases of COVID-19, researchers used the genomic structure of the virus to figure out the types of medicines and modes of action that could be effective in preventing the virus from replicating in patients (i.e., limiting the effects of the COVID-19 infection in the host).³⁷² Nations and pharmaceutical companies put resources behind the development of prophylactic and therapeutic medicines for the novel virus SARS-CoV-2 (COVID-19).³⁷³ The search for efficacious COVID-19 therapeutics continues as of mid-2023.³⁷⁴

Similar to other COVID-19-specific pharmaceuticals, the development of therapeutics specific to the treatment of COVID-19 depended on the identification of the novel virus that causes the infection, SARS-CoV-2, and the virus structure.³⁷⁵ Historically, it has been difficult for researchers to develop a therapeutic drug for a virus (e.g., colds or flu) such as antivirals (a drug for the treatment of a specific

³⁷² Mode of action is defined as the means by which a product achieves its intended therapeutic effect or action in the body. Prophylactics, such as vaccines, are intended to prevent infection and are outside the scope of this investigation. See FDA, “Definition of Primary Mode of Action of a Combination Product,” 70 Fed. Reg. 49848, August 25, 2005.

³⁷³ Even though the declaration of the pandemic was in March 2020, many of the efforts to develop medicines began before the official declaration, such as those by Gilead. Kelley, “Developing Therapeutic Monoclonal Antibodies at Pandemic Pace,” May 2020; Gilead, posthearing brief submission, May 5, 2023, 9; Gilead, “Gilead’s Efforts to Increase Supply of Remdesivir,” accessed September 27, 2023; Pfizer, written submission to the USITC, May 5, 2023, 14; Industry representatives, interviews by USITC staff, March 24, June 5, June 6, June 29, 2023.

³⁷⁴ See chapter 3 for a snapshot of the number of studies for COVID-19 therapeutics that are currently underway.

³⁷⁵ COVID-19 is a coronavirus. Structurally speaking, coronaviruses are irregularly shaped particles, approximately 60–220 nm in diameter, with an outer envelope bearing distinctive, “club-shaped” peplomers that give its “crown-like” appearance. The genomes for the virus contain the longest nonsegmented, single-stranded RNA of any RNA virus. They infect a variety of mammals and birds. Hosmane, “Antiviral Agents,” in *Kirk-Othmer Encyclopedia of Chemical Technology*, June 20, 2003, 138.

virus), and this has been the case for COVID-19.³⁷⁶ Antivirals—such as nirmatrelvir (+ ritonavir), molnupiravir, and remdesivir—can speed recovery, however, and reduce the risk of progression to severe cases.

The effectiveness of the treatment depends on the individual patient and factors such as underlying conditions (e.g., diabetes), and the variant that led to the infection.³⁷⁷ In general, the lack of a single effective therapeutic (i.e., one that has significant measurable efficacy) is due to the virus itself and the continued evolution of the virus into different variants. Viruses are small and rapidly mutate—in essence, creating a moving target in terms of drug development.³⁷⁸ Once a cell in a host is infected, thousands of copies of the virus are produced daily, which also lends to the continuing mutation of SARS-CoV-2.³⁷⁹ Despite the difficulties in developing therapeutics, a handful of medicines that target the virus have become available to those infected with COVID-19.³⁸⁰

As discussed in chapter 3, COVID-19 therapeutics that act directly on the virus to inhibit its entry into host cells—or stop the virus from replicating once inside the host cell—are referred to as “virus-directed antivirals.”³⁸¹ “Host-directed therapies” either target components of the host cell to hinder virus replication or aim to reduce the inflammatory response to infection.³⁸² Virus-directed and host-directed COVID-19 therapeutics act through a variety of mechanisms (i.e., modes of action). As stated in chapter 3, COVID-19 therapeutics consist of two categories: small-molecule drugs and biologic drugs.³⁸³

Manufacturing

In general, the first step in the large-scale synthesis of pharmaceuticals is procuring a secure supply of raw materials from qualified suppliers meeting regulatory requirements (figure 4.5).³⁸⁴ Raw materials are chosen for their quality, purity, and cost-effectiveness. The raw materials (inputs) must be tested

³⁷⁶ Separately, other pharmaceuticals that address secondary conditions caused by the virus have been developed or identified (e.g., antibiotics and corticosteroids).

³⁷⁷ Bergmen, “COVID-19 Treatment: Investigational Drugs,” June 12, 2023.

³⁷⁸ New variants of SARS-CoV-2, the virus that causes COVID-19, have emerged over time with some strains becoming dominant over others. As of July 2023, the Omicron variant is the primary strain, with new lineages that continue to emerge, leading to infection in the United States. For the first half of 2023, the XBB.1.5 “Kraken” Omicron subvariant was the most prevalent. Browne, “Why COVID’s XBB.1.5 ‘Kraken’ Variant Is So Contagious,” January 10, 2023.

³⁷⁹ Howes, “Why Are Antivirals So Hard to Develop?,” May 20, 2021.

³⁸⁰ Note that some therapeutics are only available in certain markets because of regulatory approvals and other therapeutics authorizations, recommendations, approvals, etc. have been paused or rescinded because of lack of efficacy against the latest COVID-19 variant or conclusive data. See, e.g., FDA, “Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products,” July 19, 2023.

³⁸¹ Singh and de Wit, “Antiviral Agents for the Treatment of COVID-19,” February 11, 2022.

³⁸² Immune system overreactions could be seen in instances of cytokine storms (a common ailment of patients with severe COVID-19). WIPO, *COVID-19 Vaccines and Therapeutics*, April 2023, 47; Singh and de Wit, “Antiviral Agents for the Treatment of COVID-19,” February 11, 2022. See chapter 3 for more on virus- and host-directed therapeutics.

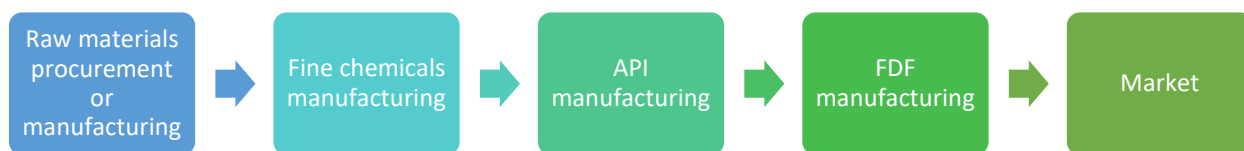
³⁸³ More specifically, both small-molecule and biologic virus-directed antivirals for COVID-19 have been prescribed in the past three years.

³⁸⁴ White House, *Building Resilient Supply Chains*, June 2021, 229.

and analyzed to ensure that they meet the required standards of purity and quality (see box 4.4 for how sourcing raw materials differs for mAbs).

Figure 4.5 Overview of finished dosage form value chain (traditional manufacturing)

API = active pharmaceutical ingredient; FDF = finished dosage form.



Source: Adapted from White House, *Building Resilient Supply Chains*, June 2021, 212.

Notes: The FDF step is where the drug is packaged for retail sale.

Next is the chemical synthesis, which can involve various types of chemical reactions (e.g., oxidation, reduction, condensation). The reaction pathway depends on the raw materials and the specific drug being produced. The commercial scale of these processes is carefully controlled to produce high yields and purity. To achieve these desired results, the reaction conditions (e.g., temperature, pressure, time) are optimized.

After the compound has been synthesized in accordance with the recipe, it is purified to produce the desired API, or API intermediates.³⁸⁵ The drugs are purified via a variety of techniques (e.g., distillation, chromatography, crystallization), and the chosen method depends on the compound and the impurities present. The goal of purification is to remove all impurities and isolate the desired product in a highly pure and concentrated form. Once synthesized and purified, the API must be formulated into a usable dosage form (e.g., tablet, capsule, injection). During the formulation stage, the API is combined with other substances, such as excipients and fillers, to yield a finished dosage form (FDF) that is safe, effective, and administrable.

Large-scale synthesis of pharmaceuticals is subject to strict regulatory requirements. Regulatory bodies such as the FDA in the United States and the European Medicines Agency in Europe oversee the production of pharmaceuticals and ensure that they are safe and effective. Large-scale production facilities must adhere to strict regulations to ensure the safety and efficacy of their products. The regulatory requirements for pharmaceutical production cover all aspects of the manufacturing process, from raw materials selection to final product formulation and packaging.³⁸⁶

Within the two primary types of therapeutics—small-molecule drugs and biologics—two main pharmaceuticals have been commercialized to combat the SARS-CoV-2 virus specifically: COVID-19 antivirals (a type of small-molecule drug) and COVID-19 mAbs (a type of biologic). The inherent

³⁸⁵ An API intermediate is a material that undergoes further molecular change or purification before it becomes an API. API intermediates may or may not be isolated and are only classified as such if produced after the point in API processing where the production of the API begins as defined by the company. FDA, “Guidance for Industry, Q7A Good Manufacturing Practice Guidance,” February 9, 2019.

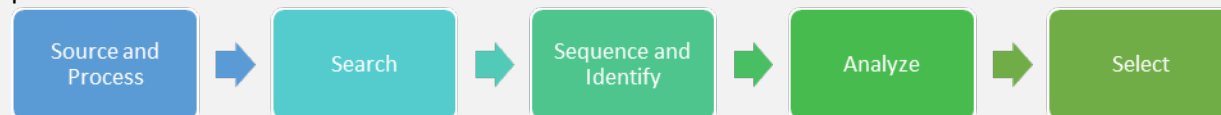
³⁸⁶ Aseptic conditions must be maintained during the manufacture of drugs to eliminate the possibility of contamination. NASEM, *Innovations in Pharmaceutical Manufacturing*, 2021, 26.

difference between the two regarding their manufacture is that small-molecule drugs are generally chemically derived, whereas biologics are extracted from living organisms (box 4.4).³⁸⁷

Box 4.4 Differences in the Development of Monoclonal Antibodies Compared to Small-Molecule Antivirals

Compared to its small-molecule drug counterparts, the supply chain for biologics, and mAbs specifically, differs in the early stages of research and development, simply because the starting material is an antibody (box figure 4.6). Sourcing the raw/starting material involves getting a COVID-19 antibody from either a human (i.e., convalescent patients) or mice exposed to SARS-CoV-2 antigens (could be a humanized mouse).^a Antibodies for COVID-19 mAbs can also be generated from vaccinated individuals, although it is unclear if that source has been used for COVID-19 therapeutics to date. Once the antibody is sourced, the material is screened for receptor-binding domain-specific single B cells. After screening, the material is sequenced and identified, which involves cloning and expression. The sequence is then analyzed, characterized, and validated. Finally, the mAb is selected and produced. The pathways of mAb generation depicted here then converge with small-molecule production in the process of selection and production, but the production needs for a mAb differ from those of classical chemical synthesis (i.e., small-molecule manufacturing).^b

Box Figure 4.6 Neutralizing monoclonal antibodies development: identification, selection, and production



Source: Gilchuk et al., “Integrated Pipeline for the Accelerated Discovery,” November 2020.

The steps described in box figure 4.6 can take months, and the literature indicates that the cost associated with producing mAbs can be prohibitively high.^c According to reports and the eventual authorization of various mAbs, it is likely that the timeline for identifying sequences of target mAbs became shorter over the course of the pandemic. In one case, in an accelerated pipeline, researchers purported that it could take as few as 17 days to identify sequences (about two months quicker than the traditional 78 days average).^d Despite the decrease in time, the potentially higher production costs that are associated with intravenous administration were cited as a hindrance to widespread adoption.^e

^a This is similar to sourcing for antibody production for diagnostic tests (see previous section on diagnostics manufacturing). Taylor et al., “Neutralizing Monoclonal Antibodies for Treatment of COVID-19,” June 2021; Allucent, “Monoclonal Antibodies,” January 23, 2018.

^b National Research Council, *Monoclonal Antibody Production*, 1999.

^c National Research Council, *Monoclonal Antibody Production*, 1999; Gilchuk et al., “Integrated Pipeline for the Accelerated Discovery,” November 2020.

^d This instance was not for a COVID-19 therapeutic. Gilchuk et al., “Integrated Pipeline for the Accelerated Discovery,” November 2020.

^e Gilchuk et al., “Integrated Pipeline for the Accelerated Discovery,” November 2020.

Many of the drugs widely available on the market are small-molecule drugs, so the existing manufacturing base for small-molecule drugs is more prevalent than those for biologics.³⁸⁸ Because of the rapid spread and high death rate of COVID-19, the scale and scope of production of these

³⁸⁷ FDA, “Biological Product Definitions,” accessed October 4, 2023; WIPO, “COVID-19 Vaccines and Therapeutics,” April 2023, 40.

³⁸⁸ To an extent, technical know-how still must be transferred even if a manufacturing base already exists. Industry representative, interview by USITC staff, May 17, 2023; government representative, interview by USITC staff, Brazil, June 26 and June 28, 2023.

therapeutics needed to be vast and as timely as possible (i.e., getting the drugs to the populations as quickly as possible).³⁸⁹ Even while waiting for approval, because of the nature of the global health emergency, the drugs' developers began taking steps to optimize and commercialize the production of their respective therapeutics.³⁹⁰

During the course of the pandemic, the production timelines for these novel COVID-19 therapeutics became extremely compressed.³⁹¹ For the commercial manufacture of COVID-19 antivirals, many of the considerations for production, which include sourcing inputs, ancillary supplies, know-how, achieving proper certifications, and meeting regulations, are generally the same among all developers. The specifics associated with the production of each antiviral is not fully known to the public because of the complicated network of supply chains associated with production agreements around the world.³⁹² In general, the originators design and optimize manufacturing processes, aiming for improved efficiency, reduced costs, enhanced product quality, and compliance assurance. The production of each antiviral differs slightly.³⁹³

Compared to small-molecule antivirals, biologics, specifically the mAbs (e.g., bebtelovimab, sotrovimab, bamlanivimab and etesevimab, casirivimab and imdevimab), do not benefit from the same infrastructure footprint as small-molecule drugs.³⁹⁴ Manufacture of mAbs generally consists of upstream processes for production of the crude protein drug via cell culture in a bioreactor followed by downstream processes for purification of the bulk drug substance and formulation. Production expansion for mAbs depends on the process mode and bioreactor type.³⁹⁵ Two common bioreactor process modes are fed-batch and perfusion.³⁹⁶ Fed-batch bioreactors, however, account for most

³⁸⁹ See chapter 2, section Regulations to Bring Diagnostics and Therapeutics to Market, for more on differences in timing of approvals of these therapeutics.

³⁹⁰ Gilead, "Gilead's Efforts to Increase Supply of Remdesivir," accessed September 27, 2023; NPR, "The COVID Antiviral Drugs are Here," December 31, 2021; industry representatives, interviews by USITC staff, March 24, June 5, June 6, June 29, 2023.

³⁹¹ In the United States, a pharmaceutical industry association estimates that building a new manufacturing facility can cost up to \$2 billion and take 5–10 years before it is operational, including the time and costs related to comply with various regulatory requirements. Traditionally, transferring the manufacture of a single product from one site to another also takes several years as it requires process transfer and scale-up, which involves validation, stability protocols, and regulatory filings. PhRMA, "Biopharmaceutical Manufacturing," accessed June 14, 2023.

³⁹² For example, Gilead—which had the first drug approved for SARS-CoV-2 in the United States—has more than 170 licensing agreements around the world to date, and each manufacturer needs its own supply chain for sourcing key ingredients for the manufacture of the drug. White House, *Building Resilient Supply Chains*, June 2021, 214; Gilead, prehearing brief submission to the USITC, March 17, 2023; industry representative, interview by USITC staff, May 25, 2023.

³⁹³ Gilead noted that remdesivir, which is administered intravenously, has the additional production consideration of vials. Gilead, prehearing brief submission to the USITC, March 17, 2023. Gilead is pursuing the development of a pill form of remdesivir. Industry representative, interview by USITC staff, May 25, 2023.

³⁹⁴ Industry representative, interview by USITC staff, February 24, 2023.

³⁹⁵ USITC, hearing transcript, March 29, 2023, 197 (testimony of George Scangos, Vir Biotechnology).

³⁹⁶ Fed-batch is where the nutrient feed is added to the bioreactor during the culture process. Perfusion mode is also known as continuous and is where the nutrient feed is constantly replaced with a fresh supply. Of these systems, perfusion has relatively low-throughput nature. As a result of space limitations, perfusion bioreactors require relatively large amounts of space to operate in a controlled environment. Sharma et al., *COVID-19 Manufacturing of Monoclonal Antibodies*, June 2020, 2–3; Dahlin et al., "Design of a High-Throughput Flow Perfusion Bioreactor," October 2012, 817.

biomanufacturing because of their scalability and volumetric output. Historically, stainless steel bioreactors have been used for large-scale production, though immediately preceding the pandemic, single-use bioreactors became more available as a result of the relatively short turnaround between batches and reduced upfront investment. Setting up new manufacturing capacity takes time—traditional fixed facilities would take more than seven years to set up—but modular platforms (e.g., single-use) can be erected in as few as 18 months.³⁹⁷ In addition to the production of biologics, these modular units also experienced high demand because the bioreactors are key in the production of certain COVID-19 vaccines.³⁹⁸ Another factor that ultimately limited the development of the infrastructure for production of biologics during the course of the pandemic relates to administration route—mAbs are typically administered via infusion, which limits outpatient demand, especially as small-molecule drugs enter the market.³⁹⁹

As mentioned earlier in the chapter, commercial-scale production of therapeutics has historically not occurred simultaneously with phase III clinical trials (or during phase II/III clinical trials). The sheer scale and scope of the pandemic, however, prompted many producers to try to safely and swiftly bring COVID-19 therapeutics to market. As a result, many companies took the step of bringing large-scale production online during clinical trials, at cost, with no guarantee that its drug would be approved for the treatment of COVID-19.⁴⁰⁰

According to the available literature, the commercial production of the antivirals remdesivir, nirmatrelvir (+ ritonavir), and molnupiravir initially occurred at cost to developers Gilead, Pfizer, and Merck.⁴⁰¹ In May 2020, Merck announced its partnership with Ridgeback Biotherapeutics to pursue development of a drug candidate in early clinical development—more specifically, an antiviral for the treatment of COVID-19.⁴⁰² Two months after that, in July 2020, Pfizer had its first clinical synthesis of nirmatrelvir.⁴⁰³

³⁹⁷ These timelines are based on trends before the COVID-19 pandemic; the current timelines could be shorter or longer than what was reported in early 2020. The capacity on the modular platforms is also lower than fixed production sites. Sharma et al., *COVID-19 Manufacturing of Monoclonal Antibodies*, June 2020, 2–3; USITC, hearing transcript, March 29, 2023, 217 (testimony of George Scangos, Vir Biotechnology).

³⁹⁸ Lead times for single use bioreactor bags were as long as 12 months in spring 2021. Stanton, “Single-Use Delay up to 12 Months,” May 3, 2021.

³⁹⁹ Drugs delivered via injection or infusion have different quality control checks than pills, such as checking for bacteria, mold, and endotoxin contamination. Additionally, a higher cost is associated with transporting liquids that often require climate control. White House, *Building Resilient Supply Chains*, June 2021, 223.

⁴⁰⁰ Kelley, “Developing Therapeutic Monoclonal Antibodies at Pandemic Pace,” May 2020; Westendorf et al., “LY-CoV1404 (Bebtelovimab) Potently Neutralizes SARS-CoV-2 Variants,” May 17, 2022; Li et al., “Therapeutic Strategies for COVID-19,” June 2023; Allais et al., “Development of the Commercial Manufacturing Process for Nirmatrelvir,” March 29, 2023, 850; Emory, “The Little Pill That Could,” November 19, 2021; industry representative, interview by USITC staff, March 7, 2023.

⁴⁰¹ “At cost” refers to the developers taking on the risk of producing the products at scale while still in clinical trials with no guarantee of approval, to ensure that product would be available immediately upon authorization or approval. Merck, “Merck and Ridgeback’s Investigational Oral Antiviral Molnupiravir,” October 1, 2021; Gilead, prehearing brief submission to the USITC, March 17, 2023; industry representatives, interviews by USITC staff, May 17, May 25, and June 5, 2023.

⁴⁰² Merck, “Merck and Ridgeback Bio Collaborate to Advance Development,” May 26, 2020.

⁴⁰³ Allais et al., “Development of the Commercial Manufacturing Process for Nirmatrelvir,” March 29, 2023, 849.

Both nirmatrelvir (+ ritonavir) and molnupiravir have been prescribed for the treatment of COVID-19 since early 2022.⁴⁰⁴

The rapid development of virus-directed small-molecule drugs also occurred with the biologics (specifically the virus-directed mAbs). Before COVID-19, a traditional timeline for discovery to proof-of-concept trials (phase I) was 10–12 months.⁴⁰⁵ The first SARS-CoV-2-specific mAb (bamlanivimab) was authorized for use in the United States in early November 2020, a period of approximately eight months from the declaration of the pandemic to availability to patients for treatment.⁴⁰⁶ Although the specifics of the development and authorization are not known, reports on speeding up the process appeared early in the pandemic.⁴⁰⁷ The steps to accelerate the timeline for mAbs were similar to the process for small-molecule drugs, because the acceleration revised some steps to occur parallel with each other instead of in sequence.

The specific costs associated with certain parts of production of COVID-19 therapeutics vary by drug and depend on supply and demand.⁴⁰⁸ Although pharmaceutical companies do not disclose specifics about their costs to develop each drug, PhRMA estimates that the costs across all pharmaceuticals, on average, are estimated to be \$2.6 billion to develop one new medicine.⁴⁰⁹ Yet, even if supply sources had already existed for an API, direct input, or the manufacture of said inputs, the amount needed to produce enough courses of a drug for initial anticipated demand meant that a rapid expansion of capacity or diversification of supply was needed.⁴¹⁰ For instance, one of the raw materials needed for the production of remdesivir, a chemically modified cyclodextrin, led to the announcement of a partnership between Hovione and Ligand in September 2020 to produce the required cyclodextrin.⁴¹¹ Under this partnership, Hovione was producing in a month the quantity that it usually produced per year.⁴¹² Because of the initial anticipated demand and amount of manufacturing required, a number of

⁴⁰⁴ Both Paxlovid and molnupiravir received an EUA in the United States in December 2021. Although both are oral antivirals, each has a different mode of action and reported efficacy against COVID-19 infections, as explained in chapter 3. For more on demand for these antivirals, see chapter 6.

⁴⁰⁵ This was 6 months quicker than the 18-month standard that had been the norm since 2015. Kelley, “Developing Therapeutic Monoclonal Antibodies at Pandemic Pace,” May 2020.

⁴⁰⁶ FDA, “Coronavirus (COVID-19) Update,” November 13, 2020.

⁴⁰⁷ Kelley, “Developing Therapeutic Monoclonal Antibodies at Pandemic Pace,” May 2020; Westendorf et al., “LY-CoV1404 (Bebtelovimab) Potently Neutralizes SARS-CoV-2 Variants,” May 17, 2022; Li et al., “Therapeutic Strategies for COVID-19,” June 2023.

⁴⁰⁸ Pfizer, written submission to the USITC, May 5, 2023, 15. Some estimates of the per-dose cost of production for certain therapeutics follow: baricitinib, \$1.83; molnupiravir, \$7.64; nirmatrelvir (+ ritonavir), \$15.81; and remdesivir, \$7.01. The methodology used for these estimates was originally commissioned by the WHO for the Fair Pricing Forum in 2017. The costing algorithm includes costs of materials (active pharmaceutical ingredients, excipients), formulation costs, a 10 percent mark-up, and tax on profit. For more see, Barber, written submission to the USITC, May 5, 2023, 1.

⁴⁰⁹ This estimate includes the cost associated with research on failed pharmaceuticals. PhRMA, “Progress toward New Medicines and Vaccines,” September 30, 2021.

⁴¹⁰ This occurred so that if the drug received authorization, manufacturing at scale was already occurring or could rapidly come online. Allais et al., “Development of the Commercial Manufacturing Process for Nirmatrelvir,” March 29, 2023; Hovione, “Hovione Announces Partnership to Support Manufacturing of Antiviral Veklury,” September 23, 2020.

⁴¹¹ Cyclodextrin is an excipient that improves the solubility, stability, bioavailability, and dosing of APIs. Hovione, “Hovione Announces Partnership to Support Manufacturing of Antiviral Veklury,” September 23, 2020.

⁴¹² Hovione, “Hovione Announces Partnership to Support Manufacturing of Antiviral Veklury,” September 23, 2020.

similar arrangements had to be made by manufacturers of COVID-19 therapeutics. Many manufacturers also made investments in their own businesses to expand existing production.⁴¹³ For instance, Pfizer announced in June 2022 a \$120 million investment at its Michigan facility to expand the production of both the API and the registered starting materials to manufacture nirmatrelvir.⁴¹⁴

Beyond the sourcing of raw materials and intermediates, the development of the production process for these drugs must be reproducible, meet quality control standards, and allow for a rate of scale that is quicker than the traditional production routes. Details of the synthetic routes from the drug developers employed for the small-molecule antiviral COVID-19 therapeutics are still being released. Some publications, however, do explain, at a high level, the development of a high-yielding commercial synthetic route such as Pfizer's development and production of Paxlovid (specifically, nirmatrelvir). The strategy for the preparation of nirmatrelvir relied on three fundamental inputs used as building blocks.⁴¹⁵ Each of these building blocks consisted of molecules that were either (1) used in the production of another pharmaceutical product, (2) sourced from existing commercial sources, or (3) used in a previously published synthesis for an internal clinical candidate.⁴¹⁶ These three factors allowed supply chains to be established rapidly when compared to previous scale-up efforts. The production processes for all the drugs were also optimized during development as well as during the brief time they have been on the market. One example of optimized production processes was the second-generation synthetic route for production of molnupiravir, which used microbial enzymes. Announced in November 2021, the route reduced the production time by 70 percent and had a seven-fold higher overall yield than when following the original route.⁴¹⁷

Global Production

As highlighted earlier in the chapter, a handful of pharmaceutical originators worldwide have been involved in the development and production of virus-directed COVID-19 therapeutics (table 4.6). The top

⁴¹³ For example, Novartis signed an agreement in April 2021 to manufacture Roche's tocilizumab (host-directed biologic therapeutic, IL-6 inhibitor). The deal involved "substantial technology transfer." Novartis, written submission to the USITC, May 5, 2023, 14.

⁴¹⁴ Pfizer, "Pfizer to Invest \$120 Million to Produce COVID-19 Oral Treatment in the U.S.," June 6, 2022.

⁴¹⁵ Allais et al., "Development of the Commercial Manufacturing Process for Nirmatrelvir," March 29, 2023. Note that other therapeutic developers or outside parties have published similar papers in which they break down the synthetic process into key molecules (i.e., building blocks) that can be used to produce the desired API. See Fier et al., "Development of a Robust Manufacturing Route for Molnupiravir, an Antiviral for the Treatment of COVID-19," December 17, 2021; Gopalsamuthiram et al., "Toward a Practical, Nonenzymatic Process for Investigational COVID-19 Antiviral Molnupiravir from Cytidine," December 17, 2021; Kawajiri et al., "Development of a Manufacturing Process Toward the Convergent Synthesis," April 7, 2023.

⁴¹⁶ More specifically, bicyclic pyrrolidine was a key component in boceprevir, which was withdrawn from the market in 2015, but those previously utilized supply chains were able to be reestablished. The second key molecule is tertiary-leucine (also referred to as pseudoleucine), which was first reported 100 years ago and is commercially available. The last building block was first reported by Pfizer La Jolla, California, in 2001 and was a key intermediate in the drug candidate rupintrivir (a rhinovirus protease inhibitor). Allais et al., "Development of the Commercial Manufacturing Process for Nirmatrelvir," March 29, 2023, 850.

⁴¹⁷ McIntosh et al., "Engineered Ribosyl-1-Kinase Enables Concise Synthesis of Molnupiravir," December 22, 2021; ACS Central Science, "A Quick, High-Yield Synthesis of Molnupiravir," November 3, 2021.

three countries with the highest number of manufacturers as enumerated through production agreements are: India (60), Bangladesh (27), and China (18).⁴¹⁸

Table 4.6 Select virus-directed COVID-19 therapeutic producers and location of headquarters

Firm	HQ	COVID-19 therapeutic
Gilead	Foster City, CA (U.S.)	Remdesivir
Pfizer	Cambridge, MA (U.S.)	Nirmatrelvir (+ ritonavir)
Merck	Rahway, NJ (U.S.)	Molnupiravir
Shionogi	Osaka (Japan)	Ensitrelvir
Lilly	Indianapolis, IN (U.S.)	Bebtelovimab; bamlanivimab and etesevimab
GlaxoSmithKline	Brentford (UK)	Sotrovimab
Vir Biotechnology	San Francisco, CA (U.S.)	Sotrovimab
Regeneron	Tarrytown, NY (U.S.)	Casirivimab and imdevimab
Roche	Basel (Switzerland)	Casirivimab and imdevimab

Sources: Gilead, “U.S. Locations,” accessed June 7, 2023; Pfizer, “Cambridge, Massachusetts,” accessed June 7, 2023; Merck, “Contact Us,” accessed June 7, 2023; Shionogi, “Global Affiliates and Locations,” accessed June 11, 2023; Lilly, “Lilly at a Glance,” accessed June 7, 2023; GSK, “Contact Us,” accessed June 7, 2023; GSK, “GSK Announces New Global Headquarters,” accessed June 7, 2023; VIR, “Contact Us,” accessed June 7, 2023; Regeneron, “Contact Us, Our Locations,” accessed June 7, 2023; Roche, “Roche R&D Locations,” accessed June 11, 2023.

Notes: Pfizer’s headquarters in Massachusetts is the global headquarters for Pfizer’s Center for Therapeutic Innovation; its administrative headquarters are in New York, NY. Outside of the United States and Canada, Merck is known as MSD. Shionogi has a “head office” in Japan as well as a corporate headquarters in Florham Park, NJ. GlaxoSmithKline is moving its headquarters to central London in 2024 and has a significant presence in the United States (Pennsylvania and North Carolina). Roche’s diagnostics headquarters is in the United States, but the majority of the firm’s pharmaceutical researchers are located in Basel, Switzerland.

The supply chains for the production of these medicines are complex networks that encompass sourcing raw materials to packaging the final drug product. Pfizer, for example, reports that its development and production of nirmatrelvir (+ ritonavir) within its own supply chain involves more than 60 materials from more than 20 supply points, which includes partners across 10 countries.⁴¹⁹ Beyond Pfizer’s own supply chain, a number of manufacturers from around the world are involved in the production of nirmatrelvir (+ ritonavir) and other COVID-19 therapeutics.⁴²⁰ Beyond the originator’s manufacturing supply chain that produces these COVID-19 therapeutics, a number of manufacturing partnership agreements or production agreements have been announced since the declaration of the pandemic in March 2020 (figure 4.7).

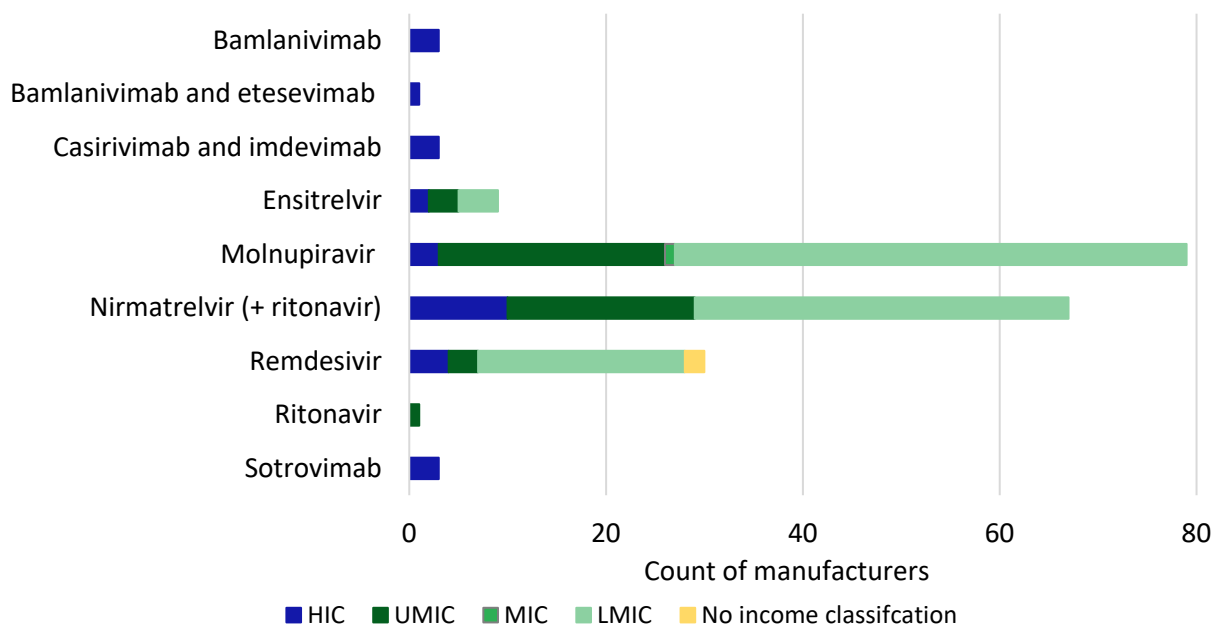
⁴¹⁸ Airfinity, “COVID-19,” accessed July 14, 2023.

⁴¹⁹ Pfizer, written submission to the USITC, May 5, 2023, ii, 2, 15, 29.

⁴²⁰ Airfinity, “COVID-19,” accessed July 14, 2023.

Figure 4.7 COVID-19 virus-directed therapeutics manufacturing, by drug

In number of manufacturers, country income level. HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; MIC = middle-income countries (see note). Underlying data for this figure can be found in appendix J, [table J.10](#).



Source: Airfinity, “Production,” accessed July 7, 2023.

Notes: Manufacturing in this instance refers to production arrangements. In aggregate, the announced production arrangements include API/excipient manufacturing, finished drug product, and fill/finish. Production arrangements that have been noted as inactive (with no production, not “launched”) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. The information presented in this chart is based on publicly available information (i.e., announced arrangements, press releases, etc.), which may not capture an originator’s/patent holder’s own production sites for manufacturing. The middle-income country (MIC) production arrangement of molnupiravir was an announcement between a UMIC and an LMIC. Venezuela was classified as a UMIC until July 2021; since then, Venezuela has been recategorized to “unclassified” by the World Bank.

Currently, it is difficult to ascertain which virus-directed COVID-19 therapeutics are still being produced. As of July 2023, a number of public arrangements were either active (i.e., production is ongoing, or the arrangement was not canceled even if production is not ongoing) or inactive (i.e., canceled, although stock of the finished drug product remains). As of summer 2023, at least 33 countries had some form of production arrangement for COVID-19 therapeutics, and within those 33 countries there were 130 unique manufacturers cited in the production arrangements.⁴²¹

Of these announced production arrangements, few establishments have indicated that production has begun.⁴²² The lack of announced production could be attributable to a number of factors, such as revoked authorization (e.g., virus-directed mAbs), ongoing clinical trials and necessary data gathering to achieve authorization in certain markets (e.g., ensitrelvir), and limited transparency regarding bilateral agreements through a third-party organization like the Medicines Patent Pool, such as molnupiravir and

⁴²¹ Airfinity, “COVID-19,” accessed July 14, 2023.

⁴²² This does not, however, necessarily mean that production has not started. Without an announcement, the start and end of production of any of these drugs is difficult to ascertain. Airfinity, “COVID-19,” accessed July 14, 2023.

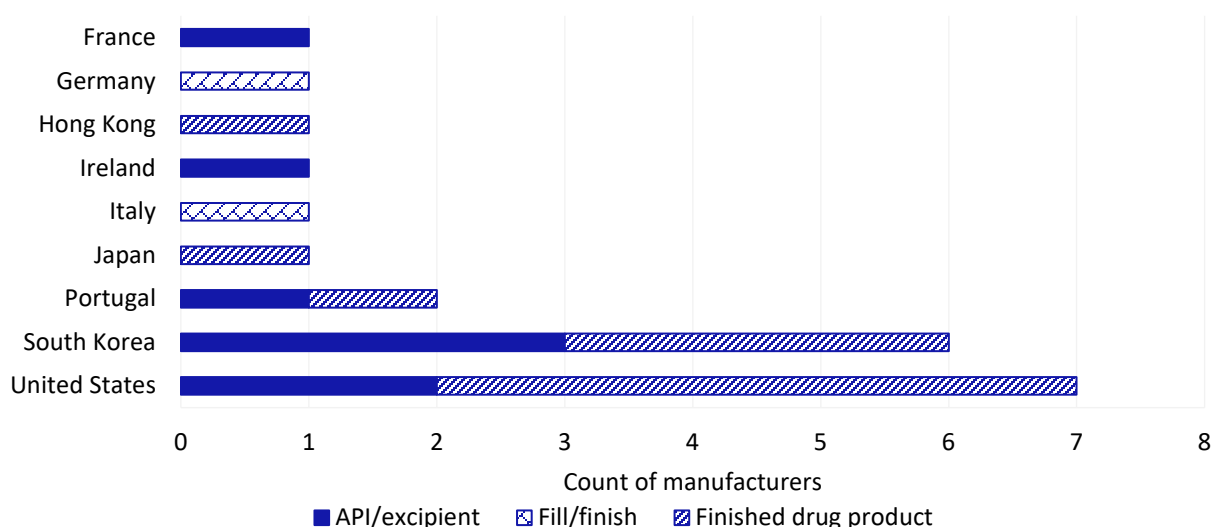
nirmatrelvir (+ ritonavir).⁴²³ India, a country known for its robust generics production, has had the highest number of reported production start dates.⁴²⁴

High-Income Country (HIC) Production

As highlighted above, all originators of COVID-19 therapeutics listed in table 4.4 are headquartered in HICs.⁴²⁵ The majority of these originators are large multinational firms that have established global supply chains and have established a presence in a number of countries other than HICs for production.⁴²⁶ Notably, as of July 2023, virus-directed mAb production (not host-directed mAbs) is solely in HICs (United States and South Korea).⁴²⁷ As shown in figure 4.8, the United States has the highest number of manufacturers for the therapeutics highlighted in table 4.2. In addition to the manufacture of mAbs, the figure also captures production (or launched production) in the United States of remdesivir (2 producers), molnupiravir (1 producer), and nirmatrelvir (+ ritonavir) (3 producers).⁴²⁸

Figure 4.8 HICs: COVID-19 virus-directed therapeutics manufacturing by production type, as of July 2023

In number of manufacturers, production type. Underlying data for this figure can be found in appendix J, [table J.11](#).



Source: Airfinity, "Production," accessed July 7, 2023.

Notes: Manufacturing in this instance refers to production arrangements. In aggregate, the announced production arrangements include API/excipient manufacturing, finished drug product, and fill/finish. Fill/finish refers to the process of filling vials with the formulated drug product and finishing by packaging the vials for distribution. Production arrangements that have been noted as inactive (with no production, not "launched") or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.), which may not capture an originator's/patent holder's production sites for manufacturing.

⁴²³ Airfinity, "Production," accessed July 7, 2023. Lack of demand is likely another factor that contributes to the lack of announced production start dates; see chapter 6.

⁴²⁴ Airfinity, "Production," accessed July 7, 2023.

⁴²⁵ For the type of manufacturing agreement/licensing agreement, see chapter 5.

⁴²⁶ WHO, *Local Production and Access to Medicines in Low- and Middle-Income Countries*, 2011, 16.

⁴²⁷ The United States has two sites for the production of the combination mAb treatment, bamlanivimab and etesevimab (Amgen and Biogen); South Korea has one manufacturer of sotrovimab (Samsung Biologics). Airfinity, "Production," accessed July 7, 2023.

⁴²⁸ This captures API/excipient and finished drug product manufacturing in the United States.

Upper-Middle-Income Country (UMIC) Production

As of July 2023, UMICs had 46 manufacturers of COVID-19 virus-directed therapeutics.⁴²⁹ Historically, pharmaceutical manufacturing in Brazil and Cuba has been substantial. The capabilities in some UMICs and regions are robust but still not as advanced or comparable to those in HICs, particularly with regard to bridging the gap from R&D to commercial production.⁴³⁰ For instance, Brazil and South Africa experienced two-month delays in purchasing reagent supplies to start manufacturing because other HICs, as the highest bidders, bought supplies in advance, as well as gaps in know-how needed to develop and bring these products to market.⁴³¹

As of July 2023, the number of production arrangements that are publicly available indicate that China was the largest producer of virus-directed COVID-19 therapeutics, with 18 manufacturers of either API or finished drug product (figure 4.9).⁴³² Analysis of the public announcements of agreements for production of these therapeutics indicate that China has manufactured, is manufacturing, or plans to manufacture nirmatrelvir (+ ritonavir), molnupiravir, and ensitrelvir.⁴³³

⁴²⁹ For the type of manufacturing agreement/licensing agreement, see chapter 5.

⁴³⁰ In some cases, capacity is there but the bridge from R&D to commercial level production or know-how is lacking. For example, in Brazil many manufacturers produce generics. WHO, *Local Production and Access to Medicines in Low- and Middle-Income Countries*, 2011; Boro and Stoll, “Barriers to COVID-19 Health Products in Low-and Middle-Income Countries,” July 22, 2022; government representatives, interviews by USITC staff, Brazil, June 27 and June 28, 2023; industry representative, interview by USITC staff, July 11, 2023; nonprofit organization representative, interview by USITC staff, Malaysia, July 24, 2023.

⁴³¹ Boro and Stoll, “Barriers to COVID-19 Health Products in Low-and Middle-Income Countries,” July 22, 2022; government representatives, interviews by USITC staff, Brazil, June 27 and June 28, 2023.

⁴³² Airfinity, “Production,” accessed July 7, 2023; Geneva Pharma Forum, interview by USITC staff, Switzerland, June 7, 2023.

⁴³³ China also produced and may still be producing remdesivir. The status of those production deals is “unknown.” Airfinity, “Production,” accessed July 7, 2023.

Figure 4.9 UMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023

In number of manufacturers, production type. Underlying data for this figure can be found in appendix J, [table J.12](#).



Source: Airfinity, “Production,” accessed July 7, 2023; Hamadeh, Van Rompaey, and Metreau, “New World Bank Country Classifications by Income Level,” July 1, 2021.

Notes: Manufacturing in this instance refers to production arrangements. In aggregate, the announced production arrangements include API/excipient manufacturing, finished drug product, and fill/finish. Production arrangements that have been noted as inactive (with no production, not “launched”) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.), which may not capture an originator’s/patent holder’s production sites for manufacturing. Not accounted for is the production of molnupiravir (finished drug product) under a joint arrangement with Jordan (UMIC) and Egypt (LMIC). Venezuela was classified as a UMIC until July 2021; since then, Venezuela has been recategorized to “unclassified” by the World Bank.

Lower-Middle-Income Country (LMIC) Production

Historically, pharmaceutical manufacturing capacity in LMICs like India, Bangladesh, Pakistan, and Vietnam has been substantial.⁴³⁴ A study by the WHO and more recent research has shown that in the aggregate, however, the capabilities in these countries and regions are still not as advanced as those in HICs.⁴³⁵ As of July 2023, 108 manufacturers in LMICs manufactured COVID-19 virus-directed therapeutics.⁴³⁶ LMIC production is limited to COVID-19 small-molecule antivirals: remdesivir, nirmatrelvir (+ ritonavir), molnupiravir, and ensitrelvir.⁴³⁷ The top producer of COVID-19 therapeutics in LMICs is India, which has a robust pharmaceutical manufacturing base, with 60 manufacturers of COVID-19 therapeutics: 26 for nirmatrelvir (+ ritonavir), 32 for molnupiravir, 7 for remdesivir, and 2 for

⁴³⁴ Reportedly, the capacity largely goes toward production of generics. Academic representative, interview by USITC staff, Bangladesh, July 17, 2023. For the type of manufacturing agreement/licensing agreement, see chapter 5.

⁴³⁵ WHO, *Local Production and Access to Medicines in Low- and Middle-Income Countries*, 2011; Boro and Stoll, “Barriers to COVID-19 Health Products in Low- and Middle-Income Countries,” July 22, 2022.

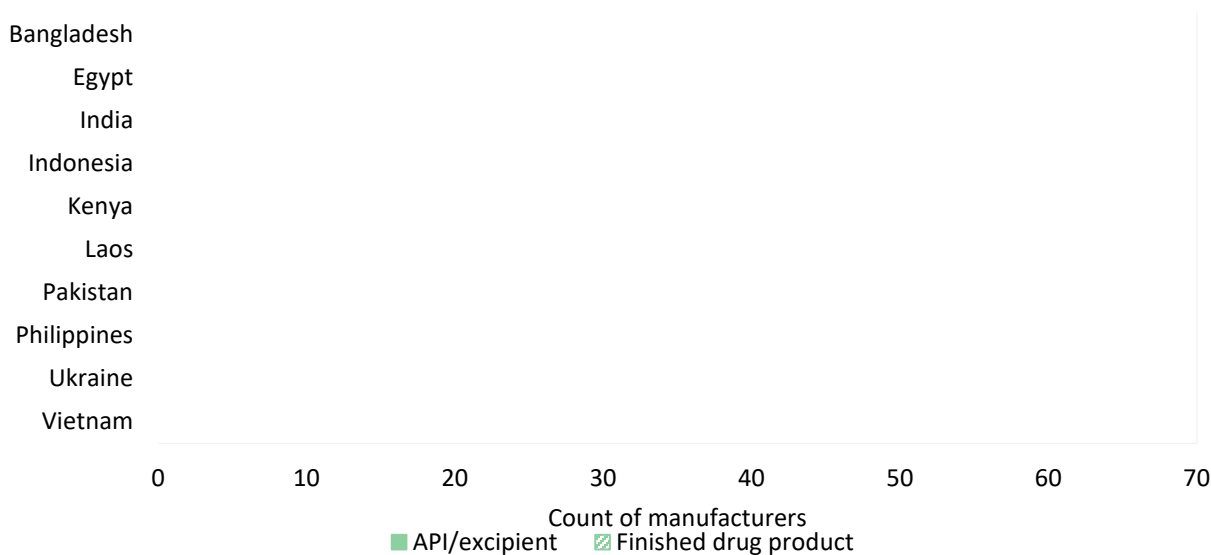
⁴³⁶ Not accounted for is the production of molnupiravir (API), which was publicized in an announcement by Hikma Pharmaceuticals (Jordan = UMIC; Egypt = LMIC). Berry, “Supersized Asia and Africa Deal to Make Merck Pill,” April 4, 2022.

⁴³⁷ When virus-directed mAbs were recommended for use, before oral COVID-19 antivirals were available, an estimated 85 percent of the global population from LMICs did not have access to mAbs. Hotez et al., “Global Public Health Security and Justice,” September 1, 2021.

ensitrelvir (figure 4.10).⁴³⁸ Bangladesh had the second-largest number of LMIC COVID-19 therapeutic manufacturers (27) in July 2023: 5 for nirmatrelvir (+ ritonavir), 11 for molnupiravir, and 11 for remdesivir.

Figure 4.10 LMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023

In number of manufacturers, production type. Underlying data for this figure can be found in appendix J, [table J.13](#).



Source: Airfinity, “Production,” accessed July 7, 2023.

Notes: Manufacturing in this instance refers to production arrangements. In aggregate, the announced production arrangements include API/excipient manufacturing, finished drug product, and fill/finish. Production arrangements that have been noted as inactive (with no production, not “launched”) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.), which may not capture an originator’s/patent holder’s production sites for manufacturing. Not accounted for is the production of molnupiravir (API), which was publicized in an announcement by Hikma Pharmaceuticals (Jordan/Egypt).

Low-Income Country (LIC) Production

As of June 2023, virus-directed COVID-19 therapeutics are not manufactured in LICs.⁴³⁹ Of the 27 countries worldwide currently designated by the World Bank as LICs, the vast majority (23) are located in Africa.⁴⁴⁰ Africa accounts for only 3 percent of global medicinal drug manufacturing capacity, and 70–90 percent of medicines consumed in sub-Saharan Africa are imported.⁴⁴¹

⁴³⁸ It is unknown whether active production is occurring. For more information on demand for these drugs, see chapter 6.

⁴³⁹ See chapter 6 for mechanisms available to LICs facilitating access to COVID-19 therapeutics.

⁴⁴⁰ Nearly half of the countries in Africa are LICs (23 of 54 nations). World Population Review, “Poorest Countries in Africa 2023,” 2023.

⁴⁴¹ Boro and Stoll, “Barriers to COVID-19 Health Products in Low-and Middle-Income Countries,” July 22, 2022.

Trade

Formulated pharmaceuticals are generally classified in HS Chapter 30 (pharmaceutical products).⁴⁴² By comparison, the bulk APIs (and API intermediates) are generally classified in other HS chapters, especially chapter 29 (organic chemicals). Chapter 30 has specific subheadings indicating whether the finished pharmaceuticals are mixed, in dosage form, and/or packaged or labeled.⁴⁴³ For the trade data, eight HS 6-digit subheadings include COVID-19 therapeutics inputs or finished drug formulations of therapeutics discussed in this chapter (bamlanivimab, tixagevimab and cilgavimab, favipiravir, molnupiravir, nirmatrelvir (+ ritonavir), remdesivir, sotrovimab, and tocilizumab).⁴⁴⁴ It is important to note that, as with trade of COVID-19 diagnostics, trade under the eight identified HS 6-digit subheadings includes goods not only for COVID-19 but immunological products for conditions other than COVID-19 as well. It is difficult to know the extent to which the data reflect mainly COVID-19 therapeutics or other kinds of therapeutics. To narrow the data somewhat, the Commission used tariff-line codes for certain countries according to the known production of COVID-19 therapeutics in those countries.⁴⁴⁵ Major exporters of products classified under HS subheadings that include COVID-19 therapeutics exported most of these goods to HICs, 81.9 percent in 2022 (figure 4.11).⁴⁴⁶ Most of these exports from HICs went to other HICs, as did most of the exports from UMICs and LMICs.

⁴⁴² For U.S. trade data of pharmaceuticals by North American Industry Classification System (NAICS), see appendix I.

⁴⁴³ They are further categorized by the type of pharmaceutical covered in the subheading (e.g., dosage-form or labeled antivirals are in HTS statistical reporting number 3004.90.92.07). Also, many of the Chapter 30 subheadings are “basket” (or “residual”) subheadings, each covering large groupings of pharmaceuticals (e.g., 3004.90.92).

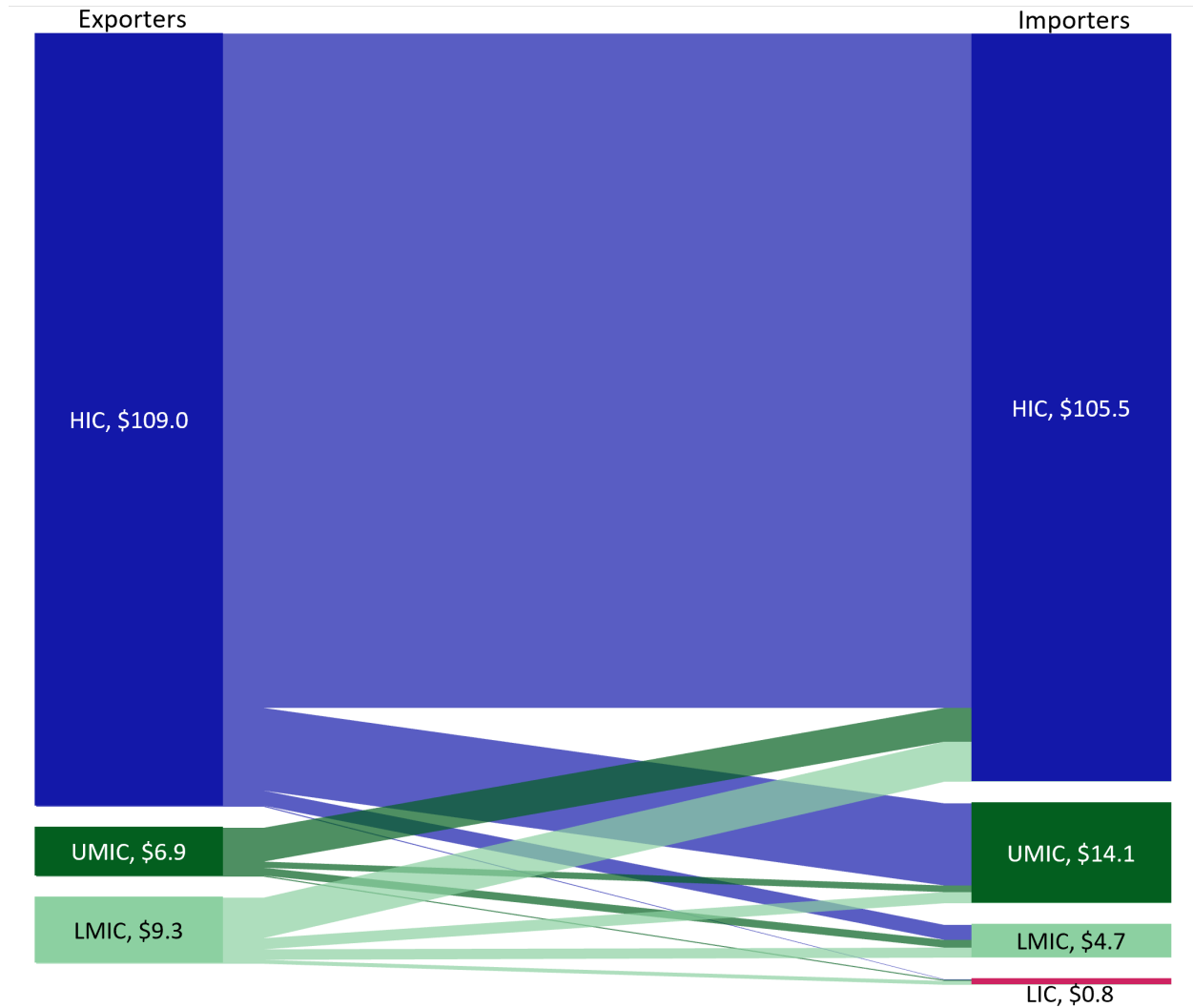
⁴⁴⁴ The trade data for therapeutics presented in this chapter are from HS subheadings 2933.79, 2933.99, 2934.10, 2934.99, 3002.13, 3002.14, 3003.90, and 3004.90. These subheadings include immunological products that are not specific to COVID-19.

⁴⁴⁵ For example, U.S. exports of nirmatrelvir (+ ritonavir) are classified under individual statistical reporting numbers in HS subheadings 3002.13 and 3002.14 and are included in the estimate, but exports under other tariff lines for COVID-19 therapeutics that are not produced in the United States (e.g., the API favipiravir traded under HS subheading 2933.99) are not included. For more information see appendix F.

⁴⁴⁶ Several outbreaks of different diseases, including monkeypox and respiratory syncytial virus, may have contributed to demand for goods covered by the same tariff codes as COVID-19-related therapeutics.

Figure 4.11 Exports and imports of HS subheadings that include COVID-19 therapeutics by income level of exporter (left) and importer (right), 2022

In billions of dollars. HIC = high-income countries, UMIC = upper-middle-income countries, LMIC = lower-middle-income countries, LIC = low-income countries. Underlying data for this figure can be found in appendix J, [table J.14](#).



Source: S&P Global, Global Trade Atlas, data under Harmonized System (HS) subheadings. 2933.79, 2933.99, 2934.10, 2934.99, 3002.13, 3002.14, 3003.90, 3004.90, accessed July 20, 2023.

Notes: Data specific to exporters were selected according to their reported production of COVID-19 therapeutics. See appendix F for more detail on selection. High-income exporters in these data include Germany, Israel, Portugal, South Korea, Switzerland, the United States, and the United Kingdom. Brazil and China are the upper-middle-income exporters, and India is the only lower-middle-income exporter. Data reported are export data by exporters and trade partners (importers).

Germany was the leading exporter of products in Harmonized System (HS) classifications that include COVID-19 therapeutics during 2018–22 (table 4.7). Germany not only produces molnupiravir, nirmatrelvir (+ ritonavir), and remdesivir but historically has been a major producer of pharmaceuticals in general (particularly innovative pharmaceuticals).⁴⁴⁷ Germany’s exports in HS classifications that

⁴⁴⁷ Pharmaceutical companies in Germany include Bayer and Merck KGaA. Merck KGaA is separate company from Merck & Co., Inc., which is known as MSD outside of Canada and the United States. Blake, “A History of . . . Merck KGaA,” April 22, 2013; Blake, “A History of Bayer,” April 2, 2013.

include COVID-19-related therapeutics in 2022 were 24 percent (\$12.7 billion) higher than in 2018 (including a 19 percent jump from 2021 to 2022), possibly because of increased COVID-19 therapeutics production.⁴⁴⁸ In comparison, India has a long history as a major producer of generic pharmaceuticals.⁴⁴⁹ India's exports of products in HS classifications that would include COVID-19 therapeutics increased by \$3.7 billion (67 percent) from 2018 to 2022.

Table 4.7 Global exports under HS subheadings that include COVID-19 therapeutics, by top exporting countries, 2018–22

In billions of dollars. — = not applicable; HIC = high-income country; UMIC = upper-middle-income country; LMIC = lower-middle-income country.

Exporter	Income level	Example COVID-19 therapeutics	2018	2019	2020	2021	2022
Germany	HIC	nirmatrelvir (+ ritonavir)	52.4	47.2	51.7	54.9	65.1
United Kingdom	HIC	sotrovimab (GSK); remdesivir	16.8	17.2	18.7	19.3	23.3
United States	HIC	molnupiravir; nirmatrelvir (+ ritonavir); remdesivir	2.8	3.0	4.3	7.4	11.5
India	LMIC	ensitrelvir; molnupiravir; nirmatrelvir (+ ritonavir); ritonavir	5.6	6.6	8.8	9.5	9.3
China	UMIC	ensitrelvir; molnupiravir; nirmatrelvir (+ ritonavir)	4.6	4.3	5.1	6.3	6.9
Top 5 exporters	—	—	82.2	78.4	88.6	97.4	116.1
All other exporters	—	—	4.3	4.8	6.3	6.0	9.2
Total	—	—	86.5	83.2	94.9	103.4	125.3

Sources: S&P Global, Global Trade Atlas, accessed May 5, 2023. Airfinity, "Production," July 20, 2023; Reuters, "UK's Hikma Starts Manufacturing COVID-19," August 7, 2020.

Notes: See appendix F for individual country codes used for each country identified as having reported production of COVID-19 therapeutics. Total in this table only represent total exports of those countries identified as having reported production of COVID-19 therapeutics, identified above.

⁴⁴⁸ S&P Global, "GTAS," accessed May 9, 2023.

⁴⁴⁹ Joshi, Shetty, and Karande, "Generic Drugs – the Indian Scenario," 2019; Issa, "The World's Pharmacy," February 12, 2020.

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Chapter 5

Approaches to Access the Intellectual Property Associated with COVID-19 Diagnostics and Therapeutics

Introduction

This chapter describes approaches to the development of, and access to, the intellectual property (IP) associated with COVID-19 diagnostics and therapeutics. It discusses the use of different types of IP-related agreements, including research and development (R&D) agreements, manufacturing partnerships, bilateral license agreements (BLAs)⁴⁵⁰ between firms, and license agreements involving the Medicines Patent Pool (MPP), a United Nations (UN)-backed public health organization. Collectively, bilateral and MPP license agreements are referred to as voluntary licenses (VLs).

This chapter largely focuses on COVID-19 therapeutics rather than diagnostics. The foundational patents for the two main types of COVID-19 diagnostic tests reportedly have expired.⁴⁵¹ According to information available, COVID-19 diagnostic producers generally did not transfer IP through manufacturing partnerships, VLs, or compulsory licenses (CLs).⁴⁵² This chapter describes specific cases in which IP-related agreements played a role in the R&D of diagnostics; however, the use of such agreements for diagnostics was less common than for therapeutics.

With respect to therapeutics, the chapter describes in detail the advantages and challenges associated with the use of VLs to increase access to COVID-19 therapeutics in developing countries. The chapter discusses CLs, and related advantages and challenges, including the experiences of countries at different income levels. Also included is a discussion of the least-developed country (LDC) exception to the TRIPS Agreement, which permits LDC members to delay implementing IP protections for pharmaceutical patents and test data—in practice, an important alternative to the voluntary and compulsory licensing

⁴⁵⁰ BLAs are agreements between licensors or owners of IP and licensees of users of IP for the authorized development, manufacture, or sale of a product subject to IP protections. GHIAA, “Issue Introduction: License Grants,” accessed August 28, 2023.

⁴⁵¹ See, e.g., FIND, written submission to the USITC, May 16, 2023, 1; FIND, *Diagnostics & Intellectual Property*, November 2022; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 7; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representatives, interviews by USITC staff, March 7, June 1, and June 14, 2023; industry representative, email message to USITC staff, June 16, 2023. See also chapters 2 and 4.

⁴⁵² BLAs between firms typically are not publicly available, as discussed below. It is therefore impossible to definitively state that no such transactions occurred, although staff interviews with diagnostics producers and the review of data from Airfinity and other sources did not unearth such transactions. By contrast, MPP licenses are publicly available. The U.S. National Institutes of Health (NIH) and the Spanish National Research Council licensed certain diagnostic technologies to the MPP; however, to date, these technologies have not been sublicensed to any diagnostics producers. Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023; industry representative, interview by USITC staff, July 5, 2023.

of COVID-19 therapeutics. This chapter responds to several elements of the request letter, including the call for information on VLS and other alternatives to compulsory licensing, as well as actions taken by World Trade Organization (WTO) members to use or attempt to use CLs for pharmaceutical products, and the outcomes of such actions. The COVID-19 diagnostics and therapeutics covered in this chapter are largely driven by the available information and the products subject to partnerships and VLS and CLs discussed.

Intellectual Property Agreements from Research and Development to Commercialization

Moving COVID-19-related discoveries from idea to market can be a complex and costly process involving a wide range of private and public actors including universities and research institutes, governmental and multilateral agencies, large firms, and small and medium-sized enterprises (SMEs).⁴⁵³ Written contracts provide the legal framework for the creation and use of IP during this process. Common types of IP-related contracts include those governing R&D collaborations, manufacturing partnerships, and license agreements.⁴⁵⁴ License agreements come in two forms particularly relevant to COVID-19 therapeutics: BLAs between firms that own IP (licensors) and those seeking to use the IP (licensees) and license agreements involving the MPP (MPP licenses). In the case of the MPP, it licenses IP from owners and then sublicenses the IP to companies who use it to produce COVID-19 therapeutics.

R&D Collaboration Agreements for COVID-19 Therapeutics and Diagnostics

An R&D collaboration agreement provides the basis for two or more entities to work together on the R&D underlying a new product or process. Among other things, agreements often specify what IP rights each party brings to the table, the ownership and use rights associated with IP that is newly developed as part of the project, and whether and how newly developed IP may be licensed to others.⁴⁵⁵ Collaborations can and do exist between different entity types. These entities can be classified into three main sectors: academic (i.e., universities), private (i.e., industry), and public (i.e., government). R&D collaborations involving academic, private, and public sector actors have spurred the development

⁴⁵³ See, e.g., Brant and Schultz, “Unprecedented,” November 2021, 8; Pfizer, written submission to the USITC, May 5, 2023, 3; Merck & Co., Inc. (“Merck”), written submission to the USITC, May 5, 2023, 14; Gilead, written submission to the USITC, May 5, 2023, 2; Lilly, prehearing brief submission to the USITC, March 17, 2023, 1; Novartis, written submission to the USITC, May 5, 2023, 1; BASF, written submission to the USITC, May 4, 2023, 2; Fraser, written submission to the USITC, May 3, 2023, 1; INTERPAT, written submission to the USITC, May 4, 2023, 3.

⁴⁵⁴ The Global Healthcare Innovation Alliance Accelerator (GHIAA) provides examples of different types of IP-related contracts that may be needed to bring a product to market. GHIAA also supplies examples of contract language that can be used to ensure sustainable, affordable, and readily available access to medicines. GHIAA, “Why Do Contracts Matter?,” November 21, 2022.

⁴⁵⁵ GHIAA, “MAPGuide: R&D Collaboration Agreement,” accessed July 18, 2023.

and commercialization of important discoveries related to COVID-19 diagnostics and therapeutics, and medical technologies more broadly.

SMEs play an important role in the R&D associated with COVID-19 therapeutics and diagnostics. For example, according to statistics compiled by the Biotechnology Innovation Organization, 87 percent of COVID-19 therapeutic R&D programs in the United States, and 75 percent of products in the global clinical development pipeline, originate from U.S.-based SMEs.⁴⁵⁶ Large firms, the U.S. federal government, and universities also have been prominent in R&D collaborations for the development of COVID-19 therapeutics, either independently or in collaboration with SMEs.⁴⁵⁷

For example, the R&D of molnupiravir involved multiple collaborations with academic researchers, SMEs, the U.S. government, and Merck & Co., Inc. (Merck). Initial research was carried out at Emory University (Emory), with funding from various government agencies.⁴⁵⁸ Emory, together with Drug Innovation Ventures at Emory, advanced molnupiravir through preclinical development, beginning in 2013. When the COVID-19 pandemic began, Ridgeback Biotherapeutics (Ridgeback), an SME, licensed the drug from Emory to continue its development.⁴⁵⁹ In May 2020, Merck partnered with Ridgeback to conduct pre-clinical and clinical studies to evaluate molnupiravir for the treatment of COVID-19.⁴⁶⁰

The U.S. government also played a substantial role in the R&D associated with remdesivir. Gilead Sciences (Gilead) began the underlying research that led to the development of remdesivir in the late 2000s, and by 2013–14, had synthesized the compound and confirmed its antiviral activity against certain viruses, initially focusing on the Ebola virus.⁴⁶¹ In 2013, the U.S. government began supporting Gilead’s preclinical remdesivir-related research.⁴⁶² In 2020, Gilead partnered in clinical trials of remdesivir for COVID-19 funded by the U.S. National Institutes of Health (NIH).⁴⁶³ According to the U.S. Government Accountability Office (GAO), federal funding for remdesivir preclinical studies and clinical trials totaled \$161.5 million from 2013 through 2020. Gilead states that it spent \$786 million in R&D from 2000 through December 2020 on remdesivir, with most spending occurring in 2020.⁴⁶⁴ IP provisions in the R&D collaboration agreements between Gilead and the U.S. government allowed the company to pursue patents for inventions during the collaboration.⁴⁶⁵ For their part, U.S. government

⁴⁵⁶ BIO, prehearing brief submission to the USITC, March 17, 2023, 2–3.

⁴⁵⁷ For example, collaborations have been prevalent in the R&D of COVID-19 mAbs, including casirivimab and imdevimab, bamlanivimab and etesevimab, and sotrovimab. Heo, “Sotrovimab,” March 2022; Deeks, “Casirivimab/Imdevimab,” November 2021; Brant and Schultz, “Unprecedented,” November 2021, 31.

⁴⁵⁸ Knowledge Ecology International (KEI) has documented U.S. government funding of the molnupiravir research conducted at Emory University and notes that Emory acknowledged that support in its patent applications. Abinader, “US Government Rights in Patents on Molnupiravir,” October 4, 2021.

⁴⁵⁹ Timmer, written submission to the USITC, May 1, 2023, 4–5.

⁴⁶⁰ Merck, written submission to the USITC, May 5, 2023, 1.

⁴⁶¹ Gilead, prehearing submission to the USITC, March 17, 2023, 5–6; GAO, “Biomedical Research,” March 31, 2021, 9–11.

⁴⁶² GAO, “Biomedical Research,” March 31, 2021, 9.

⁴⁶³ Gilead, prehearing submission to the USITC, March 17, 2023, 5–6; GAO, *Biomedical Research: Information on Federal Contributions*, March 31, 2021., 9.

⁴⁶⁴ GAO, “Biomedical Research,” March 31, 2021, 14, 15.

⁴⁶⁵ GAO, “Biomedical Research,” March 31, 2021, 16.

scientists who participated in the collaboration stated that their work did not rise to the level of co-inventor status on any of Gilead’s patents.⁴⁶⁶

Public-private collaborations also supported the development of diagnostic tests and testing platforms. For example, total U.S. government, nonprofit, and donor agency investment in the development of the GeneXpert diagnostic platform—a rapid, automated device for analyzing polymerase chain reaction (PCR) tests that is widely used in developing countries—has been estimated at \$252 million.⁴⁶⁷ The GeneXpert platform reportedly is based on technology initially developed by the U.S. government’s Lawrence Livermore National Laboratory (LLNL). A researcher involved in the initial technologies formed the U.S. company Cepheid in 1996. In exchange for a fee and royalties, the LLNL technologies formed the basis of Cepheid’s commercial products.⁴⁶⁸ Cepheid’s GeneXpert products were first approved for clinical use in 2006, with new assays for diseases approved thereafter, including SARS-CoV-2 in 2020.⁴⁶⁹ In addition to the LLNL patents, government-supported inventions from the University of Utah, Baylor College of Medicine, and the California Institute of Technology also were licensed to Cepheid.⁴⁷⁰

As set forth above, the U.S. government and universities have played an important role in some of the R&D underlying diagnostic and therapeutic discoveries.⁴⁷¹ Governments and universities, however, generally do not commercialize products. Congress enacted the Bayh-Dole Act in 1980 with the objectives of “us[ing] the patent system to promote the utilization of inventions arising from federally supported research and development” and “promot[ing] collaboration between commercial concerns and nonprofit organizations, including universities.”⁴⁷² Representatives of universities, research institutions, and other experts who provided information to the Commission focused on the importance of the Bayh-Dole framework to the development and commercialization of COVID-19 and other health-related discoveries (box 5.1).

Box 5.1 The Bayh-Dole Act

Before passage of the Bayh-Dole Act in 1980, the federal government generally took the position that inventions supported by public funding would belong solely to the government. Because of concerns that information from federally supported R&D was not being disseminated to those who could seek practical uses for it, the Bayh-Dole Act reversed this presumption and permitted universities, small businesses, and nonprofits to obtain title and patents to innovations made with federal funding.^a These

⁴⁶⁶ GAO, “Biomedical Research,” March 31, 2021, 16–18.

⁴⁶⁷ Gotham et al., “Public Investments in the Development of GeneXpert Molecular Diagnostic Technology,” August 31, 2021, 1. The GeneXpert technology is further discussed in chapters 2 and 4.

⁴⁶⁸ Gotham et al., “Public Investments in the Development of GeneXpert Molecular Diagnostic Technology,” August 31, 2021, 4–5.

⁴⁶⁹ Gotham et al., “Public Investments in the Development of GeneXpert Molecular Diagnostic Technology,” August 31, 2021, 4.

⁴⁷⁰ Gotham et al., “Public Investments in the Development of GeneXpert Molecular Diagnostic Technology,” August 31, 2021, 10.

⁴⁷¹ According to the patent landscape report prepared by the U.S. Patent and Trademark Office, 10.7 percent of COVID-19 diagnostic patent filings contain a “government interest” statement indicating that the patent application resulted from federal sponsorship. The NIH was the lead sponsor, second was the National Science Foundation, and third was the Department of Defense. Toole, et al., “Diagnosing COVID-19,” October 2023, 10–11.

⁴⁷² Bayh–Dole Act, 35 U.S.C. § 200; see generally Bayh–Dole Coalition, written submission to the USITC, April 25, 2023; Brant and Schultz, “Unprecedented,” November 2021, 15.

rights, however, came with the obligation to market actively and commercialize inventions, and universities and businesses were encouraged to work together to generate new products. The U.S. government retained a nonexclusive license to practice the invention and “march-in rights” that allow it, in specific circumstances, to grant a license to someone else to use the invention if the patent owner refuses to do so.^b The U.S. government, however, has never exercised march-in rights under Bayh-Dole.^c

Under the Bayh-Dole framework, U.S. universities have continued to participate in major medical discoveries, the development of which benefited from government funding.^d For example, medical technologies developed by the University of California, Berkeley (UC Berkeley) through public-private partnerships—including a low-cost malaria treatment and a hand-held Dengue Fever Diagnostic tool—have been deployed in developing countries at prices intended to expand access.^e In response to the COVID-19 pandemic, leading research universities have pledged to license COVID-19-related technologies “quickly, nonexclusively and royalty-free for the duration of the pandemic and for a short period thereafter.”^f In return, they asked for a commitment from licensees to distribute resulting products as widely as possible and at low cost to enable broad accessibility.^g

Relying on IP ownership rights, academic institutions have been active in developing and commercializing COVID-19 diagnostics. For example, UC Berkeley discovered a new implementation of a gene editing technology and licensed it to Mammoth Biosciences (an SME) on terms that reportedly would ensure access to the technology in developing countries.^h Mammoth Biosciences then, as part of an NIH program, used the technology to develop a high-throughput COVID-19 test called DETECTR BOOST, which received a U.S. Food and Drug Administration (FDA) emergency use authorization (EUA) in January 2022 (withdrawn in December 2022 when the market was no longer viable).ⁱ In another example, Yale University with financial support from the NIH and the National Basketball Association developed the SALIVADIRECT COVID-19 test which also received an EUA from the FDA. The test has been deployed to labs in various states, provinces, and countries free of charge.^j

Collaborations between universities and firms also reportedly have spurred litigation and restricted access to COVID-19 technologies, including in the area of lipid nanoparticle delivery systems.^k To limit disputes, observers suggest that the federal government articulate a set of standardized conditions to be included in all license agreements involving federally funded research and require greater transparency to ensure that the access principles universities and companies commit to in theory are implemented in practice.^l

^a Bayh-Dole Act, 35 U.S.C. § 202 (a); GAO, *Technology Transfer*, May 1998.

^b Bayh-Dole Act, 35 U.S.C. §§ 202(c)(4) and 203.

^c HHS, “HHS and DOC Announce Plan to Review March-In Authority,” March 21, 2023; Thomas, *March-In Rights Under the Bayh-Dole Act*, August 22, 2016, 1.

^d Ku, written submission to the USITC, May 5, 2023, 1; Winwood, written submission to the USITC, May 5, 2023, 4; Mimura, written submission to the USITC, May 5, 2023, 3; Bayh-Dole Coalition, written submission to the USITC, April 25, 2023, 3.

^e Mimura, written submission to the USITC, May 5, 2023, 3–4.

^f Stevens, “Commentary,” May 2022, 27; see also Stanford Office of Technology Licensing, “COVID-19 Technology Access Framework,” accessed August 24, 2023.

^g Stanford Office of Technology Licensing, “COVID-19 Technology Access Framework,” accessed August 24, 2023.

^h Stevens, “Commentary,” May 2022, 29–30; IPIRA, “Socially Responsible Licensing,” April 2023.

ⁱ Stevens, “Commentary,” May 2022, 30; FDA, “Revocation of Four Authorizations of Emergency Use of In Vitro Diagnostic Devices for Detection and/or Diagnosis of COVID-19,” 88 Fed. Reg. 6751, February 1, 2023.

^j Stevens, “Commentary,” May 2022, 30; Yale School of Public Health, “About SalivaDirect,” accessed October 5, 2023.

^k Herder, Gold, and Murthy, “University Technology Transfer Has Failed,” May 2022, 16, 19–21.

^l Herder, Gold, and Murthy, “University Technology Transfer Has Failed,” May 2022, 22–23; Public Citizen, “Public Citizen Comments to NIH,” July 28, 2023.

R&D collaborations involving public and private sector actors have spurred the development and commercialization of important discoveries related to COVID-19 diagnostics and therapeutics, and medical technologies more broadly. Substantial levels of U.S. government support also have raised concerns that the government has not received sufficient returns on its investments. U.S. government funding and participation in the development of molnupiravir, remdesivir, and the GeneXpert diagnostic platform have led some commentators to state that companies should be required to make their products more widely available and at lower prices, and that contract terms should be more transparent.⁴⁷³ Research and nonprofit organizations have published model contract provisions that they claim would promote equitable and affordable access to publicly and privately supported R&D.⁴⁷⁴

Manufacturing Partnership Agreements and COVID-19 Therapeutics

Rather than manufacture a product themselves, a product developer may enter into a manufacturing partnership with a specialty or contract manufacturer. These manufacturing partnerships often include provision for the manufacturer to modify and fine-tune processes to manufacture the products in a manner that meets all regulatory and quality requirements.⁴⁷⁵ Because of the importance of technical expertise, manufacturing partnership agreements typically include IP provisions that specify the background IP rights the parties bring to the transaction, as well as the terms of use and ownership of any IP created within the partnership.⁴⁷⁶ In contrast to the BLAs discussed below, manufacturing partnership agreements typically operate as part of the product originator's own supply chain; that is, they support production of the original branded product, e.g., through contract manufacturing, rather than a generic version.⁴⁷⁷

To facilitate the production of COVID-19 therapeutics, originator companies entered into manufacturing partnership agreements; as of June 26, 2023, there were reportedly 57 agreements with manufacturing partners for the production of COVID-19 therapeutics.⁴⁷⁸ These manufacturing partners are primarily

⁴⁷³ WHO, WIPO, and WTO, "An Integrated Health, Trade and IP Approach," May 2023, 18; Baker and Thrasher, "From Business as Usual to Health for the Future," March 2023, 15; Ardizzone, "U.S. Government's \$1.2 Billion Contract," October 4, 2021; multilateral organization representative, interviews with USITC staff, Switzerland, June 5, 2023; nonprofit organization representative, interview by USITC staff, Switzerland, June 7, 2023. See the "Advantages and Challenges of Bilateral License Agreements for COVID-19 Therapeutics" section in this chapter for more information on transparency of contract terms and see chapter 6 for more information on prices of COVID-19 diagnostics and therapeutics.

⁴⁷⁴ DNDi, "Pro-Access Policies for Intellectual Property and Licensing," April 17, 2020; Junod Moser et al., "Striking Fair Deals for Equitable Access to Medicines," April 1, 2023; Global Healthcare Innovation Alliance Accelerator (GHIAA), "Equitable Access Policies," accessed July 18, 2023; Public Citizen, "Public Citizen Comments to NIH," July 28, 2023.

⁴⁷⁵ BIO, written submission to the USITC, May 5, 2023, 6.

⁴⁷⁶ For examples of COVID-19-related contract manufacturing agreements, see GHIAA, "MAPGuide: Contract Manufacturing Agreements," accessed July 18, 2023.

⁴⁷⁷ Manufacturing partnership agreements involving the transfer of IP have not been reported as an important feature in the production of COVID-19 diagnostics.

⁴⁷⁸ Given the waning demand for COVID-19 products, some reported partnerships are likely to be inactive. Airfinity, "COVID-19," accessed June 26, 2023; see chapters 4 and 6 for discussions of manufacturing, trade, demand, and supply trends.

located in high-income countries (HICs) (70.8 percent), followed by upper-middle-income countries (UMICs) (14.6 percent), and lower-middle-income countries (LMICs) (14.6 percent). Currently, no reported manufacturing partnerships are in low-income countries (LICs).⁴⁷⁹

Bilateral License Agreements and COVID-19 Therapeutics

BLAs between licensors—who own IP rights associated with COVID-19 therapeutics—and licensees using the IP to develop, manufacture, and sell the product to patients in LICs, LMICs, and UMICs have been an important mechanism used to offer therapeutics in these countries. BLAs have not been a major feature of COVID-19 diagnostic test production for at least two reasons. First, BLAs transferring IP reportedly were not needed for foundational technologies because the patents for those technologies underlying PCR and rapid antigen tests have expired.⁴⁸⁰ Second, the technology transfer that has occurred to improve the capabilities of developing country diagnostic producers has mainly been in the form of donor- and government-supported initiatives.⁴⁸¹ Some commentators stated that more technology transfers are needed, including under Article 66.2 of the TRIPS Agreement, which requires developed countries to incentivize technology transfer from enterprises and institutions to developing countries.⁴⁸²

Overview of Bilateral License Agreements for COVID-19 Therapeutics

The primary purpose of COVID-19 therapeutic BLAs is the voluntary grant of IP rights from the licensor to the licensee to enable the development, manufacture, and sale of a licensed version of the therapeutic.⁴⁸³ This licensed version is offered as a generic and typically can be offered for a lower price

⁴⁷⁹ Airfinity, manufacturing partnership data accessed June 26, 2023; see section on global production of therapeutics in chapter 4 for more information.

⁴⁸⁰ For example, the foundational patents for PCR tests reportedly expired more than 15 years ago. FIND, written submission to the USITC, May 16, 2023, 1; FIND, *Diagnostics & Intellectual Property*, November 2022; PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023, 18; MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021, 7; AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5; industry representatives, interviews by USITC staff, March 7, June 1, and June 14, 2023; industry representative, email message to USITC staff, June 16, 2023; see also box 2.2 in chapter 2 for more information on patented diagnostic technology.

⁴⁸¹ MSF Access Campaign, *Local Diagnostics to Meet Local Health Needs*, July 8, 2021; Unitaid, “FIND and Unitaid Invest to Support Technology Transfer,” July 15, 2021; Watal, written submission to the USITC, May 3, 2023, 5 (describing support from the Indian government and the Rockefeller Foundation that enabled India’s local industry to scale-up production and manufacture more than a million PCR tests per day at substantially lower prices than at the beginning of the pandemic); multilateral organization representative, interview by USITC staff, Switzerland, June 6, 2023; nonprofit organization representative, interview by USITC staff, Switzerland, June 7, 2023; see also chapters 2 and 4.

⁴⁸² FIND, written submission to the USITC, May 16, 2023, 1; Access to Medicine Foundation, written submission to the USITC, May 4, 2023, 1; Embassy of Bangladesh, written submission to the USITC, April 5, 2023, 3; nonprofit organization, interview by USITC staff, Switzerland, June 8, 2023; nonprofit organization, interview by USITC staff, Switzerland, June 7, 2023; government representative, interview by USITC staff, Bangladesh, July 17, 2023.

⁴⁸³ For purposes of this report, these licensed versions may also be called “generics” to distinguish them from the originator company’s product. In the industry, a “generic” is also used to refer to a product that is authorized, for

for a number reasons, including because the licensee did not have to invest in the R&D and regulatory expenses associated with the discovery and approval of the new drug. Lower labor rates and costs of production also enable lower prices in locations, like India, where many licensees are located.⁴⁸⁴ The rights granted under BLAs typically include the right to use patented processes, make (or have made) and sell the patented product, and, in some cases, also provide for the sharing of trade secrets, expertise, data, or other technical information needed to produce the product and obtain regulatory approval.⁴⁸⁵

BLAs have been granted for remdesivir (Gilead), molnupiravir (Merck) and baricitinib (Eli Lilly and Company (Lilly)). Patented COVID-19 therapeutics that have been included in WHO recommendations but reportedly have not been produced under BLAs (or MPP licenses) include sarilumab (patent holders Regeneron Pharmaceuticals and Sanofi) and tocilizumab (patent holders Roche and Chugai). Roche and Chugai have announced a decision not to assert their patent rights in low- and middle-income countries.⁴⁸⁶ Other COVID-19 therapeutics that have not been the subject of BLAs are part of the MPP, such as nirmatrelvir (+ ritonavir) (Pfizer). Common elements of BLAs are described in box 5.2. Generally, however, only limited information is available on the actual terms of these agreements between private companies. The only agreement that is published, in model form, involves Gilead and remdesivir; the actual executed contracts are not publicly available.⁴⁸⁷ The other bilateral agreements, involving Merck and molnupiravir as well as Lilly and baricitinib, are not publicly available. Some information regarding their terms has been provided in hearing testimony and written submissions to the Commission, as detailed below.⁴⁸⁸

Box 5.2 Common Elements of Bilateral License Agreements

- **IP description:** BLAs (bilateral license agreements) typically describe the types of IP covered by the agreement that are explicitly excluded from the agreement (for example, trademarks or trade names). Some BLAs include detailed lists of patent applications and granted patents. They also may reference a technology transfer package, or other technical information and expertise that may be shared. The agreement may include only IP existing at the time the agreement was concluded or extend to future developments. The agreement may also grant the originator a license to IP developed by the licensee (e.g., improvements to the manufacturing process).
- **Covered territories:** BLAs may provide for worldwide sales of products, limit covered territories to a list of countries, or cover only a single country. The covered territory may be different than where the

example, because patent protection has expired or because the production does not violate an existing patent. Industry representative, interview by USITC staff, July 6, 2023.

⁴⁸⁴ Industry representatives, interviews by USITC staff, July 6, July 7, and July 10, 2023; Merck, written submission to the USITC, May 5, 2023, 4.

⁴⁸⁵ Although agreements that involve only the transfer of trade secrets, data, knowledge, or other materials are sometimes referred to separately as technology transfer agreements, here, the phrase BLA broadly refers to licenses for the transfer of all types of IP. GHIAA, “Why Do Contracts Matter?,” November 21, 2022.

⁴⁸⁶ Unitaid, WHO, and ML&P, *Improving Access to Novel COVID-19 Treatments*, April 11, 2023, 10; see also MSF, written submission to the USITC, May 17, 2023, 4.

⁴⁸⁷ Gilead, “2020 Original COVID–19 Voluntary License Agreement,” 2020.

⁴⁸⁸ See, e.g., Merck, written submission to the USITC, May 5, 2023; Lilly, prehearing brief submission to the USITC, March 17, 2023.

licensed product is manufactured. For example, some BLAs permit production in countries not within the territory covered by the license for export to covered territories.

- **Exclusivity:** BLAs may be exclusive (limited to a single licensee) or nonexclusive (allowing the licensor to grant IP rights to multiple licensees).
- **Use restrictions:** BLAs may describe the activities for which the IP may be used, such as to develop, manufacture, and sell the product. They may preclude attempting to reverse-engineer or design around the licensed IP.
- **Sublicensing:** BLAs may include provisions on sublicensing—that is, the onward grant of the license to a third party. Conditions of a sublicense may include obtaining the licensor’s consent, sublicense terms that are consistent with those of the main license, licensee responsibility for the performance of the sublicensee, and evidence demonstrating that the sublicensee has the capability to fulfill the terms.
- **Payment:** BLAs may provide for the payment of a royalty for the use of the IP. Some BLAs may provide for the royalty-free use of IP only for a specified amount of time or for sales to particular locations.

Source: GHIAA, “MAPGuide: Issue Introduction: License Grants,” accessed August 29, 2023.

Gilead Bilateral License Agreements

The first BLAs for the licensing of COVID-19 therapeutics involved Gilead and remdesivir. In May 2020, four months after the identification of remdesivir as a potential treatment for COVID-19, Gilead entered into BLAs with nine licensees in India, Pakistan, and Egypt.⁴⁸⁹ Under the terms of the agreements, the licensed product could be sold in 127 countries—the broadest territorial coverage available under any BLA or MPP license. The 127 countries included most LICs and LMICs, as well as more than half of UMICs, but among those countries excluded are several UMICs with large populations.⁴⁹⁰ To determine territorial coverage, Gilead states that it considered various factors including economic status, levels of economic inequality, incidence of COVID-19, health infrastructure, and the ability to ensure that the product would reach the intended patients.⁴⁹¹ The Gilead BLAs also include active engagement with licensees including the transfer of expertise and information on manufacturing processes to scale up production quickly, support with suppliers as appropriate, and other knowledge sharing as needed.⁴⁹²

Gilead does not collect royalties for the licensing of the IP, and licensees set their own prices for finished products.⁴⁹³ Gilead reports that the name brand and licensed product together have been made available to 13 million patients globally, with the licensed product available to more than 8 million patients in LICs and LMICs.⁴⁹⁴ Gilead and the licensees reported surpluses of advanced pharmaceutical

⁴⁸⁹ Gilead, prehearing brief submission to the USITC, March 17, 2023, 10–11, 29.

⁴⁹⁰ The countries are identified in appendix H.

⁴⁹¹ Gilead, prehearing brief submission to the USITC, March 17, 2023, 26.

⁴⁹² Gilead, written submission to the USITC, May 5, 2023, 10; industry representatives, interviews by USITC staff, June 13, July 7, July 10, and August 23, 2023.

⁴⁹³ Gilead, prehearing brief submission to the USITC, March 17, 2023, 11–12; Gilead, written submission to the USITC, May 5, 2023, 3, 7, and 13.

⁴⁹⁴ Gilead, prehearing brief submission to the USITC, March 17, 2023, 15. Gilead’s submissions provide no further information on delivery of products made available. It is unclear whether the products made available were delivered.

ingredients and finished product and that demand has been dropping since 2022, in line with the state of the pandemic during that time.⁴⁹⁵

Merck Bilateral License Agreements

In April 2021, before regulatory approval of the product, Merck entered into BLAs for the production of molnupiravir with licensees in India. Merck selected licensees who met the following criteria: World Health Organization (WHO) prequalified manufacturing facilities or a demonstrated commitment to securing WHO prequalification for their products, and a history of supplying quality-assured products to international procurement agencies. Some of the eight current bilateral licensees began manufacturing “at risk” before regulatory approval was certain to ensure rapid access in LICs and LMICs upon approval. The licensees are authorized to sell the licensed version of the product in 106 LICs, LMICs, and UMICs.⁴⁹⁶ As with the Gilead license agreement, many UMICs are excluded.⁴⁹⁷ Merck worked with its licensees to facilitate the development and regulatory authorization of the licensed products by providing technical packages describing the molecule and manufacturing process, and by providing data from its clinical program to regulators to support approval. Merck also provided information to support licensees’ own clinical trials and to facilitate regulatory submissions.⁴⁹⁸ The first WHO prequalification for a licensed COVID-19 antiviral was for molnupiravir in September 2022, with additional WHO prequalifications in December 2022 and April 2023.⁴⁹⁹ Merck did not receive royalties for sales of molnupiravir by licensees under BLAs (or under MPP licenses) for as long as COVID-19 remained classified as a Public Health Emergency of International Concern (PHEIC) by the WHO.⁵⁰⁰

Lilly Bilateral License Agreements

In May 2021, Lilly entered into BLAs with eight Indian companies to produce baricitinib (a rheumatoid arthritis drug for which Lilly obtained an EUA for use as a COVID-19 treatment) for distribution in India.⁵⁰¹ Within weeks of signing the agreements, however, Lilly discovered that Indian-manufactured baricitinib was being offered for sale in countries outside of India and for indications other than COVID-19, reportedly in violation of the terms of the BLAs.⁵⁰² Local manufacturers reportedly produced millions more doses than were necessary to treat COVID-19 in India.⁵⁰³ According to Lilly, this product diversion

⁴⁹⁵ Gilead, prehearing brief submission to the USITC, March 17, 2023, 12–13; industry representatives, interviews by USITC staff, June 13, July 6, July 10, and August 23, 2023.

⁴⁹⁶ Merck, written submission to the USITC, May 5, 2023, 4, appendix B. The covered countries are identified in appendix H.

⁴⁹⁷ The territorial coverage of Merck’s BLAs and the MPP licenses, discussed below, is the same. Merck, written submission to the USITC, May 5, 2023, appendix B.

⁴⁹⁸ Merck, written submission to the USITC, May 5, 2023, 5–6.

⁴⁹⁹ Merck, written submission to the USITC, May 5, 2023, 5.

⁵⁰⁰ Merck, written submission to USITC, May 5, 2023, 6; WHO, “Statement on the Fifteenth Meeting of the IHR,” May 5, 2023; HHS, “Fact Sheet,” May 9, 2023. The PHEIC classification ended in May 2023. It is not known whether Merck has started requiring or receiving royalty payments after that time.

⁵⁰¹ Lilly, prehearing brief submission to the USITC, March 17, 2023, 3; U.S. Food and Drug Administration, “Fact Sheet for Health Care Providers,” May 2022.

⁵⁰² Lilly, prehearing brief submission to the USITC, March 17, 2023, 3; industry representative, interview by USITC staff, June 28, 2023.

⁵⁰³ Lilly, prehearing brief submission to the USITC, March 17, 2023, 3; industry representative, interview by USITC staff, June 28, 2023.

can pose significant risks to product quality and patient safety.⁵⁰⁴ The BLAs expired in May 2022 and are no longer in force.⁵⁰⁵

Advantages and Challenges of Bilateral License Agreements for COVID-19 Therapeutics

BLAs have been an important mechanism used to offer COVID-19 therapeutics in LICs, LMICs, and some UMICs. From the standpoint of the licensor, BLAs have several key advantages, particularly when facing the prospect of CLs. First, they enable the licensor to provide access to valuable IP only to producers it trusts and that it believes will adhere to quality-control standards and respect IP rights.⁵⁰⁶ Second, they enable the licensor to build trusted partners for future licensing deals. Third, by retaining control over the selection of licensees, the licensor determines the number of manufacturers who are competing to sell licensed versions of the product in each market and potentially can address concerns that a large number of licensees may not be sustainable from the standpoint of demand or the supply of inputs.⁵⁰⁷

BLAs also may provide advantages in the areas of technology transfer and regulatory approval, as compared to CLs, which involve only patent rights and not the transfer of knowledge or technology. Traditional small-molecule drugs potentially can be reverse-engineered by producers in developing countries; however, transfer of know-how is often valuable in maintaining quality control and meeting regulatory requirements. Drugs based on more complex technologies, such as biologics, often require access to expertise and trade secrets for their safe and efficient reproduction.⁵⁰⁸ Licensees generally placed a high value on the access to expertise and trade secrets licensors provided under the BLAs.⁵⁰⁹

Some BLAs include terms that seek to minimize delays associated with regulatory processes. Such terms include waiving data exclusivity rights so the licensee can rely on data from clinical trials for the branded version when seeking marketing approval for the licensed product and sharing regulatory expertise.⁵¹⁰ Licensees also are bound by pharmacovigilance or product quality standards that include an obligation to report adverse events to the licensor. Some originators expressed concern that because CLs do not include the sharing of know-how, the licensees under CLs might not have the capacity to meet quality control and regulatory standards and bad actors may use less regulated environments to produce substandard or counterfeit medicines.⁵¹¹ No specific examples were provided, however, and pharmaceuticals produced under CLs may still be subject to regulatory safeguards in the relevant

⁵⁰⁴ Lilly, prehearing brief submission to the USITC, March 17, 2023, 3; industry representative, interview by USITC staff, June 28, 2023.

⁵⁰⁵ Lilly, prehearing brief submission to the USITC, March 17, 2023, 3; industry representative, interview by USITC staff, June 28, 2023.

⁵⁰⁶ Task Force on Voluntary Licensing and Access to Medicines, “Report of the Task Force on Voluntary Licensing and Access to Medicines,” version 1.1, April 22, 2023, 23; industry representative, interview by USITC staff, Switzerland, June 6, 2023.

⁵⁰⁷ Task Force, “Report of the Task Force,” April 22, 2023, 23.

⁵⁰⁸ Task Force, “Report of the Task Force,” April 22, 2023, 29–30; industry representative, interview by USITC staff, Switzerland, June 6, 2023.

⁵⁰⁹ Industry representatives, interviews by USITC staff, July 7, July 10, and August 23, 2023.

⁵¹⁰ Task Force, “Report of the Task Force,” April 22, 2023, 31–32.

⁵¹¹ Pfizer, written submission to the USITC, May 5, 2023, 25; AmCham EU, consultation response, May 2023, 5; Galen Centre for Health and Social Policy, written submission to the USITC, May 1, 2023, 5; EFPIA, written submission to the USITC, May 4, 2023, 4.

country, depending on the jurisdiction. On the other hand, the substantial control maintained by the licensor can give rise to disadvantages in terms of access to medicine in LICs, LMICs, and UMICs. First, the licensor determines what IP rights and products are made available to licensees. There is no assurance that the most successful or most needed treatments will be made available for licensing.⁵¹² Second, licensors control the countries to which licensees may export their products and the countries that may obtain access through imports from licensees. With respect to COVID-19, this option may exclude countries for which access to licensed products would be valuable from a public health perspective, as discussed in further detail below. Third, BLAs generally are not published; this means complete information about the terms and conditions of the agreements is not available.⁵¹³ This lack of transparency makes it difficult for the public to assess competing claims about the advantages and limitations of the agreements' terms and conditions.⁵¹⁴

The Medicines Patent Pool and COVID-19 Therapeutics

Overview of Medicines Patent Pool Licensing

Another avenue for the voluntary licensing of COVID-19 therapeutics and diagnostics is through the MPP.⁵¹⁵ Rather than negotiating individual license agreements directly with producers, licensors authorize the MPP to sublicense their technologies to third parties. In turn, the MPP solicits applications for sublicense agreements, reviews prospective producers, and handles all aspects of implementation of the sublicense agreements with selected companies.⁵¹⁶ The coverage territory of MPP license agreements may be worldwide, or limited to a list of countries or even a single country; while the MPP

⁵¹² See generally Abbott and Reichman, "Facilitating Access to Cross-Border Supplies of Patented Pharmaceuticals," September 28, 2020, 549; People's Vaccine Alliance, written submission to the USITC, May 4, 2023, 8; Rethink Trade, written submission to the USITC, May 5, 2023, 6; public health organization representative, interview by USITC staff, Switzerland, June 6, 2023; nonprofit organization representatives, interviews by USITC staff, Switzerland, June 7 and June 8, 2023; nonprofit organization representative, interview by USITC staff, South Africa, June 26, 2023.

⁵¹³ Gilead publishes a model BLA; however, the specific terms and conditions ultimately agreed upon with its licensees are not publicly available. By contrast, the MPP publishes the executed versions of its agreements with originator companies and its sublicense agreements with producers. Compare Gilead, "2020 Original COVID-19 Voluntary License Agreement," 2020; MPP, "Nirmatrelvir," License Agreement, November 2021; MPP, "35 Generic Manufacturers Sign Agreements," March 17, 2022; nonprofit organization representative, interview by USITC staff, Switzerland, June 7, 2023.

⁵¹⁴ This report is based on access to additional data and information on the terms of the BLAs obtained through hearing testimony, written submissions, and informational interviews—data that would not be available in the absence of this investigation.

⁵¹⁵ Academic research on the effects of the MPP is limited, and available literature has generally analyzed the case of HIV/AIDS drugs. Overall, studies on the impact of the MPP on pharmaceutical products showed that the MPP increased the share of generic drugs and encouraged technology diffusion. See chapter 8 for further information. See also Martinelli and Romito, "Collective Licensing and Asymmetric Information," 2021; Wang, "Global Drug Diffusion and Innovation with the Medicines Patent Pool," September 2022.

⁵¹⁶ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023; industry representative, interview by USITC staff, Switzerland, June 6, 2023; see generally 't Hoen, *Private Patents and Public Health*, 2016, 73–77 (describing the genesis and operation of the MPP).

generally advocates for broad coverage, the decision is up to the licensor.⁵¹⁷ Unlike the BLAs described above, terms of the executed MPP licenses and sublicenses are generally available on the MPP website.⁵¹⁸

In 2010, Unitaid established the MPP to facilitate global access to life-saving treatments specifically in the context of HIV/AIDS, particularly for patients in low- and middle-income countries.⁵¹⁹ The organization's statute established the patent pool "through which intellectual property is available, in order to reduce prices, improve access, and facilitate the development and production of quality, safe, and efficacious health products for use in low- and middle-income countries, considering the importance of technology transfer mechanisms, capacity building, and local manufacturing in developing countries."⁵²⁰

In March 2020, the MPP expanded its mandate to work on health technologies relevant to the COVID-19 pandemic.⁵²¹ Thereafter, the MPP secured licenses from the NIH and the Spanish National Research Council for research tools for the development of diagnostic technologies related to COVID-19 and other viruses. To date, however, the MPP has not awarded any sublicenses for access to these technologies.⁵²²

In September 2020, the MPP joined the therapeutics pillar of the Access to COVID-19 Tools Accelerator (ACT-A), contributing its expertise to facilitate equitable access to innovative therapeutics in low- and middle-income countries.⁵²³ The MPP reached out to patent owners when their products were still under development, with the goal of reducing the gap between when the original product received regulatory approval and when a sublicensee could obtain approval for its product.⁵²⁴ Thus far, the MPP has secured licenses for three patent-protected therapeutics: molnupiravir (patent holder Merck), nirmatrelvir (+ ritonavir) (patent holder Pfizer), and ensitrelvir fumaric acid (ensitrelvir) (patent holder Shionogi & Co. (Shionogi)).⁵²⁵

The MPP typically receives 10–15 sublicense applications for a particular pharmaceutical; for COVID-19 therapeutics, MPP received a record number of applications.⁵²⁶ As of June 2023, the MPP had awarded

⁵¹⁷ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

⁵¹⁸ MPP, "35 Generic Manufacturers Sign Agreements," March 17, 2022.

⁵¹⁹ Unitaid is a global health partnership that works to prevent, diagnose, and treat major diseases in LICs and MICs. The plan for a pool of patents for medicines was raised at Unitaid in 2006 in presentations made by Knowledge Ecology International and Médecins Sans Frontières. 't Hoen, *Private Patents and Public Health*, 2016, 74.

⁵²⁰ MPP, "Foundation Statutes," November 23, 2020.

⁵²¹ The MPP's expanded mandate includes treatments for HIV/AIDS, hepatitis C, tuberculosis, cancer, cardiovascular disease, diabetes, and COVID-19. MPP, "Disease Areas," accessed July 18, 2023.

⁵²² The MPP is still accepting applications for sublicenses for the Spanish National Research Council's COVID-19 serological antibody technology and for the NIH sublicenses for High-Throughput COVID-19 Diagnostic Test that Detects Both Viral and Host Nucleic Acid. The license for NIH's RNASEH-Assisted Detection Assay for RNA is no longer available for applications, as NIH abandoned the technology. See MPP, "ELISA ANTIBODY TECHNOLOGY," November 2021; MPP, "HIGH-THROUGHPUT DIAGNOSTIC TEST (Diagnostic)," May 2022; MPP, "RNASEH-ASSISTED DETECTION ASSAY FOR RNA (Diagnostic)," May 2022; public health organization, interview by USITC staff, Switzerland, June 9, 2023.

⁵²³ MPP, written submission to the USITC, May 5, 2023, 2, 8–9. For more information on ACT-A, see chapter 6.

⁵²⁴ MPP, written submission to the USITC, May 5, 2023, 9.

⁵²⁵ MPP, written submission to the USITC, May 5, 2023, 2.

⁵²⁶ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

72 sublicenses for therapeutics under its COVID-19 mandate.⁵²⁷ The high interest in applications is attributed to the timing of the license announcement at the height of the pandemic. The MPP also targeted a wider geographic area than in BLAs to stimulate competition between generic producers to drive down prices.⁵²⁸

According to the MPP, a total of 119 countries with an aggregate population of more than 4.35 billion people are covered by at least one of the three MPP licenses for COVID-19 therapeutics.⁵²⁹ All three licenses provide for a waiver of royalty payments until the end of the WHO PHEIC, with differing royalty arrangements following that time.⁵³⁰ Decreased testing and incidence of COVID-19, and other changes in supply and demand conditions, reportedly impacted the market for licensed products before the formal end of the PHEIC in May 2023.⁵³¹

Merck Medicines Patent Pool License

In October 2021, Merck became the first company to sign an agreement with the MPP for COVID-19 therapeutics. The U.S. Food and Drug Administration (FDA) granted an EUA for Lagevrio (molnupiravir) in December 2021. By January 2022, MPP had signed sublicense agreements with an initial group of 27 producers.⁵³² The license authorized product sales in 106 countries including all LICs, most LMICs, 20 UMICs, and all of sub-Saharan Africa.⁵³³ Many UMICs were excluded.⁵³⁴ Merck stated that it licensed through the MPP to diversify the geographic footprint of the licensed manufacturers for molnupiravir beyond India.⁵³⁵

With regard to regulatory requirements, the MPP sublicenses include a regulatory waiver, which enables a sublicensee to request a temporary waiver of the requirement to receive prior WHO prequalification or Stringent Regulatory Authority (SRA) approval if it satisfies certain conditions.⁵³⁶ These conditions include the sublicensee's certification that its manufacturing is consistent with WHO prequalification or SRA standards, and that it has complied with regulatory requirements in the countries of manufacture and sale.⁵³⁷ The licenses also waive data exclusivities in countries with such forms of protection and

⁵²⁷ MPP, written submission to the USITC, May 5, 2023, 6–7 (65 sublicenses for molnupiravir and nirmatrelvir); MPP, “Seven Manufacturers Sign Sublicense Agreements,” June 26, 2023 (seven sublicenses for ensitrelvir).

⁵²⁸ Nonprofit organization representative, interview by USITC staff, Switzerland, June 9, 2023; public health organization, email message to USITC staff, August 23, 2023.

⁵²⁹ MPP, written submission to the USITC, May 5, 2023, 2.

⁵³⁰ Merck-MPP License Agreement, October 26, 2021, par. 5A.4; Pfizer-MPP License Agreement, November 15, 2021, par. 7.3; Shionogi-MPP License Agreement, October 3, 2022, par. 7.3.

⁵³¹ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023; WHO, “Statement on the Fifteenth Meeting of the IHR,” May 5, 2023; HHS, “Fact Sheet,” May 9, 2023.

⁵³² MPP, written submission to the USITC, May 5, 2023, 6.

⁵³³ MPP, written submission to the USITC, May 5, 2023, 2.

⁵³⁴ MPP, “Molnupiravir (MOL),” October 2021, Exhibit B.

⁵³⁵ Merck, written submission to the USITC, May 5, 2023, 6.

⁵³⁶ An SRA is a regulatory agency that is a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), an ICH observer, or an agency associated with an ICH member through a legally binding mutual recognition agreement. For more information on SRAs, see chapter 2. See also MPP, written submission to the USITC, May 5, 2023, 6.

⁵³⁷ MPP, “Molnupiravir,” Waiver of Section 3.2 of the Form Sublicense Agreement, January 24, 2022; MPP, written submission to the USITC, May 5, 2023, 6.

disallow sublicensees from seeking exclusivities.⁵³⁸ According to the MPP, as of the first quarter of 2023, four companies among the 27 sublicensees have launched production of molnupiravir, producing 548,051 courses of treatment in 2022, and two companies have filed for WHO prequalification.⁵³⁹ Seven licensees have placed further work on the product on hold, and four sublicensees have terminated their agreements. Sublicensees generally report that low demand signals from the market, as testing rates have gone down, have caused them to terminate or place work on hold.⁵⁴⁰

Pfizer Medicines Patent Pool License

In November 2021, Pfizer and the MPP announced a license agreement for nirmatrelvir (+ ritonavir) (Paxlovid). The FDA granted an EUA for nirmatrelvir (+ ritonavir) in December 2021. By March 2022, the MPP had signed sublicense agreements with an initial group of 38 producers. The license authorizes product sales in 95 countries, including in UMICs that transitioned to UMIC status from LMIC status during the preceding five years—Armenia, Georgia, Guatemala, Kosovo, and Moldova—and most UMICs in sub-Saharan Africa; some large UMICs, however, were excluded.⁵⁴¹

As with molnupiravir, the agreements waive data exclusivities in countries with such forms of protection and prohibit sublicensees from seeking exclusivities.⁵⁴² Unlike the Merck MPP agreement, it does not include the possibility of a waiver of the requirement for WHO prequalification or SRA approval.⁵⁴³ According to the MPP, as of the end of the first quarter of 2023, six sublicensees have filed for WHO prequalification and one has secured approval and subsequently has begun production.⁵⁴⁴ Two sublicensees have terminated their agreements, and nine have placed further work on the product on hold. Again, sublicensees generally reported low demand signals because of lower testing rates as their reasons for stopping work under the agreements.⁵⁴⁵

Shionogi Medicines Patent Pool License

In October 2022, the MPP and Shionogi announced a license agreement for Shionogi's Xocova (ensitrelvir), which had already been granted regulatory approval in Japan. The license agreement covers 117 countries, including all LICs, almost all LMICs, 35 UMICs, and all countries in sub-Saharan Africa.⁵⁴⁶ As with the Merck agreement, the sublicensee can request a temporary waiver of the requirement to receive prior WHO prequalification or SRA approval if it satisfies certain conditions.⁵⁴⁷ In

⁵³⁸ For a discussion of data exclusivity, see chapter 2. MPP, written submission to the USITC, May 5, 2023, 6.

⁵³⁹ MPP, Annual Report, 2022.

⁵⁴⁰ MPP, written submission to the USITC, May 5, 2023, 8; public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

⁵⁴¹ MPP, written submission to the USITC, May 5, 2023, 7; public health organization representative, email message to USITC staff, August 24, 2023.

⁵⁴² MPP, written submission to the USITC, May 5, 2023, 7.

⁵⁴³ MPP, "Molnupiravir," License Agreement," October 2021.

⁵⁴⁴ Industry representative, interview by USITC staff, June 13, 2023.

⁵⁴⁵ MPP, written submission to the USITC, May 5, 2023, 8; public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

⁵⁴⁶ MPP, written submission to the USITC, May 5, 2023, 8.

⁵⁴⁷ The conditions include proof of filing for WHO prequalification or SRA approval, certification that manufacturing is consistent with WHO or SRA standards, proof of marketing approval, registration, or compassionate sale permit

June 2023, MPP initially awarded sublicenses to seven firms in five countries to manufacture and sell ensitrelvir.⁵⁴⁸ The status of sublicensed production is unknown at the time of this report's publication.

Advantages and Challenges of Medicines Patent Pool Licensing

A key advantage to the MPP licensing structure is that it streamlines the license solicitation and negotiation process by eliminating the need for licensors to individually identify and negotiate terms with potential producers. Originator companies and the MPP generally took advantage of streamlined processes and began negotiations early in the product development process, thereby reducing the lag between when therapeutics became available in high- and low-income countries.⁵⁴⁹ Previously, MPP-licensed products had taken three to four years to earn regulatory approval. The first MPP-licensed COVID-19 antiviral was approved just one month after the regulatory approval of the innovator product.⁵⁵⁰

The MPP also has established procedures to govern the application and selection of sublicensees who will manufacture the products. Although applicants for sublicenses do not need to have a previous track record for prequalification of a product, the MPP does scrutinize applicants' plans and potential to achieve qualification. To avoid the appearance of favoritism, many identifying details for applicants are removed during the review process.⁵⁵¹ Although licensors can engage with the MPP in the selection process for sublicensees, some defer entirely to the MPP's recommendations.⁵⁵² Furthermore, MPP licenses contain management features, such as uniform dispute resolution procedures and mechanisms to monitor compliance and safety.⁵⁵³

As with BLAs, an important advantage over CLs is that MPP licenses provide opportunities for technology transfer beyond what can be gleaned from the patent itself. All three COVID-19 therapeutic licenses allow the sublicensee to receive access to licensed know-how and support, and the nirmatrelvir (+ ritonavir) and ensitrelvir licenses also grant access, upon request, to a data package.⁵⁵⁴ The MPP and sublicensees credit technology transfer—and the sharing of innovators' own products with sublicensees to enable them to undertake the needed studies to show bioequivalence—for accelerating regulatory approvals.⁵⁵⁵ According to the MPP, development of quality-assured licensed products happened in

in the countries of manufacture and of sale, and certification that the product planned for commercialization and the product for which regulatory approval has been sought are the same. MPP, "Ensitrelvir Fumaric Acid," Sublicense Agreement - Form, October 2022, par. 3.8.

⁵⁴⁸ MPP, "Ensitrelvir Fumaric Acid," Generic Partners and Product Developers, October 2022; MPP, "Seven Manufacturers Sign Sublicense Agreements," June 26, 2023.

⁵⁴⁹ Pincombe and Guzman, *Lessons from Expanding Access to COVID-19 Treatments*, December 14, 2022; MPP, written submission to the USITC, May 5, 2023, 2, 8–9.

⁵⁵⁰ MPP, written submission to the USITC, May 5, 2023, 9.

⁵⁵¹ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

⁵⁵² Industry representative, interview by USITC staff, June 5, 2023; public health organization representative, interview by USITC staff, Switzerland, June 9, 2023.

⁵⁵³ See, e.g., MPP, Pfizer–MPP License and Sublicense, November 15, 2021, pars. 4.1, 4.2, 4.3, 4.4, and 8.6.

⁵⁵⁴ Merck–MPP License Agreement, October 26, 2021, par. 2.1; Pfizer–MPP License Agreement, November 15, 2021, pars. 2.1 and 3.6; Shionogi–MPP License Agreement, October 3, 2022, pars. 2.1 and 3.6.

⁵⁵⁵ MPP, written submission to the USITC, May 5, 2023, 6; industry representative, interview by USITC staff, July 10, 2023; industry representative, interview by USITC staff, July 6, 2023; industry representative, interview by USITC staff, August 23, 2023.

record time and facilitated procurement by governments.⁵⁵⁶ The technology transfer reportedly was particularly beneficial for the nirmatrelvir (+ ritonavir) sublicensees, as limited public information about development was available at the time of licensing.⁵⁵⁷

In addition to the technology transfer options available via MPP license agreements, the MPP is a partner in the mRNA technology transfer program. Via the program's technology transfer "hub" (Afrigen, located in South Africa), the MPP aims to facilitate technology development, training, and technology transfer. Currently, 15 program partners from developing countries receive training and technology from the hub with the goal of commercial production. The program is currently focused on vaccine development for COVID-19 and aims to incorporate therapeutics for diseases that threaten low- and middle-income countries in the future.⁵⁵⁸

The geographical scope of MPP licenses is a challenging aspect of the program, with many calling for licensors to increase the scope and authorize sales in more UMICs, given high rates of infection that occurred in those countries and high prices for medicines in those countries (as compared to countries within the geographical scope).⁵⁵⁹ According to one analysis in fall 2022, only 10 percent of global diagnoses of COVID-19 occurred in LICs, LMICs, and UMICs included in the Pfizer-MPP deal but 29 percent of diagnoses came from LMICs and UMICs not included in the agreement.⁵⁶⁰

Access to IP in UMICs, LMICs, and LICs

Figure 5.1 identifies UMICs, LMICs, and LICs where products licensed under MPP licenses or BLAs cannot be offered for sale under the terms of MPP licenses or BLAs. It illustrates the substantial number of UMIC countries excluded under MPP licenses for molnupiravir (28 of 54 UMICs), nirmatrelvir (+ ritonavir) (41 of 54 UMICs), and ensitrelvir (19 of 54 UMICs), as well as countries outside the scope of the remdesivir BLAs (22 of 54 UMICs).

⁵⁵⁶ MPP, written submission to the USITC, May 5, 2023, 2.

⁵⁵⁷ Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023; industry representative, interview by USITC staff, July 10, 2023.

⁵⁵⁸ MPP, "MRNA Technology Transfer Programme," accessed July 18, 2023. For more information on the mRNA technology transfer program, see the South Africa section below.

⁵⁵⁹ TWN, written submission to the USITC, April 12, 2023, 3; Public Citizen, written submission to the USITC, May 5, 2023, 16–17; Rethink Trade, written submission to the USITC, May 5, 2023, 6; nonprofit organization representative, interview by USITC staff, Switzerland, June 7 and June 8, 2023; intergovernmental organization representative, interview by USITC staff, Switzerland, June 6, 2023; government representative, interview by USITC staff, Brazil, June 28, 2023; multilateral organization representative, email message to USITC staff, July 28, 2023.

⁵⁶⁰ Pepperrell et al., "Barriers to Worldwide Access for Paxlovid, a New Treatment for COVID-19," September 2022, 1.

Figure 5.1 UMICs, LMICs, and LICs where COVID-19 therapeutics licensed under MPP licenses or BLAs cannot be offered for sale under the terms of those licenses/agreements, by treatment type and income levels

Ensitrelvir = Ensitrelvir fumaric acid; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC=low-income countries; underlying data for this figure can be found in appendix J, [table J.15](#).

Treatment type	UMIC	LMIC	LIC
Ensitrelvir Fumaric Acid	Albania, American Samoa, Argentina, Belarus, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Malaysia, Mexico, Montenegro, North Macedonia, Palau, Russia, Serbia, Thailand, Turkey, Turkmenistan	Indonesia, Lebanon	None
Molnupiravir	Albania, American Samoa, Argentina, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Costa Rica, Dominican Republic, Ecuador, Georgia, Jordan, Kazakhstan, Kosovo, Malaysia, Mexico, Montenegro, North Macedonia, Palau, Peru, Russia, Serbia, Turkey, Turkmenistan	Kyrgyzstan, Lebanon, Ukraine, West Bank and Gaza	None
Nirmatrelvir	Albania, American Samoa, Argentina, Azerbaijan, Belarus, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, Fiji, Grenada, Guyana, Iraq, Jamaica, Kazakhstan, Libya, Malaysia, Maldives, Marshall Islands, Mauritius, Mexico, Montenegro, North Macedonia, Palau, Paraguay, Peru, Russia, Saint Lucia, Saint Vincent and the Grenadines, Serbia, Suriname, Thailand, Turkey, Turkmenistan, Tuvalu	Lebanon	None
Remdesivir	Albania, American Samoa, Argentina, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Ecuador, Iraq, Jordan, Kosovo, Malaysia, Mexico, Montenegro, North Macedonia, Paraguay, Peru, Russia, Serbia, Thailand, Turkey	Iran, Lebanon, West Bank and Gaza	Syrian Arab Republic, Yemen

Source: MPP, Nirmatrelvir, “Country List,” <https://medicinespatentpool.org/licence-post/pf-07321332>, accessed June 26, 2023; MPP, Molnupiravir, “Country List,” <https://medicinespatentpool.org/licence-post/molnupiravir-mol>, accessed June 26, 2023; MPP, Ensitrelvir Fumaric Acid, “Country List,” <https://medicinespatentpool.org/licence-post/ensitrelvir>, accessed June 26, 2023; Gilead, Access Partnerships, “2020 Original COVID-19 Voluntary License Agreement,” <https://www.gilead.com/-/media/files/pdfs/other/original-covid-19-voluntary-license-agreement.pdf>, accessed June 26, 2023.

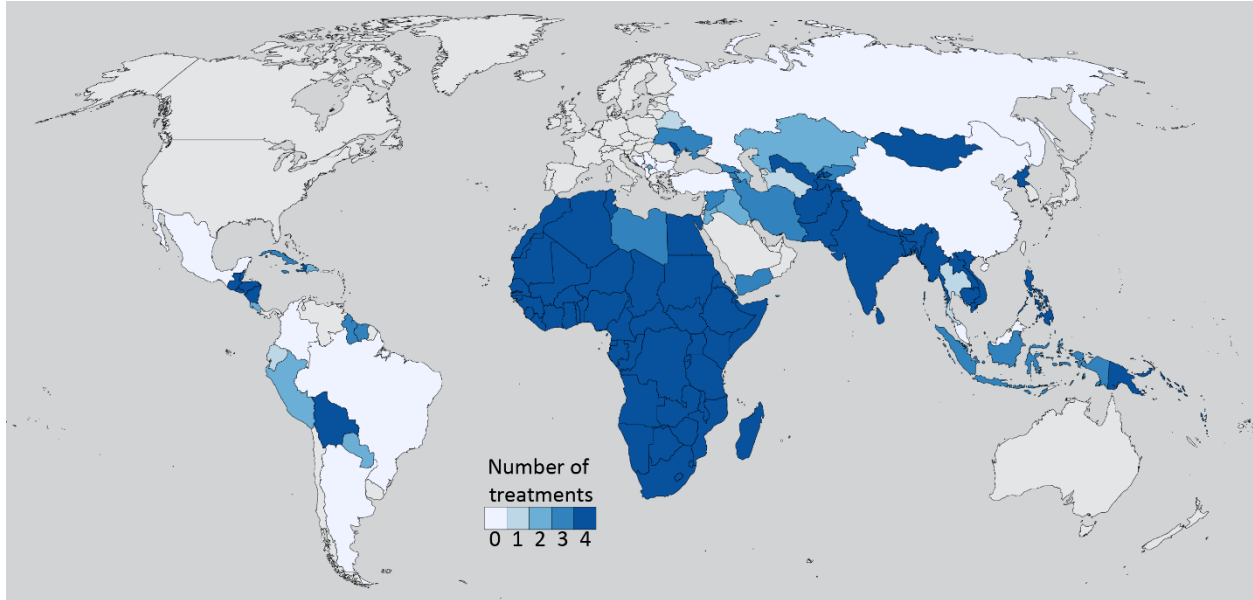
Notes: BLAs for the production and sale of baricitinib in India expired in May 2022 and are not included in this figure. The geographic scope of the MPP licenses for molnupiravir is the same as the scope of the BLAs. HICs within the scope of the remdesivir license are not included in this figure. Venezuela is included in the scope of the remdesivir license and was classified as a UMIC until July 2021. Its income level is now unclassified by the World Bank. Anguilla, the Cook Islands, and Montserrat are included in the ensitrelvir, molnupiravir, and nirmatrelvir licenses, but their income levels are not classified by the World Bank. Treatment names are the international nonproprietary names (INNs).

Figure 5.2 provides a map of the UMICs, LMICs, and LICs where four COVID-19 therapeutics—ensitrelvir, molnupiravir, nirmatrelvir (+ ritonavir), and remdesivir—may be offered for sale under the geographic coverage terms of the VLs. The map does not show whether the therapeutics were offered for sale in these locations, only whether they could be under the terms of VLs. Supply and demand factors—such as procurement priorities, regulatory approvals, testing and treatment infrastructure, and the course of

the pandemic—affected whether licensed therapeutics were available in these countries.⁵⁶¹ Figure 5.2 shows substantial coverage of Africa, where in most countries all four therapeutics could be offered for sale under VLs. On other continents, coverage is more mixed. Large UMICs with no licensed therapeutics available for sale under VLs include Argentina, Brazil, China, Colombia, Mexico, Russia, and Turkey.

Figure 5.2 UMICs, LMICs, and LICs where four COVID-19 therapeutics can be offered for sale under MPP licenses and BLAs, by count of treatment types

UMIC = upper-middle-income countries, LMIC = lower-middle-income countries, LIC = low-income countries. Underlying data for this figure can be found in appendix J, [table J.16](#).



Source: Airfinity, “COVID-19,” accessed August 9, 2023.

Notes: The four therapeutics are ensitrelvir, molnupiravir, nirmatrelvir (+ ritonavir), and remdesivir. HICs are not included in this map. The World Bank did not include the following countries in their list of income levels, therefore, they are not included in this figure: Anguilla, Cook Islands, Montserrat (one therapeutic each), and Venezuela (three therapeutics).

From a population standpoint, the potential availability of COVID-19 therapeutics under the geographic coverage terms of the VLs varies substantially by country income level.⁵⁶² At least one of the four therapeutics could be offered for sale to all, or virtually all, of the LIC and LMIC populations. In UMICs, at least one of the four therapeutics could be offered for sale to 14.7 percent of the collective UMIC population, but for 85.3 percent of the UMIC population none of the four therapeutics could be offered for sale under the terms of the VLs.⁵⁶³

Many of the countries not included in the scope of the VLs may hold promise as a market for the branded product, according to originator companies. For example, Merck states that it proactively approached all UMICs that are neither included in the coverage of VLs nor in global public health

⁵⁶¹ See chapter 6.

⁵⁶² This population calculation does not show whether the therapeutics were offered for sale in these locations, only whether they could be under the terms of VLs. Supply and demand factors—such as procurement priorities, regulatory approvals, testing and treatment infrastructure, and the course of the pandemic—affected whether licensed therapeutics were available in these countries.

⁵⁶³ Calculated using population data obtained from World Bank, World Development Indicators, “Population, total,” accessed May 10, 2023 (2021 population data).

programs, to explore their interest in procuring the branded product through advance supply agreements.⁵⁶⁴ Some countries, particularly UMICs in the Asia-Pacific region, entered into agreements to procure the branded product. Others, particularly many Latin American UMICs, reportedly did not prioritize procuring molnupiravir.⁵⁶⁵ For its part, Pfizer offered its branded product through a tiered-pricing approach based on each country's national income level and entered into supply agreements with UNICEF and the Global Fund to enable supply of its product in certain UMICs, LMICs, and LICs.⁵⁶⁶

Public health and nonprofit organizations raise concerns about differential pricing for branded products, stating that it generally results in much higher prices compared to licensed or generic products.⁵⁶⁷ In the case of COVID-19 therapeutics, tiered prices reportedly were multiples higher than the price negotiated by the Clinton Health Access Initiative.⁵⁶⁸ Concerns also have been raised about the exclusion of UMICs from the coverage territory of VLs because the exclusion may limit necessary economies of scale to make production of licensed products financially viable. According to advocacy organizations, the markets covered by VLs may not be valuable enough to support the multiple competitors they believe are needed for adequate supplies and lower prices for developing countries.⁵⁶⁹ Some suggest instead that licensed producers could pay higher royalty payments for sales made in UMICs rather than excluding them from VLs.⁵⁷⁰ Some Indian producers, however, consider the geographical scope of MPP licenses and BLAs to be sufficiently broad to support the production of licensed products. These licensees reported that a decline in demand as COVID-19 cases declined, consistent with the course of the pandemic, was the primary cause of constrained sales.⁵⁷¹

An additional feature of MPP licenses is that the locations where products can be offered for sale differ from where production is authorized.⁵⁷² This is particularly true for UMICs, which are generally excluded from the territorial coverage of VLs but may be authorized to produce licensed products for export. For example, there are 17 authorized production sites in China under MPP licenses.⁵⁷³ China is, however, outside the coverage territories of all MPP licenses for COVID-19 therapeutics (see figure 5.1). Most production sites are in India, an LMIC within the territorial coverage of all VLs.⁵⁷⁴ Indian producers

⁵⁶⁴ These global public health programs are described in chapters 1 and 6; Merck, written submission to the USITC, May 5, 2023, 9.

⁵⁶⁵ Merck, written submission to the USITC, May 5, 2023, 9–10.

⁵⁶⁶ Pfizer, written submission to the USITC, May 5, 2023, 17. For additional details on originator companies' equitable access programs, see Lilly, prehearing brief submission to the USITC, March 17, 2023, 2; Gilead, prehearing brief submission to the USITC, March 17, 2023, 10–13; and chapter 6.

⁵⁶⁷ Public Citizen, written submission to the USITC, May 5, 2023, 16–7; Rethink Trade, written submission to the USITC, May 5, 2023, 5; TWN, prehearing brief submission to the USITC, March 20, 2023, 7–8, 16–17.

⁵⁶⁸ For more information on the Clinton Health Access Initiative, please see table 1.1. See chapter 6 for a discussion of tiered pricing and access issues for COVID-19 therapeutics.

⁵⁶⁹ Public Citizen, written submission to the USITC, May 5, 2023, 16; People's Vaccine Alliance, written submission to the USITC, May 4, 2023, 8.

⁵⁷⁰ Pincombe and Guzman, *Lessons from Expanding Access to COVID-19 Treatments*, December 14, 2022; multilateral organization representative, interview by USITC staff, Switzerland, June 6, 2023.

⁵⁷¹ Industry representatives, interviews by USITC staff, July 7, July 10, and August 23, 2023.

⁵⁷² See also Rethink Trade, written submission to the USITC, May 5, 2023, 6; MSF, written submission to the USITC, May 17, 2023, 3; public health organization representative, interview by USITC staff, Switzerland, June 9, 2023; nonprofit organization representatives, interviews by USITC staff, Switzerland, June 7, 2023.

⁵⁷³ Airfinity, "COVID-19," accessed August 9, 2023.

⁵⁷⁴ Airfinity, "COVID-19," accessed August 9, 2023.

attribute their central role in licensed production to prior trusted relationships with licensors, a large and knowledgeable work force with capabilities in chemistry and pharmaceutical manufacturing, integrated production along the entire value chain, and substantial experience with quality standards and regulatory approval requirements.⁵⁷⁵ Licensees also are found in the Americas, the Asia-Pacific region, the Middle East, and Africa.⁵⁷⁶

Regulatory approval requirements, particularly at SRAs and the WHO, may be considered both an advantage—because they support the distribution of safe therapeutics—and a challenge—because of the difficulties and delays that may be associated with regulatory review. MPP agreements with sublicensees specify that products under the agreements must obtain approval from an SRA or WHO prequalification, as applicable.⁵⁷⁷ Some MPP licenses, such as the Merck and Shionogi agreements, permit conditional waivers on regulatory requirements to allow commercialization of the product before WHO prequalification or SRA approval.⁵⁷⁸

Compulsory Licenses

Overview

Compulsory licensing is the practice of a government allowing an entity aside from the patent owner, including the government itself, to produce a patented product or process without the consent of the owner.⁵⁷⁹ No compulsory licenses (CLs) have been used with respect to COVID-19 vaccines or diagnostics, though as discussed later in this chapter, COVID-19 therapeutics have been the subject of CLs in several instances.

As discussed in chapter 2, the TRIPS Agreement Article 31 allows member states to issue CLs to authorize use of a patent without the owner's consent, subject to certain conditions, including that the use be primarily for supplying the domestic market,⁵⁸⁰ and TRIPS Agreement Article 31*bis* waives this condition for pharmaceutical products exported to certain members in accordance with specified terms.⁵⁸¹ As also discussed in chapter 2, WTO members at the 12th Ministerial Conference adopted the 2022 Ministerial Decision, which provides additional flexibilities focused on compulsory licensing of patents for COVID-19 vaccines, including not subjecting the use of such patents for export to certain terms set forth in the Annex to Article 31*bis*.⁵⁸² TRIPS authorizes CLs, but domestic laws and regulations are typically needed to implement a CL program and to make individual CL determinations within that country. These laws take various forms. For example, laws making a CL an available remedy for different kinds of litigation, such as antitrust claims, exist in various jurisdictions.⁵⁸³ Procedural provisions for CL

⁵⁷⁵ Industry representatives, interviews by USITC staff, June 13, July 7, and July 10, 2023.

⁵⁷⁶ Airfinity, "COVID-19," accessed August 9, 2023.

⁵⁷⁷ MPP, "Foundation Statutes," November 23, 2020, art. 4l.

⁵⁷⁸ MPP, written submission to the USITC, May 5, 2023, 6, 9.

⁵⁷⁹ WTO, "Compulsory Licensing of Pharmaceuticals and TRIPS," accessed July 18, 2023.

⁵⁸⁰ TRIPS Agreement, arts. 31 and 31*bis*.

⁵⁸¹ TRIPS Agreement, art. 31*bis*.

⁵⁸² WTO, "Ministerial Decision on the TRIPS Agreement," WT/L/1141, WT/MIN(22)/30 (June 17, 2022), paras. 3.

⁵⁸³ See, e.g., Government of South Africa, Patents Act No. 57, 1978, § 56; industry representative, interview by USITC staff, South Africa, June 26, 2023.

issuance can also be a major legal component in CL usage by easing or complicating the requirements to pursue a CL for domestic use or export.⁵⁸⁴

Advantages and Challenges Associated with the Use of Compulsory Licenses

CLs are one of several ways to access IP, as explained throughout this chapter. This section will highlight some of the main benefits and challenges of relying on CLs for access to patented products and processes.

The primary, commonly cited benefit for countries utilizing CLs is the reduced cost of the pharmaceutical product or products at issue and improved access.⁵⁸⁵ By introducing generic drug manufacturing under a CL, some argue that drug prices come down.⁵⁸⁶ Research typically supports that CLs reduce prices, though certain tradeoffs are involved, as discussed below.⁵⁸⁷ Some research, however, indicates that the benefit of CL use in terms of lower prices is nonexistent among HICs for the most expensive category of pharmaceuticals (those newly patented or just entering the market).⁵⁸⁸ VLs also introduce generic drug manufacturing and typically, in addition, provide needed know-how for the generic's manufacturing and regulatory approval, as discussed above. VLs are not available, however, for the sale of COVID-19 therapeutics in a substantial number of UMICs.

It was also noted that the use of CLs, or potential use of CLs, can act as leverage.⁵⁸⁹ One of the more prominent ways this leverage can be exercised is in negotiating the inclusion of the potential CL-using producer into a VL and potentially lowering the price of the products of those arrangements.⁵⁹⁰ The utility of this leverage in terms of price negotiations is limited to a certain degree by various factors, including the availability of technical expertise to make use of the IP or the availability of a supplier.⁵⁹¹

⁵⁸⁴ See subsections on Zambia and Canada below for more information.

⁵⁸⁵ See the India and Malaysia subsections below for more information.

⁵⁸⁶ See, e.g., USITC, hearing transcript, March 30, 2023, 116–117, 122 (testimony of Sonya Reid Smith, Social Watch), 117–118 (testimony of Sangeeta Shashikant, TWN), 111–112 (testimony of James Love, KEI), 113–114 (testimony of Peter Maybarduk, Public Citizen); Watal, “Pharmaceutical Patents, Prices and Welfare Losses,” 2000, 742–746.

⁵⁸⁷ Watal, “Pharmaceutical Patents, Prices and Welfare Losses,” 2000, 742–746; see e.g., Mohara et al., “Impact of the Introduction of Government Use Licenses on the Drug Expenditure on Seven Medicines in Thailand,” January 2012; Sarmah, De Giovanni, and De Giovanni, “Compulsory Licenses in the Pharmaceutical Industry,” May 1, 2020, 28.

⁵⁸⁸ Qunaj, Kaltenboeck, and Bach, “Compulsory Licensing of Pharmaceuticals in High-Income Countries,” 2022, 284–285.

⁵⁸⁹ Industry representative, interview by USITC staff, South Africa, June 26, 2023; Martins, Almeida, and Valadao, “The Right to Health versus the Right to Property,” 2014, 390–392. See the Brazil, India, and South Africa sections below for more information.

⁵⁹⁰ Shadlen, Sampat, and Kapczynski, “Patents, Trade and Medicines,” January 2, 2020, 83; Ramani and Urias, “Access to Critical Medicines,” June 2015, 76; USITC, hearing transcript, March 29, 2023, 248, 262–263, (testimony of Tahir Amin, I-MAK); nonprofit organization representative, interview by USITC staff, May 8, 2023; see generally Urias and Ramani, “Access to Medicines after TRIPS,” December 1, 2020; multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023.

⁵⁹¹ Urias and Ramani, “Access to Medicines after TRIPS,” December 1, 2020, 377. See the India section below for more details.

The threat of a CL will not hold as much weight in a negotiation on either price or inclusion if it is apparent that a CL alone would not be adequate to allow the CL-issuing country to manufacture the pharmaceutical product, as occurred with COVID-19 vaccines.⁵⁹²

While not as frequently acknowledged as price reduction or negotiating leverage, development of a country's domestic manufacturing capacity has been said by some to be another potential benefit of that country utilizing CLs.⁵⁹³ When prices of the patented product are unaffordable and VIs are not granted, CLs can provide an avenue of developing a local solution and then increasing access.⁵⁹⁴ This approach might not lead to significant decreases in cost due to the necessary scaling-up that a local manufacturer would need to undergo, but the long-term benefit to the CL-issuing country may be more substantial in regards to price reduction.⁵⁹⁵ Development of domestic manufacturing can be limited, however, when know-how or trade secrets are necessary to manufacture the specific product.⁵⁹⁶

Countries that use CLs often encounter political and economic pressure when granting a CL or attempting to issue a CL.⁵⁹⁷ According to witness testimony and submissions, countries utilizing a CL have faced this pressure in various forms, including the threat of sanctions, claims of expropriation under investment law, and withdrawal of financial support on unrelated matters.⁵⁹⁸ In addition to the detrimental effects of these actions after CL implementation, commentators also note a chilling effect on the use of CLs by developing countries in the first place.⁵⁹⁹ Furthermore, the pharmaceutical sector reportedly has publicly retaliated against countries for utilizing CLs by withdrawing investment or withholding pharmaceutical products from the relevant market.⁶⁰⁰ The implementation of the 2022

⁵⁹² Nonprofit organization representative, interview by USITC staff, April 12, 2023; industry representative, interview by USITC staff, May 16, 2023. See chapter 6 for further information on pricing.

⁵⁹³ See India section and box 5.3 below for more information. Box 5.3 discusses flexibilities for LDCs that are distinct from CLs but allow the country to circumvent IP restrictions in a similar way.

⁵⁹⁴ See generally Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020; Davey, "Overcoming Patent Barriers to Increase Access to Medicines," Spring 2022, 691–703; Reichman, "Compulsory Licensing of Patented Inventions," Summer 2009, 257; see also Baker, "Don't Be Afraid of Compulsory Licenses Despite US Threats," February 20, 2018.

⁵⁹⁵ Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020, 376–377.

⁵⁹⁶ USITC, hearing transcript, March 29, 2023, 100–101 (testimony of Ashley Miller, AdvaMed), 115–116 (testimony of Zachary Rothstein, AdvaMed); industry representative, interview by USITC staff, May 16, 2023; Novak, Knall, "Will the Patent Waiver Proposal Really Help Third World Countries?," September 8, 2021.

⁵⁹⁷ CAMD, written submission to the USITC, May 5, 2023; USITC, hearing transcript, March 29, 2023, 313–314 (testimony of Rachel D. Thrasher), 25–26, 91–94 (testimony of James Love, KEI), 32 (testimony of Jennifer Reid, Oxfam America); Baker, "Don't Be Afraid of Compulsory Licenses Despite US Threats," February 20, 2018; Baker and Thrasher, "From Business as Usual to Health for the Future," March 2023, 9–10; Mermelstein and Stevens, "TRIPS to Where?," December 27, 2021, 1.1; Wong, Cole, and Kohler, *TRIPS Flexibilities and Access to Medicines*, October 28, 2022; Rosenberg, "Patent Laws Are Malleable," January 28, 2001, 693. See South Africa and Thailand sections below for more information.

⁵⁹⁸ USITC, hearing transcript, March 29, 2023, 91–94 (testimony of James Love, KEI), 313–314 (testimony of Rachel D. Thrasher); industry representative, interview by USITC staff, South Africa, June 26, 2023; Public Citizen, written submission to the USITC, May 5, 2023, 18–21.

⁵⁹⁹ Baker and Thrasher, "From Business as Usual to Health for the Future," March 2023, 9–10; Wong, Cole, and Kohler, *TRIPS Flexibilities and Access to Medicines*, October 28, 2022, 14–18; Reichman, "Compulsory Licensing of Patented Pharmaceutical Inventions," Summer 2009, 249.

⁶⁰⁰ Schuettler, "Angered U.S. Firm Excludes Thailand from New Drugs," March 14, 2007; nonprofit organization representative, interview by USITC staff, Switzerland, June 8, 2023. See South Africa and Thailand sections below for more information.

Ministerial Decision has been highlighted as a potential means of reducing both this political pressure and potentially limiting retaliation from the pharmaceutical sector, as it reaffirms the right to issue a CL in a similar way to the 2003 Doha Declaration on the TRIPS Agreement and Public Health.⁶⁰¹

A key challenge to effectively utilizing a CL is that the flexibility only covers patents and does not include know-how.⁶⁰² Know-how—which can include (but is not limited to) trade secrets, technical specifications and training, instructions, process controls, test data, and quality control procedures—is often necessary to reproduce more complex pharmaceutical products, such as vaccines.⁶⁰³ Other, less complex pharmaceutical products, such as certain small-molecule therapeutics, may be more readily manufactured without know-how from the patent holder.⁶⁰⁴ Industry representatives and others have pointed to the challenge of meeting domestic regulatory approval requirements when using a CL without the know-how of the patent holder, or concerns associated with producing a less safe product if such regulatory scrutiny does not exist domestically.⁶⁰⁵

Another challenge faced by countries attempting to successfully issue a CL is the potential lack of a qualified generic drug manufacturer interested in serving the available market.⁶⁰⁶ This issue could be either domestic (if attempting to use a CL under TRIPS Agreement Article 31) or foreign (if seeking exports under a CL issued through Article 31*bis*). In domestic markets, the challenge would essentially be the know-how problem described above; the country could not manufacture the pharmaceutical domestically without the necessary technical expertise.⁶⁰⁷ If seeking to import, a country could successfully issue a CL domestically to import under Article 31*bis* and then attempt to secure a foreign manufacturing partner to export the product at issue but ultimately not succeed. Either the lack of a

⁶⁰¹ USITC, hearing transcript, March 29, 2023, 95–97 (testimony of Patrick Kilbride, U.S. Chamber of Commerce); nonprofit organization representative, interview by USITC staff, April 12, 2023; nonprofit organization representative, interview by USITC staff, South Africa, June 26, 2023. See chapter 2 for more information on the Doha Declaration.

⁶⁰² USITC, hearing transcript, March 29, 2023, 100–102 (testimony of Ashley Miller, AdvaMed); academic representative, interview by USITC staff, May 16, 2023; see generally Perehudoff et al., “A Pandemic Treaty for Equitable Global Access to Medical Countermeasures,” July 14, 2022; Garrison, “What Is the ‘Know-How Gap’ Problem,” December 16, 2020, 6; nonprofit organization representative, interview by USITC staff, April 12, 2023. See Brazil section below for more information.

⁶⁰³ Perehudoff et al., “A Pandemic Treaty for Equitable Global Access to Medical Countermeasures,” July 14, 2022, 2.

⁶⁰⁴ Academic representative, interview by USITC staff, May 16, 2023; nonprofit organization representative, interview by USITC staff, April 12, 2023; Perehudoff et al., “A Pandemic Treaty for Equitable Global Access to Medical Countermeasures,” July 14, 2022, 2; Garrison, “What Is the ‘Know-How Gap’ Problem,” December 16, 2020, 8–10.

⁶⁰⁵ Academic representative, interview by USITC staff, May 16, 2023; USITC, hearing transcript, March 29, 2023, 20 (testimony of Joshua Teitelbaum, Alliance for Trade Enforcement), 171 (testimony of Cynthia Cardona, Lilly); Pfizer, written submission to the USITC, May 5, 2023, 25.

⁶⁰⁶ USITC, hearing transcript, March 29, 2023, 91–92 (testimony of James Love, KEI); Ramani and Urias, “Access to Critical Medicines,” June 2015, 76; Wong, Cole, and Kohler, *TRIPS Flexibilities and Access to Medicines*, October 28, 2022, 8–9. See Canada section below for more information.

⁶⁰⁷ Perehudoff et al., “A Pandemic Treaty for Equitable Global Access to Medical Countermeasures,” July 14, 2022; Ramani and Urias, “Access to Critical Medicines,” June 2015, 76.

willing generic drug manufacturer, or the country of jurisdiction of a willing manufacturer not granting a corresponding CL for export, could essentially nullify the CL for import.⁶⁰⁸

Legal and procedural hurdles in various forms present another substantial challenge for countries to utilize CLs.⁶⁰⁹ On the multilateral front, the requirement of Article 31(f) that a CL issued under that provision be used predominantly for the domestic market limits the extent to which countries without a capable domestic manufacturing base can benefit from the flexibility.⁶¹⁰ Article 31*bis* states that, for pharmaceutical products, the requirement that use be predominantly for domestic supply shall not apply for the purpose of exporting to eligible importing members subject to certain conditions.⁶¹¹ However, the conditions imposed by Article 31*bis* on the CL grantor and the CL beneficiary (i.e., importer) are considered particularly burdensome and prevent utilization of that flexibility, according to various commentators.⁶¹² On the domestic front, utilizing TRIPS Agreement flexibilities requires domestic implementation of a process to issue CLs.⁶¹³ A number of countries have not implemented such a process in their domestic law, while others have established a process but done so in such a way that the mechanism is challenging to use.⁶¹⁴ A number of countries and the EU, however, have updated or sought to update their domestic laws regarding CL usage to simplify and ease the process in response to the pandemic, potentially alleviating this problem for those countries.⁶¹⁵ Other specific requirements of domestic law can pose challenges to the implementation of a CL.⁶¹⁶

The impact of CL usage on innovation has been explored at length by various commentators.⁶¹⁷ Some state that CLs hurt innovation by removing the incentive for firms to invest in R&D, while others assert that CLs increase competition and thus foster innovation.⁶¹⁸ Others argue that there is no evidence CLs

⁶⁰⁸ Gurgula and Hull, “Compulsory Licensing of Trade Secrets,” November 1, 2021. Ramani and Urias, “Access to Critical Medicines,” June 2015, 76. Schouten, “Canada Based Biolyse Pharma Seeks to Manufacture COVID-19 Vaccines,” March 12, 2021. For more information, see Canada/Bolivia example in the Canada subsection below.

⁶⁰⁹ See Ecuador, India, South Africa, and Zambia sections below for more information.

⁶¹⁰ TRIPS Agreement art. 31(f); USITC, hearing transcript, March 29, 2023, 91–92 (testimony of James Love, KEI).

⁶¹¹ TRIPS Agreement art. 31*bis*(1).

⁶¹² TRIPS Agreement art. 31*bis*; USITC, hearing transcript, March 29, 2023, 376 (testimony of Brook K. Baker, Health Global Access Project, Inc.), 99 (testimony of Sangeeta Shashikant, TWN); Wong, Cole, and Kohler, *TRIPS Flexibilities and Access to Medicines*, October 28, 2022, 7; WTO, Council for Trade-Related Aspects of Intellectual Property Rights, “Annual Review of the CL System,” IP/C/84, November 14, 2019, 6.1(2); nonprofit organization, interview by USITC staff, Switzerland, June 7, 2023.

⁶¹³ TRIPS Agreement art. 31; Baker and Thrasher, “From Business as Usual to Health for the Future,” March 2023, 9.

⁶¹⁴ Baker and Thrasher, “From Business as Usual to Health for the Future,” March 2023, 9–10; academic representative, interview by USITC staff, Switzerland, May 2, 2023; USITC, hearing transcript, March 29, 2023, 25–26 (testimony of James Love, KEI).

⁶¹⁵ Baker and Thrasher, “From Business as Usual to Health for the Future,” March 2023; Gabriele, “The European Commission’s New Compulsory Licensing Proposal,” May 5, 2023; intergovernmental organization representative, interview by USITC staff, Switzerland, June 6, 2023.

⁶¹⁶ Baker and Thrasher, “From Business as Usual to Health for the Future,” March 2023; multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023. See the Ecuador section below for more information.

⁶¹⁷ See chapter 8 for more information on the effects of CLs on access, innovation, and global health.

⁶¹⁸ See Pfizer, written submission to the USITC, May 5, 2023, 24–25; USITC, hearing transcript, March 29, 2023, 95–96 (testimony of Patrick Kilbride, U.S. Chamber of Commerce); but see also USITC, hearing transcript, March 29, 2023, 31–32 (testimony of Jennifer Reid, Oxfam America).

harm innovation.⁶¹⁹ The specific factors at play in each CL usage—including the relevant laws, pharmaceutical products at issue, and context—influence how using a CL impacts innovation.⁶²⁰

Academic research on the effects of compulsory licensing is limited.⁶²¹ In the available literature on the impact of CLs on pharmaceutical products, researchers have generally found that CLs are associated with decreased pharmaceutical prices in the countries that used CLs.⁶²² The available research also associates CLs with increases in the number of people with access to patented products.⁶²³ There is some evidence that CLs encouraged innovation, where the literature has generally focused on the broader chemical industry.⁶²⁴

Compulsory Licensing Attempts and Outcomes

The following section profiles various actions taken by WTO Members since 2001 to use or attempt to use CLs for the production, importation, or exportation of pharmaceutical products. While CLs can be used for any patented invention, they are most often used in the context of public health.⁶²⁵ As noted, CLs have not been used with respect to any COVID-19 diagnostics or vaccines and, although COVID-19 therapeutics have been the subject of CLs in several instances, little information is available as to the impact of the CLs on prices or access. This chapter, therefore, provides examples of CLs for other pharmaceutical products, particularly in the context of HIV/AIDs, where more information is available. Each example will examine the context and outcomes of those actions, including the effects on product access, innovation, and global health where information is available.

Since 2001, there have been approximately 121 attempts to issue a public health CL, including four by the United States.⁶²⁶ The majority of these attempts were ultimately executed and resulted in a CL, but about a quarter of the attempts never came to fruition (figure 5.3).

⁶¹⁹ USITC, hearing transcript, March 29, 2023, 97–98 (testimony of Sangeeta Shashikant, TWN).

⁶²⁰ See South Africa and Thailand sections below for more information.

⁶²¹ See chapter 8 for a review of the academic literature on the effects of CLs, including information on product access, innovation, and global health.

⁶²² Urias and Ramani, “Access to Medicines after TRIPS,” December 1, 2020, 1; Tenni et al., “What Is the Impact of Intellectual Property Rules on Access to Medicines?,” April 15, 2022, 11.

⁶²³ Tenni et al., “What Is the Impact of Intellectual Property Rules on Access to Medicines?,” April 15, 2022, 11. See chapter 8 for more information on the available literature.

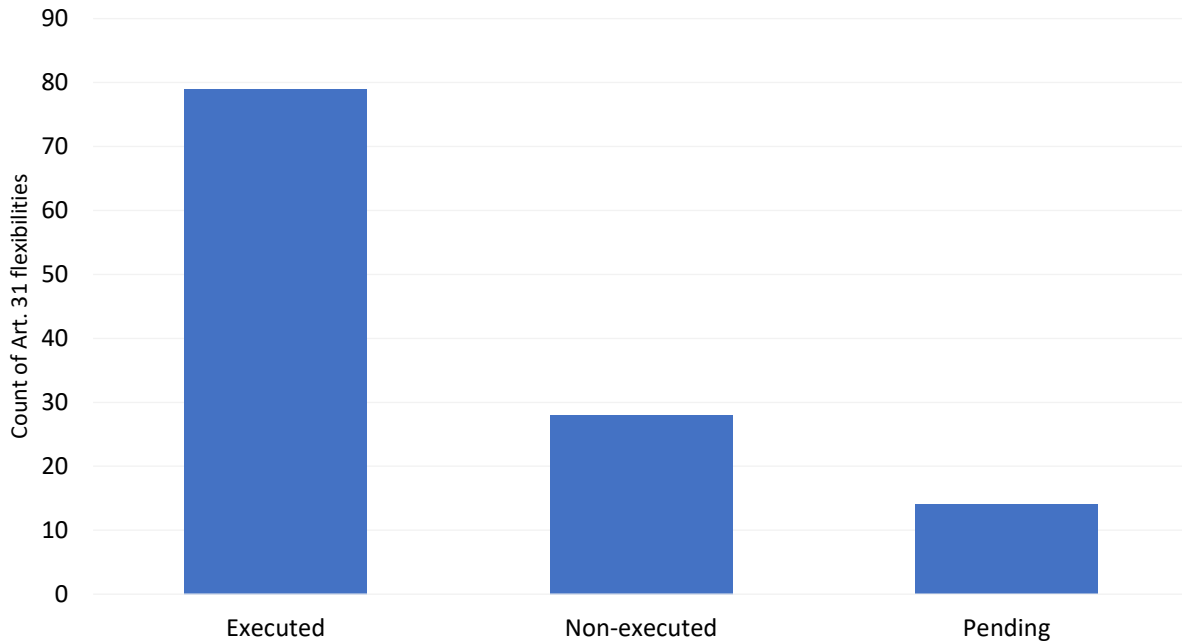
⁶²⁴ Baten, Bianchi, and Moser, “Compulsory Licensing and Innovation,” May 2017; Moser and Voena, “Compulsory Licensing,” February 1, 2012.

⁶²⁵ Thomas, *Compulsory Licensing of Patented Inventions*, January 14, 2014. A number of countries also expressly limit in their domestic laws the basis for which a CL can be granted to public health issues. See e.g., Government of Ecuador, Resolution No. 10-04 P-IEPI, January 15, 2010, art. 5.

⁶²⁶ ML&P, The TRIPS Flexibilities Database, accessed July 12, 2023. Medicines Law & Policy (ML&P), a nonprofit research organization based in the Netherlands, maintains the TRIPS Flexibilities database of instances when authorities have invoked, planned to invoke, or have been asked to invoke a TRIPS Agreement flexibility for public health reasons. This database is thorough in its coverage but is not an exhaustive list of all CL uses or attempts to use a CL. Because of the differences in national IP laws, the rules regarding TRIPS Agreement reporting requirements, and the role of private actors in potential CL uses through litigation, among other factors, certain actions may be omitted. Additionally, certain included actions might not be characterized as a CL or an attempt to use a CL by some parties. As a result, the database should be treated as an informative resource and not an authoritative summation of all relevant measures or attempts to implement measures.

Figure 5.3 Number of public health uses of TRIPS Agreement Art. 31 flexibilities since 2001, by execution status in count of Art. 31 flexibilities

Underlying data for this figure can be found in appendix J, [figure J.17](#).

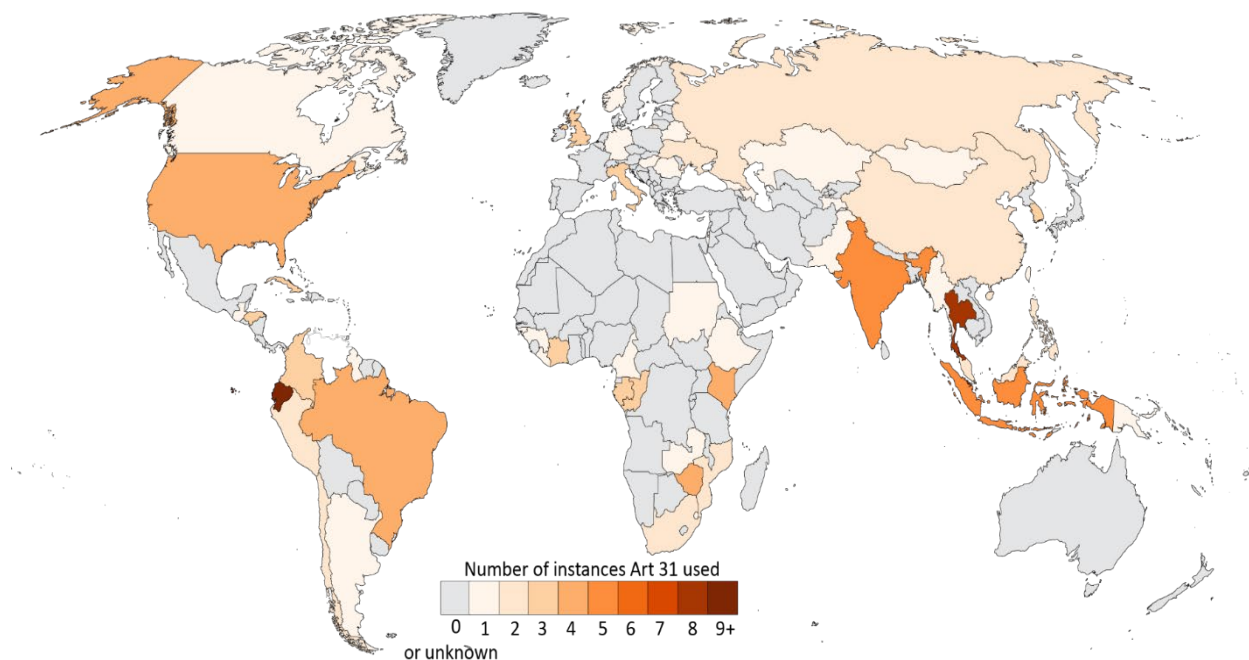


Source: ML&P, The TRIPS Flexibilities Database, accessed July 12, 2023.

As highlighted in figure 5.4 below, CL usage is spread throughout the world and includes countries of all World Bank income groups.

Figure 5.4 Number of public health uses and attempts to use TRIPS Agreement Art. 31 flexibilities since 2001, by country

In number of CL uses and attempts. Underlying data for this figure can be found in appendix J, [table J.18](#).



Source: ML&P, The TRIPS Flexibilities Database, accessed July 12, 2023.

Notes: While the Medicines Law & Policy database from which this map is derived is thorough in its coverage, it is not an exhaustive list of all CL uses or attempts to use a CL. Due to the differences in national IP laws, the rules regarding TRIPS Agreement reporting requirements, and the role of private actors in potential CL uses through litigation, among other factors, certain actions may be omitted. Additionally, certain included actions might not be characterized as a CL or attempt to use a CL by some parties, including the governments associated with the CL. As a result, the database should be treated as an informative resource and not an authoritative summation of all relevant measures or attempts to implement measures.

The following section profiles certain actions taken by WTO members to use or attempt to use CLs for the production, importation, or exportation of pharmaceutical products since 2001. This section first covers CL usage during the COVID-19 pandemic and then outlines CL usage through examples in a selection of countries in order of country income level: Zambia, India, Brazil, Ecuador, Malaysia, South Africa, Thailand, and Canada. Each example will examine the context and outcomes of those actions, including the effects on product access, innovation, and global health as information is available. The examples below were selected based on several factors, including the public availability of information, illustrative value, and representation in terms of both geography and economic status.

CL Usage During COVID-19 Pandemic

As noted throughout this report, the 2022 Ministerial Decision waived and clarified specific requirements for issuing CLs pertaining to COVID-19 vaccines.⁶²⁷ To date, however, CLs have not been used to access patents pertaining to COVID-19 vaccines. Bolivia did give notice of its intent to use TRIPS Agreement Article 31*bis* flexibilities to partner with a Canadian firm to source COVID-19 vaccines, but

⁶²⁷ WTO, “Ministerial Decision on the TRIPS Agreement,” WT/MIN(22)/30, June 22, 2022. See chapter 2 for more details on the 2022 Ministerial Decision.

the attempt did not come to fruition.⁶²⁸ CLs have also not been used to access patents associated with COVID-19 diagnostics.⁶²⁹

COVID-19 therapeutics have been the subject of CLs in several instances, though detailed information on the outcomes is often limited due to several factors, most notably the recency of the CLs. CLs in Hungary (remdesivir), Israel (Kaletra), and Russia (remdesivir) are some of the most documented instances.⁶³⁰ Reportedly, Hungary's CL allowed a domestic manufacturer to begin local production of remdesivir, and Hungary was able to treat patients and begin clinical trials as a result.⁶³¹ Reportedly, Israel's CL led, in part, to the patent holder pledging to not enforce the patent globally while Kaletra was being used for COVID-19 treatment.⁶³² Russia issued a CL for remdesivir, but evidence of the impact on access is limited.⁶³³ An Indian firm requested that a CL be granted for baricitinib, and the patent holder ultimately offered a VL to the firm.⁶³⁴ There are also CL attempts for COVID-19 therapeutics pending in a number of countries including Chile, Colombia, the Dominican Republic, and Peru.⁶³⁵

Zambia

Zambia, a LIC and LDC (see box 5.3), issued a CL in September of 2004 to manufacture a triple fixed-dose combination of three antiretrovirals for the treatment of HIV/AIDS.⁶³⁶ Despite its LIC status, Zambia agreed to pay some of the highest royalty rates for the products covered by its CL in a comparison of similarly situated countries as well as wealthier developing countries.⁶³⁷ Notwithstanding the issuance of the CL, the compound was never manufactured at a meaningful scale in Zambia.⁶³⁸ While the company that was granted the CL received the necessary patent rights, it ultimately did not have access to the manufacturing capacity or know-how to begin manufacturing the compound.⁶³⁹ Thus, despite the issuance of the CL, there was no subsequent impact on product access.

⁶²⁸ See Canada section below for further information.

⁶²⁹ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023. For more detail, see the discussion earlier in this chapter regarding the primary underlying patents for COVID-19 diagnostics.

⁶³⁰ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023; Bonadio and Contardi, "Compulsory Licences during the COVID-19 Pandemic: A European and International Perspective," November 21, 2022, 4–6.

⁶³¹ Bonadio and Contardi, "Compulsory Licences during the COVID-19 Pandemic: A European and International Perspective," November 21, 2022, 4–5.

⁶³² Bonadio and Contardi, "Compulsory Licences during the COVID-19 Pandemic: A European and International Perspective," November 21, 2022, 4.

⁶³³ Bonadio and Contardi, "Compulsory Licences during the COVID-19 Pandemic: A European and International Perspective," November 21, 2022, 5–6; Chheda, "Russia Compulsory License," July 12, 2021.

⁶³⁴ Bonadio and Contardi, "Compulsory Licences during the COVID-19 Pandemic: A European and International Perspective," November 21, 2022, 6.

⁶³⁵ Public Citizen, prehearing brief submission to the USITC, March 20, 2023, 14; ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

⁶³⁶ This report bases country classifications by income level off of the World Bank's 2022 list. Government of Zambia, Ministry of Commerce, Trade and Industry, Compulsory License no. CL 01/2004, September 22, 2004.

⁶³⁷ WHO, "Improving Access to Medicines in Thailand," February 6, 2008, 20.

⁶³⁸ Government representative, interview by USITC staff, Zambia, June 21, 2023; nonprofit organization representative, interview by USITC staff, Zambia, June 22, 2023.

⁶³⁹ Government representative, interview by USITC staff, Zambia, June 21, 2023; nonprofit organization representative, interview by USITC staff, Zambia, June 22, 2023.

The country's legal framework for issuing CLs currently presents another potential hurdle to the use of CLs. Specifically, the requirement for a mandatory three-year delay after the initial issuance of the patent in question before a CL can be granted has reportedly prevented quick usage of a CL.⁶⁴⁰ Zambian scholars have called for the country to update its IP law to follow in the footsteps of other countries like Canada, Chile, and Ecuador, which all made legislative changes to streamline CL issuance in response to the COVID-19 pandemic.⁶⁴¹ There are efforts within Zambia to address this potential delay for future public health emergencies, but the law in its current form would prevent a CL from quickly increasing product access even if the issues of manufacturing capacity and know-how were addressed.⁶⁴²

Box 5.3 Least-Developed Country Status

Least Developed Countries (LDCs) are a special classification of countries, as determined by the United Nations (UN).^a LDCs receive differential treatment under various WTO agreements; most relevant to this investigation are the flexibilities provided by the TRIPS Agreement that allow LDCs to postpone implementing most of their legal obligations under the TRIPS Agreement.^b This transition period was initially set at 10 years from a country's date of application, but has since been repeatedly extended by the WTO, with the most recent extension to expire no earlier than July 1, 2034.^c LDCs can use this transition period in multiple ways, depending on how they enact domestic legislation. Until the end of the transition, an LDC could for example provide no patent protection at all or provide patent protection for a period that is less than the 20-year minimum required under the TRIPS Agreement.^d LDCs that extend patent protection to processes and not products could continue in that manner until the end of the transition, despite TRIPS Agreement obligations typically applying to both products and processes.^e

Some LDCs, such as Bangladesh, have made use of these flexibilities. In 2008, Bangladesh suspended the issuance of pharmaceutical patents, and in 2022, made pharmaceutical and chemical products exempt from patent protection.^f Prior to the passage of a 2022 law, the term of patent protection in Bangladesh was only 16 years; the 2022 law extended it to 20 years for all patents aside from those covering pharmaceutical and chemical products.^g By copying or reverse-engineering foreign technologies while exempted from the patent protection obligations of the TRIPS Agreement, Bangladesh has been able to build the technological base of its pharmaceutical sector into a substantial industry.^h The sector's output has grown substantially from 1982 to 2017 comprising about 1 percent of gross domestic product, becoming the biggest white-collar employer in the country, and producing 97 percent of the country's pharmaceutical needs.ⁱ Bangladesh's pharmaceutical sector also supplies over 100 other countries including the United States.^j

Utilizing the LDC transition period, Bangladeshi manufacturers produce generic versions of nirmatrelvir (+ ritonavir), remdesivir, and baricitinib.^k Bangladesh also relies on the LDC transition period to export these pharmaceutical products to jurisdictions where the products are not covered by patents or where an applicable CL has been issued.^l According to the Embassy of Bangladesh, the country can also provide these drugs to other countries through parallel importation, which is the process of manufacturing the drugs legally and then exporting them without the permission of the patent holder.^m Manufacturers in Laos, Myanmar, and Paraguay also leverage their respective countries' LDC status to manufacture generic versions of COVID-19 therapeutics without a VL or having to issue a CL. The Paraguayan

⁶⁴⁰ Government of Zambia, The Zambia Patent Act of 2016, December 27, 2016, § 99(1); Mutale, "Access to COVID-19 Vaccines in Zambia through the Strategic Use of Patent Law," December 29, 2020.

⁶⁴¹ Mutale, "Access to COVID-19 Vaccines in Zambia through the Strategic Use of Patent Law," December 29, 2020.

⁶⁴² Government representative, interview by USITC staff, Zambia, June 21, 2023; Mutale, "Access to COVID-19 Vaccines in Zambia through the Strategic Use of Patent Law," December 29, 2020.

manufacturer produces a generic version of remdesivir; the Laos and Myanmar firms manufacture generic versions of molnupiravir.ⁿ

Other LDC countries, such as Zambia, have not used the flexibilities to the same degree. For example, Zambia issues pharmaceutical patents, with certain limitations, despite the LDC transition period.^o Zambia's patent law, however, previously limited patent protections to 16 years instead of the 20 years required under the TRIPS Agreement, with an option for the patent holder to extend the length of the patent protection. The patent term is now 20 years, however, and the terms of extension are more limited.^p The law also authorizes the government to declare a period of emergency and subsequently use any patented invention for the maintenance or the securing of supplies and services essential to the life of the community.^q Despite currently being an LDC, Zambia met the criteria for graduation from LDC status in 2021 and will be reassessed in 2024.^r If Zambia graduates out of its LDC status, it may have to reformulate its laws to make them TRIPS Agreement compliant.^s

Similarly, Bangladesh is expected to graduate from LDC status in 2026.^t The government is expecting challenges from having to come into compliance with standard TRIPS Agreement obligations, but actively is working to mitigate them before the graduation deadline.^u A number of Bangladeshi firms relying on the LDC transition period, however, have yet to chart a path for the post-LDC status manufacturing environment.^v

ⁿ UN, "Department of Economic and Social Affairs, LDC Identification Criteria & Indicators," accessed August 8, 2023; WTO, "Least-Developed Countries," August 8, 2023.

^o WTO, "Notification Portal, LDC Flexibilities Concerning Notification Obligations," accessed August 8, 2023; TRIPS Agreement, art. 66.1; WTO, "Analytical Index, TRIPS Agreement – Article 66 (Practice)," accessed August 8, 2023.

^p TRIPS Agreement art. 66.1; WTO, Council for Trade-Related Aspects of Intellectual Property Rights, "Extension of the Transition Period for LDCs," IP/C/88, June 29, 2021.

^q ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006, at 26; TRIPS Agreement, art. 33; nonprofit organization representative, interview by USITC staff, Switzerland, June 7, 2023.

^r ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006, at 26; TRIPS Agreement, art. 27(1).

^s Thrasher, "Bangladesh's Pharmaceutical Sector and Access to Medicines," September 23, 2021; Azam and Richardson, "Pharmaceutical Patent Protection and Trips Challenges for Bangladesh," January 1, 2011; Embassy of Bangladesh, written submission to the USITC, May 10, 2023, 4.

^t UN, "LDC Portal, What LDC Graduation Will Mean for Bangladesh's Drugs Industry," 2017; Hasan and Chakma, "New Patents Bill Passed," April 4, 2022; Government of Bangladesh, "Bangladesh Patents Act of 2022," April 11, 2022.

^u UN, "LDC Portal, What LDC Graduation Will Mean for Bangladesh's Drugs Industry," 2017.

^v Embassy of Bangladesh, written submission to the USITC, May 10, 2023, 1; UN, "LDC Portal, What LDC Graduation Will Mean for Bangladesh's Drugs Industry," 2017.

^w UN, "LDC Portal, What LDC Graduation Will Mean for Bangladesh's Drugs Industry," 2017.

^x Industry representative, interview by USITC staff, Bangladesh, July 19, 2023.

^y Government representative, interview by USITC staff, Bangladesh, July 17, 2023; ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006, 29; Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020, 370; nonprofit organization representative, interview by USITC staff, Switzerland, June 7, 2023.

^z Embassy of Bangladesh, written submission to the USITC, May 10, 2023, 1-2; WTO, "Glossary Term: Parallel Imports," August 8, 2023. Note that the use of parallel importation will depend on the domestic laws of the countries involved. See chapter 2 for more information on parallel imports.

^{aa} Airfinity, "COVID-19," accessed July 14, 2023.

^{ab} Government of Zambia, "The Zambia Patent Act of 2016," December 27, 2016. §§ 15–17. See Zambia section for more information.

^{ac} Government of Zambia, "The Zambia Patent Act of 2016," December 27, 2016. § 65 (previously §§ 29–30); ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006.

^{ad} Government of Zambia, "The Zambia Patent Act of 2016," December 27, 2016. § 105; ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006, 29.

^{ae} ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006.

^{af} ICTSD-UNCTAD, *The Ability of SSA Countries to Use TRIPS Flexibilities*, 2006.

^{ag} Embassy of Bangladesh, written submission to the USITC, May 10, 2023, 2; UN, General Assembly, "Graduation of Bangladesh from the LDC Country Category," A/RES/76/8, November 24, 2021, at para. 4.

^{ah} Embassy of Bangladesh, written submission to the USITC, May 10, 2023, 2; government representative, interview by USITC staff, Bangladesh, July 17, 2023.

^{ai} Industry representative, interview by USITC staff, Bangladesh, July 18, 2023; industry representative, interview by USITC staff, Bangladesh, July 19, 2023.

India

India, an LMIC, has made moderate use of CLs over the last 15 years to mixed results. Of the five attempts to secure a CL, one was granted, one was withdrawn, two were rejected, and one is currently pending.⁶⁴³ India's IP law gives the government a broad scope of potential rationales for granting a CL, including that the reasonable requirements of the public regarding the patented invention have not been satisfied, that the patented invention is not available to the public at a reasonably affordable price, and that the patented invention is not worked (e.g., put into use at commercial scale) in India.⁶⁴⁴ The government can, on the same grounds, sanction a patent holder by revoking the patent.⁶⁴⁵ In spite of this broad authority, the government has rarely issued CLs, and legal cases requesting the grant of CLs are seldom reported.⁶⁴⁶

This low usage could be the result of several factors. One explanation is that the previous iteration of India's patent law made CLs unnecessary for pharmaceuticals, as patents could not be granted for medicine or drugs until the law was amended in 2005 to implement the country's new obligations under the TRIPS Agreement.⁶⁴⁷ Pharmaceutical process patents were allowed, however, but only granted five to seven years of protection.⁶⁴⁸ Because CLs can only be granted three years after the patent is granted, the small window of utility has likely dissuaded CL issuance.⁶⁴⁹ The threat of retaliation by other governments has also been highlighted by the Indian government (in response to a request for comment by the Indian Supreme Court) as well as various commentators.⁶⁵⁰

Regardless of the low usage of CLs, India plays a prominent role in international IP and public health discussions, notably spearheading, along with South Africa, the initial waiver proposal to the TRIPS Council that resulted in the 2022 Ministerial Decision.⁶⁵¹ India's substantial manufacturing capacity allows it to bill itself as the "pharmacy to the world."⁶⁵² Furthermore, India's patent law makes CLs

⁶⁴³ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

⁶⁴⁴ Government of India, The Patents Act, 1970 (as amended in 2005), art. 84(1).

⁶⁴⁵ Government of India, The Patents Act, 1970 (as amended in 2005), art. 85(1).

⁶⁴⁶ Mueller, "The Tumultuous Transformation of India's Patent System," April 26, 2007, 581.

⁶⁴⁷ Government of India, The Patents Act, 1970, art. 5 (stating that "for substances intended for use or capable of being used as food, or as medicine or drug, no patent could be granted"); TRIPS art. 70, paras. 8–9; Watal, "Patents: An Indian Perspective," October 2015, 303.

⁶⁴⁸ Government of India, The Patents Act, 1970, art. 53(a) (stating "in respect of an invention claiming the method or process of manufacture of a substance, where the substance is intended for use, or is capable of being used, as food or as a medicine or drug, be five years from the date of sealing of the patent, or seven years from the date of the patent whichever period is shorter."); Mueller, "The Tumultuous Transformation of India's Patent System," April 26, 2007.

⁶⁴⁹ Government of India, The Patents Act, 1970 (as amended in 2005), art. 84(1); Mueller, "The Tumultuous Transformation of India's Patent System," April 26, 2007.

⁶⁵⁰ Government of India, Ministry of Home Affairs, Affidavit in the Matter of In Re: Distribution of Essential Supplies and Services during Pandemic, May 9, 2021, para. 46; Médecins Sans Frontières, "Compulsory Licenses, The TRIPS Waiver and Access to COVID-19 Medical Technologies," May 2021; Chintan, "Making Drugs and Vaccines Accessible, Affordable," June 20, 2021.

⁶⁵¹ WTO, Council for Trade-Related Aspects of Intellectual Property Rights, "Communication Regarding the Waiver from Certain Provisions of the TRIPS Agreement, Revised Decision Text," IP/C/W/669/Rev.1, May 25, 2021; WTO, Council for Trade-Related Aspects of Intellectual Property Rights, "Communication from India and South Africa Regarding the Waiver from Certain Provisions of the TRIPS Agreement," IP/C/W/669, October 2, 2020.

⁶⁵² India Global Business, "Reasons Why India Is the Pharmacy to the World," June 3, 2016.

available for the manufacture and export of pharmaceuticals to any country with insufficient pharmaceutical manufacturing capacity to address public health problems if the importing country has issued a CL.⁶⁵³ The potential of India supplying generic pharmaceutical products to a country that issues a CL reportedly is a major tool for the importer in negotiations for either price reductions on the branded product or securing a VL, though this leverage is typically only available when the pharmaceutical product in question is not protected by a patent in India or the importing country does not have the requisite manufacturing capacity.⁶⁵⁴ Indian firms seeking a CL have also been associated with the expansion of existing VLs to include more firms as sublicensees.⁶⁵⁵ This combination of manufacturing capacity and a readily available legal avenue for export means that India looms large in addressing public health needs throughout the world.⁶⁵⁶ This substantial presence can have a detrimental effect on other countries' attempts to develop their own pharmaceutical manufacturing sectors, however, when cheaper, readily available imports from India overwhelm the domestic industry.⁶⁵⁷

Brazil

Brazil, a UMIC, had mixed results with CLs during the past two decades. Of the four efforts to have CLs granted, two were not issued, one ultimately came to fruition in 2007, and one is currently pending.⁶⁵⁸ The two attempts that were not issued reportedly led to negotiated VLs with the patent holders and ultimately lower prices for the two HIV/AIDS drugs in question, both compared to the original price and to the prices paid by similarly situated countries.⁶⁵⁹ According to various stakeholders, the CL that was granted in 2007 did not achieve its primary purpose of improving access, in large part because of the 2–3 years it took to begin local production.⁶⁶⁰ Despite the issuance of the CL and efforts by the government to translate various patents into Portuguese for the use of domestic manufacturers of generic drugs, the patented technology reportedly was not used because of the lack of necessary know-how and technical expertise to manufacture the products.⁶⁶¹ That CL has since been revoked. The only

⁶⁵³ Government of India, The Patents Act, 1970 (as amended in 2005), art. 92a.

⁶⁵⁴ Ramani and Urias, "Is Compulsory Licensing an Effective Mechanism to Lower Drug Prices?," September 3, 2020, 368–369.

⁶⁵⁵ Bonadio and Contardi, "Compulsory Licences during the COVID-19 Pandemic: A European and International Perspective," November 21, 2022, 8.

⁶⁵⁶ See generally Waning, "The Role of Indian Generic Manufacturers in Supplying ARVs to Developing Countries," September 14, 2010. For example, Malaysia imports a hepatitis C drug that was the subject of a CL from India. Industry representative, interview by USITC staff, Malaysia, July 25, 2023.

⁶⁵⁷ Industry representative, interview by USITC staff, South Africa, June 28, 2023; industry representative, interview by USITC staff, South Africa, June 28, 2023.

⁶⁵⁸ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

⁶⁵⁹ Agência Saúde, "Statement of the Brazilian Minister of Health," August 7, 2005; Brazilian Ministry of Health, "Brazilian Statement on Compulsory License for Nelfinavir," August 22, 2001; Petersen, "Brazil Will Defy Patent on AIDS Drug Made by Roche," August 23, 2001; Nunn et al., "Evolution of Antiretroviral Drug Costs," November 2007, 1805; multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023.

⁶⁶⁰ Industry representatives, interviews by USITC staff, Brazil, June 27 and June 28, 2023; government representative, interview by USITC staff, Brazil, June 26, 2023.

⁶⁶¹ Government of Brazil, Decree No. 6.108, May 4, 2007 (revoked in 2019 by Government of Brazil, Decree No. 9.917, July 18, 2019); Jorda, "Trade Secrets and Trade-Secret Licensing," 2007, 1051.

subsequent attempt to issue a CL has come from a civil society request for a CL as a remedy to alleged monopolistic behavior by the patent holder.⁶⁶²

Like several other countries, there were various legislative efforts in Brazil to update domestic IP law to ease the use of CLs in response to the COVID-19 pandemic. These efforts ultimately led to little substantive changes, however, as the more potentially impactful provisions of the legislation were struck from the final bill by way of a veto.⁶⁶³ The Brazilian legislature eventually upheld the veto.⁶⁶⁴ Brazilian manufacturers of generic pharmaceuticals generally did not support the more substantive changes, because they stated they do not find CLs to be useful without the necessary know-how and technical expertise.⁶⁶⁵

Ecuador

Ecuador, a UMIC, has been one of the most active countries in issuing or attempting to issue CLs.⁶⁶⁶ From 2003 to 2021, Ecuador issued or attempted to issue 13 CLs related to public health, the majority of which came to fruition.⁶⁶⁷ The CLs and attempted CLs covered treatments for various ailments, including cancer, rheumatoid arthritis, COVID-19, and HIV/AIDS; treatments for HIV/AIDS were by far the most common subject of a CL, comprising seven of the 13 actions.⁶⁶⁸ The one CL attempt related to COVID-19 appears to not have come to fruition, despite a resolution from the Education, Science, and Technology Commission of the National Assembly requesting the government and the Ministry of Health to take action.⁶⁶⁹

One potential reason for the CL related to COVID-19 not coming to fruition is Ecuador's domestic law. Because the IP at issue must first be covered by an Ecuadorian patent, a process that reportedly takes

⁶⁶² Government of Brazil, Decree No. 9.917, July 18, 2019; Associação Brasileira de Assistência à Mucoviscidose, "Letter to Brazilian Minister of Health," February 6, 2023.

⁶⁶³ Government of Brazil, Law No. 14,200, September 2, 2021; Library of Congress, "Brazil: Patent Law Amended to Allow for Compulsory Licensing of Patents," October 12, 2021. Note that Brazilian law allows for line-item vetoes. Government of Brazil, Constitution of Brazil, art. 66 (§§ 1–2), October 5, 1988.

⁶⁶⁴ Leonardos, "Compulsory License: Patent Owners in Brazil Are under No Obligation to Provide Know-How and Raw Materials," July 6, 2022; industry representative, interview by USITC staff, Brazil, June 28, 2023.

⁶⁶⁵ Industry representatives, interviews by USITC staff, Brazil, June 27 and June 28, 2023.

⁶⁶⁶ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

⁶⁶⁷ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023. The ML&P database includes 11 CL actions for Ecuador. Additionally, Ecuador granted a CL for an HIV/AIDS medication in 2021 and attempted a CL related to COVID-19 in 2020. See Government of Ecuador, Resolution No. LO-001-2021-DNPI-SENADI, February 25, 2021; Knowledge Ecology International, "Ecuador Grants Compulsory License over HIV Drug Raltegravir," March 4, 2021; Government of Ecuador, Ministry of Health, "Ecuador Granted Nine Compulsory Licenses for Strategic Medicines," accessed August 8, 2023; Abinader, "Legislative Committee in Ecuador Approves Resolution on Compulsory Licensing of Patents Relating to the Coronavirus," March 20, 2020.

⁶⁶⁸ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023; Government of Ecuador, Resolution No. LO-001-2021-DNPI-SENADI, February 25, 2021.

⁶⁶⁹ Government of Ecuador, National Assembly, "Resolution to Require the National Government to Establish Compulsory Licenses," March 20, 2020; Abinader, "Legislative Committee in Ecuador Approves Resolution on Compulsory Licensing of Patents Relating to the Coronavirus," March 20, 2020; Ponce, "Ecuador: Patent, Compulsory Licenses and the Covid-19," accessed August 8, 2023.

several years, Ecuador could not quickly grant a CL for COVID-19 therapeutics.⁶⁷⁰ Unlike Brazil and other countries in the region, Ecuador currently has no fast-track process for patents.⁶⁷¹ This delay makes the effective use of a CL in Ecuador for novel IP during a public health emergency highly challenging.⁶⁷² In addition, one commentator pointed to Ecuador as a target of political pressure from the United States regarding its use of CLs.⁶⁷³ Others have noted that Ecuador's use of CLs led to political difficulties between the United States and Ecuador in the past.⁶⁷⁴

Malaysia

Malaysia, a UMIC, has issued two public health CLs: one in 2003 for a combination of drugs to treat HIV/AIDS and the other in 2017 for a drug to treat hepatitis C.⁶⁷⁵ The former CL reportedly resulted in a substantial reduction in cost for the drugs.⁶⁷⁶ The latter CL for a hepatitis C drug reportedly resulted in an even greater cost reduction and allowed the Malay government to provide the drug free of cost.⁶⁷⁷ Other similarly situated countries that were able to negotiate VLs with the patent owner of the hepatitis C drug, however, were each reportedly able to treat 10 times more people than was Malaysia in the year the license was issued, and the VL negotiated price was lower than the CL price.⁶⁷⁸ About the time of the issuance of the CL for the hepatitis C pharmaceutical, however, Gilead expanded its VLs for the treatment to include Malaysia, reportedly as a result of Malaysia's pursuit of the CL.⁶⁷⁹ To date, it is estimated that between 18,000 and 20,000 patients have been treated for hepatitis C in Malaysia, but fewer than 200 had been treated before the issuance of the relevant CL.⁶⁸⁰ After the 2017 issuance of the hepatitis C CL, which expired in October 2020, Malaysia issued no additional CLs because the

⁶⁷⁰ Government of Ecuador, Resolution No. 10-04 P-IEPI, art. 4, January 15, 2010; Ponce, "Ecuador: Patent, Compulsory Licenses and the Covid-19," accessed August 8, 2023.

⁶⁷¹ Szymczak, "Patent Applicant Pendency in Various Countries: Part 1," August 31, 2022; Ponce, "Ecuador: Patent, Compulsory Licenses and the Covid-19," accessed August 8, 2023. Ecuador is reportedly in negotiations with the USPTO to join the Patent Prosecution Highway (PPH), however, which could potentially expedite the Ecuadorian patent examination process. For more information on the PPH see USPTO, "Patent Prosecution Highway (PPH) - Fast Track Examination of Applications," August 8, 2023.

⁶⁷² Ponce, "Ecuador: Patent, Compulsory Licenses and the Covid-19," accessed August 8, 2023.

⁶⁷³ Public Citizen, written submission to the USITC, May 5, 2023, 18–20; Public Citizen, "Leaked Cables Show U.S. Tried, Failed to Organize Against Ecuador Compulsory Licensing," May 10, 2011.

⁶⁷⁴ Oser, "The COVID-19 Pandemic: Stress Test for Intellectual Property and Pharmaceutical Laws," July 19, 2021, 3.

⁶⁷⁵ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

⁶⁷⁶ WHO, "Improving Access to Medicines in Thailand," February 6, 2008, 21. The drugs covered by the CL were didanosine (ddI), lamivudine and zidovudine (combivir), and zidovudine (AZT).

⁶⁷⁷ USITC, hearing transcript, March 29, 2023, 98 (testimony of Sangeeta Shashikant, TWN); industry representative, interview by USITC staff, Malaysia, July 25, 2023. The drug covered by the CL was sofosbuvir.

⁶⁷⁸ USITC, hearing transcript, March 29, 2023, 110–111 (testimony of Kevin Haninger, PhRMA), 214 (testimony of Anu Osinusi, Gilead); Galen Center, written submission to the USITC, May 5, 2023, 4; industry representative, interview by USITC staff, Malaysia, July 25, 2023.

⁶⁷⁹ USITC, hearing transcript, March 29, 2023, 117–118 (testimony of Sangeeta Shashikant, TWN), 215 (testimony of Melissa Barber); Galen Center, written submission to the USITC, May 5, 2023, 4; Thiru, "WTO Trade Policy Review," April 27, 2018; Brennan, "Malaysia Issues Compulsory License for Gilead Hepatitis C Drug," September 15, 2017; Saez, "Malaysia Grants Compulsory Licence For Generic Sofosbuvir," September 15, 2017; Gilead, *Chronic Hepatitis C Treatment Expansion*, November 2017.

⁶⁸⁰ Government representative, correspondence with USITC staff, Malaysia, July 26, 2023.

government had sufficient supply of the hepatitis C drug, and a CL during COVID-19 was deemed unnecessary.⁶⁸¹

Some industry representatives believed the CLs ultimately did not improve access and were concerned about the impact on IP-related investment in Malaysia.⁶⁸² This may be in part due to the scope of the Malaysian CLs covering only government use, and not use by private industry.⁶⁸³ Another stakeholder who formerly supported the issuance of CLs in Malaysia ultimately concluded that IP was not the problem facing Malaysia's healthcare system. Instead, they pointed to various other issues like the public's lack of desire to receive treatment, the burnout of Malaysian healthcare workers, and the deteriorating healthcare infrastructure as more pressing issues related to Malaysian healthcare access.⁶⁸⁴

South Africa

South Africa, a UMIC, has never granted a CL to manufacture or export pharmaceutical products, despite having one of the most advanced regulatory frameworks for issuing CLs on the continent.⁶⁸⁵ The country has not yet taken steps to make use of the 2022 Ministerial Decision.⁶⁸⁶

During the HIV/AIDS pandemic when South Africa was heavily impacted and, as a result, suffered substantial loss of life and a significant economic downturn, no CLs were issued (box 5.4).⁶⁸⁷ The threat of a CL was sufficient to secure access to various antiretrovirals through VLs.⁶⁸⁸ In 2003, when a complaint was filed with the South African Competition Commission (SACC) against multinational biopharma company GSK (formerly GlaxoSmithKline) and others for abusing their market dominance by refusing to grant VLs to South African generic drug manufacturers, the SACC agreed with the complaint and referred the case to the Competition Tribunal for determination.⁶⁸⁹ The SACC requested that the tribunal grant, among other things, a general use CL for the drugs at issue.⁶⁹⁰ Before the tribunal acted on the referral, however, the parties settled the dispute. The settlement included, among other things,

⁶⁸¹ Government representative, interview by USITC staff, Malaysia, July 25, 2023.

⁶⁸² Industry representatives, interviews by USITC staff, Malaysia, July 21, 2023.

⁶⁸³ Industry representatives, interviews by USITC staff, Malaysia, July 21, 2023.

⁶⁸⁴ Industry representative, interview by USITC staff, Malaysia, July 21, 2023.

⁶⁸⁵ ML&P, *The TRIPS Flexibilities Database*, accessed July 19, 2023; Nkomo, "The Under-Utilization of TRIPS Flexibilities by Developing Countries: The Case of Africa," *WIPO-WTO Colloq. Pap. Vol. 1 2010*, in *WIPO-WTO Colloquium Papers, Volume 1 (2010)*, 2010, 134.

⁶⁸⁶ Avafia, Berger, Hartzenberg, "The Ability of Select Sub-Saharan African Countries to Utilise TRIPs Flexibilities," September 20, 2006; DOC, "South Africa – Protecting Intellectual Property," May 6, 2023; industry representative, interview by USITC staff, South Africa, June 26, 2023; government representative, interview by USITC staff, South Africa, June 29, 2023; Kizor-Akaraiwe, "South Africa Compulsory Licensing," May 17, 2021.

⁶⁸⁷ Academic representative, interview by USITC staff, May 16, 2023; Dixon, McDonald, and Roberts, "The Impact of HIV and AIDS on Africa's Economic Development," January 26, 2002.

⁶⁸⁸ Industry representative, interview by USITC staff, South Africa, June 26, 2023; academic representative, interview by USITC staff, May 16, 2023.

⁶⁸⁹ Government of South Africa, *Hazel Tau & Others v GlaxoSmithKline and Boehringer Ingelheim*, Case No. 2002Sep226, September, 2002; UNCTAD, "Hazel Tau & Others v. GlaxoSmithKline, Boehringer Ingelheim & Others, 2002," December 2020.

⁶⁹⁰ Government of South Africa, *Hazel Tau & Others v GlaxoSmithKline and Boehringer Ingelheim*, Case No. 2002Sep226, September, 2002; UNCTAD, "Hazel Tau & Others v. GlaxoSmithKline, Boehringer Ingelheim & Others, 2002," December 2020.

the issuance of VLs to generic drug manufacturers for various antiretrovirals as well as permission to export them to other sub-Saharan African countries.⁶⁹¹ A similar complaint in 2007 against Merck and its South African subsidiary resulted in an agreement with multiple licensees to bring to market a wide range of generic products used as part of first-line antiretroviral treatment in South Africa.⁶⁹² In the wake of these actions, however, South Africa suffered from pharmaceutical firms pulling investment from the country, increased pharmaceutical import costs, and loss of talent in the country. This adverse reaction to these VLs led to the view that South Africa would ultimately suffer a net loss from using CLs.⁶⁹³

Another potential motivation for South Africa to not utilize CLs within the context of the COVID-19 pandemic was Moderna's pledge to not enforce its patent rights for its mRNA vaccine during the duration of the pandemic, which was potentially done as a preemptive measure by Moderna to prevent countries using CLs.⁶⁹⁴ This allowed South Africa to develop its own mRNA vaccine based on the Moderna vaccine through Afrigen with the help of the NIH, the WHO, and the MPP, despite Moderna's not participating in any technology transfer or conveyance of know-how.⁶⁹⁵ Moderna updated its pledge after the WHO declared the end of the COVID-19 pandemic as a global health emergency, stating that it will "never enforce our patents for COVID-19 vaccines against companies manufacturing in or for the 92 low- and middle-income countries in the Gavi COVAX Advance Market Commitment (AMC), provided that the manufactured vaccines are solely for use in the AMC 92 countries."⁶⁹⁶ As South Africa is not included in the 92 AMC countries, it remains unclear if Moderna will act to enforce its rights against Afrigen or other similarly situated manufacturers producing mRNA vaccines for COVID-19 or other diseases going forward.⁶⁹⁷

⁶⁹¹ OECD, "Generic Pharmaceuticals, Note by South Africa," May 19, 2014, 4; industry representative, interview by USITC staff, South Africa, June 26, 2023; CPTech, "Competition Commission Finds Pharmaceutical Firms in Contravention of the Competition Act," October 16, 2003.

⁶⁹² Government of South Africa, *Treatment Action Campaign v Bristol-Myers Squibb*, Case No. 2007Nov 3328, November 2007; OECD, "Generic Pharmaceuticals, Note by South Africa," May 19, 2014, 4; industry representative, interview by USITC staff, South Africa, June 26, 2023. Note that this complaint was not referred to the Competition Tribunal with the request of a general use CL like the 2003 complaint against GSK. Subsequently, this complaint does not show up in the ML&P database.

⁶⁹³ Industry representative, interview by USITC staff, South Africa, June 26, 2023; government representative, interview by USITC staff, South Africa, June 29, 2023.

⁶⁹⁴ Moderna, "Moderna's Updated Patent Pledge," March 7, 2022; government representative, interview by USITC staff, South Africa, June 29, 2023; industry representatives, interviews by USITC staff, South Africa, June 26 and June 27, 2023.

⁶⁹⁵ Acharya, "South Africa's Afrigen Partners with U.S. on mRNA Vaccine Research," July 8, 2022; industry representatives, interviews by USITC staff, South Africa, June 26 and June 27, 2023; government representative, interview by USITC staff, South Africa, June 29, 2023.

⁶⁹⁶ Moderna, "Moderna's Updated Patent Pledge," March 7, 2022; UN, "WHO Chief Declares End to COVID-19 as a Global Health Emergency," May 5, 2023.

⁶⁹⁷ Government representative, interview by USITC staff, South Africa, June 29, 2023; industry representative, interview by USITC staff, South Africa, June 26 and June 27, 2023. Moderna told Politico that despite South Africa not being included in the list of eligible countries, the pledge regarding COVID-19 vaccines would also include the WHO mRNA Tech Transfer Hub, which is located in Cape Town, South Africa. mRNA vaccines developed in the future are not covered by the pledge. Furlong, "Moderna to Share Vaccine Tech, Commits to Never Enforce COVID-19 Jab Patents," March 8, 2022.

One more potential reason for the lack of CL usage in South Africa is the country's own IP interests.⁶⁹⁸ The relationship between the government and the pharmaceutical sector has been mixed, with various firms suing the government to block the 1997 amendment to South Africa's patent laws that would make issuing CLs easier, among other things (though the suit was eventually dropped due to public pressure).⁶⁹⁹ However, South Africa has become an innovator in its own right and wants to protect its own firms as well as the IP they originate.⁷⁰⁰ This balance between innovation and access has been at issue in the drafting of new patent laws in South Africa, which would potentially allow for South Africa to utilize the 2022 Ministerial Decision, and has led to lengthy debates publicly and within the government about the content of the pending legislation since a framework document was released in 2018.⁷⁰¹ The government is also mindful of the negative responses it received after securing VLS for antiretrovirals with the threat of issuing CLs, as well as the retaliation from the pharmaceutical industry that Thailand reportedly faced when it issued CLs for HIV/AIDS treatments from 2006 to 2008.⁷⁰²

While the South African government has not made use of CLs, this has not prevented several individuals and civil society groups from attempting to do so through litigation. There have been a handful of attempts, primarily in the 1990s, to sue for the grant of a CL as the requested remedy for alleged abuse of a patent by the patent holder.⁷⁰³ These suits were all unsuccessful due to failure by the litigants to meet the various statutory requirements under South African law.⁷⁰⁴ In 2023, civil society organizations initiated litigation seeking a CL for a cystic fibrosis treatment, which is pending.⁷⁰⁵

Thailand

Thailand, a UMIC, has been one of the more prolific users of CLs.⁷⁰⁶ The bulk of this usage came between 2006 and 2008, when the Thai government issued eight CLs for pharmaceutical products to treat cancer,

⁶⁹⁸ Government representative, interview by USITC staff, South Africa, June 29, 2023; industry representatives, interviews by USITC staff, South Africa, June 26 and June 29, 2023.

⁶⁹⁹ Bird, "Developing Nations and the Compulsory License: Maximizing Access to Essential Medicines while Minimizing Investment Side Effects," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009) at 212; Government of South Africa, "Medicines and Related Substances Control Act Amendment 90," December 1997.

⁷⁰⁰ Government representative, interview by USITC staff, South Africa, June 29, 2023; industry representatives, interviews by USITC staff, South Africa, June 26, June 27, June 28, and 2023.

⁷⁰¹ Chaskalon, "FTPL Patent Law Reform June 2022," June 12, 2022; government of South Africa, "Intellectual Property Policy of the Republic of South Africa Phase I," August 2018; Fix The Patent Laws, *The Report*, accessed July 19, 2023; government representative, interview by USITC staff, South Africa, June 29, 2023; nonprofit organization representative, interview by USITC staff, South Africa, June 26, 2023; industry representative, interview by USITC staff, South Africa, June 26, 2023.

⁷⁰² Government representative, interview by USITC staff, South Africa, June 29, 2023; industry representatives, interviews by USITC staff, South Africa, June 26 and June 27, 2023. See box 5.3 and Thailand subsection for more information.

⁷⁰³ Kizor-Akaraiwe, "South Africa Compulsory Licensing," May 17, 2021; industry representative, interview by USITC staff, South Africa, June 26, 2023.

⁷⁰⁴ Kizor-Akaraiwe, "South Africa Compulsory Licensing," May 17, 2021; Government of South Africa, Patents Act No. 57, 1978, § 56.

⁷⁰⁵ Right to Breathe, "2023 Campaign Briefing," March 23, 2023.

⁷⁰⁶ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023. See generally Reichman, "Compulsory Licensing of Patented Inventions," Summer 2009.

HIV/AIDS, and cardiovascular disease.⁷⁰⁷ The CLs collectively reduced the cost of the pharmaceutical products in Thailand substantially, bolstering access for the Thai populace.⁷⁰⁸ However, delays in production due to objections from the patent holders and the confusion of generic drug manufacturers reportedly delayed access.⁷⁰⁹

Thailand's CLs and subsequent reduction in the market returns of pharmaceutical industries have collectively been noted by researchers in the Thai Ministry of Health as a disincentive for pharmaceutical investment in the country.⁷¹⁰ In this vein, Abbott reportedly withheld new drugs from the Thai market in 2007 after the government made use of CLs.⁷¹¹ According to one industry representative, Abbott's action did not go unnoticed by other similarly situated countries, creating a reticence in some to make use of CLs for fear of a similar outcome.⁷¹² Thailand issued three more CLs in 2012, but none thereafter (box 5.4).⁷¹³

Box 5.4 Lessons from the HIV/AIDS Epidemic

The national and global actions taken to address the ongoing HIV/AIDS epidemic may convey lessons for responses to both COVID-19 and future global health emergencies.

One such lesson is the role that CLs can play in providing countries leverage to negotiate prices or secure VLs. In some of the countries most affected by the epidemic—such as South Africa, where one in five adults was HIV-positive as of the early 2000s—the medicines necessary to treat HIV/AIDS were patented and unaffordable for most patients.^a South Africa was able to leverage the threat of a CL as the result of antitrust action to secure VLs for antiretrovirals, and subsequently more affordable prices, on two separate occasions.^b Similarly, Brazil and Thailand were also able to use the threat of CLs to negotiate lower prices for HIV/AIDS drugs.^c Despite these successes regarding VLs and price reductions, both South Africa and Thailand reportedly received backlash from pharmaceutical firms as a result of their actions with detrimental effects on both countries' pharmaceutical sectors, as mentioned above.^d

Another lesson is the potential price-lowering effect of expanded generic drug manufacturing. The Gilead Access Program to improve developing country access to antiretrovirals for HIV/AIDS treatment began in 2003 with a tiered-pricing strategy of “no-profit prices.”^e Despite these efforts, prices were still too high for many developing countries to afford.^f In 2006, Gilead shifted to a VL strategy, through a series of bilateral contracts, by authorizing trusted generic drug manufacturers to produce and sell its HIV/AIDS drugs in designated countries throughout the world.^g With competition among licensees, prices reportedly dropped from \$17/month under Gilead's no-profit pricing of its branded medicines to

⁷⁰⁷ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023; Mohara et al., “Impact of the Introduction of Government Use Licenses on the Drug Expenditure on Seven Medicines in Thailand,” January 2012.

⁷⁰⁸ ML&P, “The TRIPS Flexibilities Database,” accessed July 19, 2023.

⁷⁰⁹ Mohara et al., “Impact of the Introduction of Government Use Licenses on the Drug Expenditure on Seven Medicines in Thailand,” January 2012; WHO, “Improving Access to Medicines in Thailand,” February 6, 2008, 31.

⁷¹⁰ Mohara et al., “Impact of the Introduction of Government Use Licenses on the Drug Expenditure on Seven Medicines in Thailand,” January 2012; Schuettler, “Angered U.S. Firm Excludes Thailand From New Drugs,” March 14, 2007; Lybecker and Fowler, “Compulsory Licensing in Canada and Thailand: Comparing Regimes to Ensure Legitimate Use of the WTO Rules,” *Journal of Law, Medicine & Ethics* 37, 2009, 222–240; but see also generally Reichman, “Compulsory Licensing of Patented Inventions,” Summer 2009.

⁷¹¹ Schuettler, “Angered U.S. Firm Excludes Thailand From New Drugs,” March 14, 2007.

⁷¹² Industry representative, interview by USITC staff, South Africa, June 26, 2023.

⁷¹³ ML&P, The TRIPS Flexibilities Database, accessed July 19, 2023.

\$4/month for licensed generic product. Two factors reportedly were important in achieving this price decrease: generic drug manufacturers were able to provide antiretrovirals more cheaply than Gilead, and the Global Fund and The U.S. President’s Emergency Plan for AIDS Relief radically increased their procurement under their 90/90/90 Treatment for All campaign.^h Similarly, generic drug manufacturers in India began producing antiretrovirals cocktails and selling them cheaply in other countries, which increased access to the lifesaving treatment.ⁱ Médecins Sans Frontières monitored the prices for antiretroviral treatment from 2007 to 2014 and found that the generic drug price steadily declined, while the price of the originator products remained the same during that period.^j

Notwithstanding these lessons, there are differences between the HIV/AIDS epidemic and the COVID-19 pandemic. For example, COVID-19 vaccines and monoclonal antibodies are more complex than antiretrovirals, thus requiring the know-how to manufacture the good, and not just protection against a suit for patent infringement.^k There are stronger similarities, however, between antiretrovirals and small-molecule therapeutics for COVID-19.^l This overlap enables existing frameworks, such as VLs, to play a similar role with COVID-19 as they did with HIV/AIDS.

^a Shadlen, “Patents, Trade and Medicines: Past, Present and Future,” June 27, 2019, 76.

^b See South Africa section for more details.

^c Wong, “The Case for Compulsory Licensing,” June 2020.

^d Industry representative, interview by USITC staff, South Africa, June 26, 2023; government representative, interview by USITC staff, South Africa, June 29, 2023; Schuettler, “Angered U.S. Firm Excludes Thailand from New Drugs,” March 14, 2007.

^e Task Force on VLAM, *Report of the Task Force*, April 22, 2023, 8–9.

^f Task Force on VLAM, *Report of the Task Force*, April 22, 2023, 9–10.

^g Task Force on VLAM, *Report of the Task Force*, April 22, 2023, 10–11. The VLs for HIV/AIDS treatment granted the right to manufacture, transfer, and distribute within an agreed area (the area covered 68 countries in 2003, increased to 95 countries in 2007, and ultimately encompassed 116 countries).

^h Task Force on VLAM, *Report of the Task Force*, April 22, 2023, 11–12.

ⁱ Task Force on VLAM, *Report of the Task Force*, April 22, 2023, 8–9.

^j Nonprofit organization representative, interview by USITC staff, April 12, 2023.

^k Academic representative, interview by USITC staff, May 2, 2023; industry representative, interview by USITC staff, South Africa, June 26, 2023.

^l Academic representative, interview by USITC staff, May 2, 2023; see also, generally, Rutschman, Barnes-Weise, “The COVID-19 Vaccine Patent Waiver,” May 5, 2021.

Canada

Canada, a HIC, has been involved with two attempts to use CLs, only one of which came to fruition. In October of 2007, Canada notified the TRIPS Council that it granted a CL under TRIPS Agreement Article 31*bis* to provide the HIV/AIDS drug TriAvir to Rwanda, which had filed a related notification previously.⁷¹⁴ This is the only completed attempt to use Article 31*bis* since its implementation.⁷¹⁵ To implement the CL under Article 31*bis*, Canada had to make various modifications to its domestic law.⁷¹⁶ The results of the agreement were ultimately underwhelming for both sides. Rwanda, for its part, reportedly in the end could have accessed a similar combination drug from India for roughly one-third the price per unit that the CL yielded with less procedural hurdles, so the CL reportedly did not improve pharmaceutical access in Rwanda.⁷¹⁷ The Canadian generic drug manufacturer, Apotex, reportedly found the Canadian process to utilize Article 31*bis* too burdensome to be effective.⁷¹⁸ Similarly, the Director

⁷¹⁴ WTO, “Canada Is First to Notify Compulsory Licence to Export Generic Drug,” October 4, 2007.

⁷¹⁵ Igbokwe and Tosato, “Access to Medicines and Pharmaceutical Patents,” accessed August 8, 2023, 1823.

⁷¹⁶ Hestermeyer, “Canadian-Made Drugs for Rwanda,” December 10, 2007.

⁷¹⁷ Hestermeyer, “Canadian-Made Drugs for Rwanda,” December 10, 2007.

⁷¹⁸ BioSpace, “Apotex Inc. Life Saving AIDS Drug,” September 21, 2007; Hestermeyer, “Canadian-Made Drugs for Rwanda,” December 10, 2007.

General of the European Generic Medicines Association pointed to the hurdles of the Article 31*bis* process and concluded at a hearing on the TRIPS Agreement and access to medicine by the European Parliament that it is unlikely that any company in Europe would make use of the mechanism.⁷¹⁹ While the patent owners did not oppose the application for a CL, they opted to not grant a VL without certain conditions being met, which ultimately did not occur and placed an administrative burden on Apotex, according to the firm.⁷²⁰

Canada has updated its relevant laws in light of the COVID-19 pandemic.⁷²¹ The change allows the Canadian government to license, produce, sell, and use a patented invention during a public health emergency.⁷²² It also allows the government to issue a license without having to first negotiate with the patent owner or establish its own ability to manufacturer a product.⁷²³ Despite these changes, a 2021 attempt by Bolivia to secure an arrangement for COVID-19 vaccines similar to Rwanda's 2007 efforts failed to materialize. Bolivia gave notice to the TRIPS Council of a desire to use TRIPS Agreement Article 31*bis* and secured an agreement with a Canadian manufacturer, but Canada never issued a CL, and the arrangement never came to fruition.⁷²⁴ Canada's decision not to issue a CL reportedly was due to the lack of the manufacturer's experience with vaccines, as well as requirements under Canadian law that the product at issue have full regulatory approval, as opposed to the EUA COVID-19 vaccines had received.⁷²⁵

⁷¹⁹ Hestermeyer, "Canadian-Made Drugs for Rwanda," December 10, 2007.

⁷²⁰ BioSpace, "Apotex Inc. Life Saving AIDS Drug," September 21, 2007.

⁷²¹ Government of Canada, An Act Respecting Certain Measures in Response to COVID-19, March 25, 2020; Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020.

⁷²² Government of Canada, An Act Respecting Certain Measures in Response to COVID-19, March 25, 2020, part 12; Houldsworth, "The Key Covid-19 Compulsory Licensing Developments So Far," April 7, 2020.

⁷²³ Government of Canada, An Act Respecting Certain Measures in Response to COVID-19, March 25, 2020, part 12; Houldsworth, "The Key Covid-19 Compulsory Licensing Developments So Far," April 7, 2020.

⁷²⁴ WTO, Council for Trade-Related Aspects of Intellectual Property Rights, "Notification under the TRIPS Agreement (Bolivia)," IP/N/9/BOL/1, February 17, 2021; Bruce, "Canadian Firm Scathing On Obstacles To Compulsory Licensing," May 27, 2021; Abinader, "Bolivia Seeks to Import COVID-19 Vaccines from Biolyse," May 11, 2021.

⁷²⁵ Government of Canada, "Jean Chrétien Pledge to Africa Act," May 14, 2004; government representative, interview by USITC staff, Switzerland, June 13, 2023; multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023; Cotter, "The Implications of Rwanda's Paragraph 6 Agreement with Canada for Other Developing Countries," January 1, 2008, 185–188.

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Chapter 6

Availability and Consumption of COVID-19 Diagnostics and Therapeutics

Introduction

The U.S. Trade Representative’s request letter identifies several areas where data and information are requested regarding availability and consumption of COVID-19 diagnostics and therapeutics. Specifically, the letter asks for information on global demand, consumption, and the factors that explain the trends in availability, such as prices and how testing can impact the demand for treatment. It also asks for information on access to diagnostic and therapeutic products through donations or via procurement programs run by multilateral organizations. In providing this information, the letter requested that global demand and consumption be delineated by low-income countries (LICs), lower-middle-income countries (LMICs), upper-middle-income countries (UMICs), and high-income countries (HICs).⁷²⁶

This chapter begins with a presentation of information that relates to the need and demand for these products, as well as the uncertainties in assessing future demand. Subsequently, this chapter covers available information on current prices, purchases, donations, and consumption for diagnostics and therapeutics, with separate information for HICs, UMICs, LMICs, and LICs. It concludes with information on principal demand factors, including prices, regulations and approvals, competing healthcare priorities, existence of test-to-treat programs, and last mile delivery.

The data provided are from a variety of sources. For therapeutics, much of the data on procurements, donations, and consumption were obtained from Airfinity Infectious Disease Analytics (Airfinity), a healthcare data and analytics company, whose activities include closely monitoring global market and industry trends, tracking research activities, and following intellectual property (IP) developments.⁷²⁷ For diagnostics tests, Airfinity coverage is limited, and no other comprehensive source of consolidated procurement data was found. However, certain data were obtained from the Foundation for Innovative New Diagnostics (FIND), a nongovernmental organization (NGO) based in Geneva, Switzerland, that tracks the development and commercialization of COVID-19 test kits, global testing rates, and global testing policies.⁷²⁸ The COVID-19 diagnostics and therapeutics covered in this chapter are largely driven by the availability of data from these sources. Several data gaps were identified, including consumption of diagnostics and therapeutics for all but a few HICs. The data provided by Airfinity reflect public statements from new releases and other sources concerning supply agreements and procurements.

⁷²⁶ While the letter specified these four income groups based on World Bank classifications, other sources use additional terms, including middle-income countries (MICs), lesser developed countries, and developing countries. In this report, when referring to countries, we use the terms specified by the individual entities and sources.

⁷²⁷ Airfinity, “COVID-19,” accessed various dates.

⁷²⁸ FIND, “Dashboards,” accessed July 11, 2023.

Visibility, however, is poor with respect to amounts actually delivered, distributed within country, and administered to patients. COVID-19 diagnostic and therapeutic prices are not very transparent either.

Demand for Diagnostics and Therapeutics

Definition of Demand

In the debate over access and whether the 2022 Ministerial Decision should be extended to COVID-19 diagnostics and therapeutics, an important issue is how demand is defined and measured. The definition matters because how demand is measured determines the extent to which it can be met by existing supply and, if it cannot be met, whether extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would lead to increased production, lower prices, and greater access. One way to measure demand for COVID-19 diagnostics and therapeutics is by actual market purchases and donated procurements by countries across all income groups.⁷²⁹ Another method is in terms of a population-based public health “need,”⁷³⁰ measured by estimating the maximum number of people that may benefit from the treatment to avoid hospitalization and death.⁷³¹

Opponents of extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics point to the apparent lack of global demand as measured by purchases and donated procurement. Indeed, data from several monitoring organizations indicate that current levels of manufacturing far exceed purchases. For example, the COVID Global Accountability Platform (COVID GAP) reported that, for 2022, 30 million courses of molnupiravir were manufactured (i.e., 30 million patients diagnosed with COVID-19 could be treated with the volume manufactured), compared to purchases of only 12.5 million.⁷³² It also projected Pfizer would manufacture 120 million doses of nirmatrelvir (+ ritonavir) in 2022, compared to confirmed purchases of only 44.2 million.⁷³³ UMICs, LMICs, and LICs made procurements through the Access to COVID-19 Tools Accelerator (ACT-A) partnership (a global collaboration launched by the World Health Organization (WHO)). As of July 2023, of 2.2 million courses of molnupiravir offered, only about 150,000 have arrived in country, and of 2.1 million courses of nirmatrelvir (+ ritonavir) offered, only 140,000 have been confirmed.⁷³⁴

Opponents and proponents of extending the 2022 Ministerial Decision disagree on the reasons for the lack of global consumption.⁷³⁵ Opponents—including pharmaceutical manufacturers, a number of industry associations, and some academics—typically view actual market purchases and donated

⁷²⁹ AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 7–8.

⁷³⁰ Public Citizen Access to Medicine, written submission to the USITC, May 5, 2023, 3; Rethink Trade, written submission to the USITC, May 5, 2023, 2.

⁷³¹ Public Citizen Access to Medicine, written submission to the USITC, May 5, 2023, 3; USITC, hearing transcript, March 29, 2023, 30 (testimony of Jennifer Reid, Oxfam America).

⁷³² The COVID Global Accountability Platform (COVID GAP) COVID-19 is led by Duke University and COVID Collaborative. The goal of COVID GAP is to “improve and accelerate global pandemic response by serving as a source of insights and actionable recommendations, convening key stakeholders to galvanize actions and collaborations, and strengthening transparency and accountability.” COVID GAP, “About COVID GAP,” accessed July 2023.

⁷³³ COVID GAP, “COVID GAP Accountability Report,” Issue 24, April 19, 2023.

⁷³⁴ Real time data on procurements under multilateral programs can be found at WHO, “ACT-A Tx Allocation Dashboard,” accessed August 11, 2023, and UNICEF, “COVID-19 Market Dashboard,” accessed August 11, 2023.

⁷³⁵ USTR, “Summary of Consultations,” accessed August 9, 2023.

procurement as the appropriate measures of demand to compare with supplies. They claim that supplies are ample, including from production under voluntary license agreements, such as bilateral license agreements between firms and licenses through the Medicines Patent Pool (MPP), and available at affordable prices.⁷³⁶ These opponents note several reasons for low purchases and procurements, such as poor healthcare systems and last mile delivery infrastructure, as well as inadequate financial support to establish robust test-to-treat programs.⁷³⁷ They also say that low procurement levels exist in part because currently available COVID-19 therapeutics are only authorized for use in certain countries and some can be prescribed only following confirmation of infection with COVID-19 in high-risk patients.⁷³⁸ These opponents claim that supplies are sufficient given current capacity of countries to receive, store, distribute, and administer tests and therapeutics.⁷³⁹ Some opponents have noted a communication from Mexico and Switzerland to the WTO TRIPS Council in November 2022.⁷⁴⁰ This communication states that, “[n]o shortage of therapeutics exists. Instead, large parts of innovators’ production capacity remain idle due to lack of demand. Global demand for tests has reduced, and no evidence suggests that the supply is constrained relative to actual demand.” The communication concludes that, “we do not face a situation where we have an IP-induced lack of access to or a lack of manufacturing capacity of COVID-19 therapeutics and diagnostics. As a consequence, no adjustments to the IP system seem to be required.”⁷⁴¹

Proponents of extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics, such as public health and other civil society organizations, as well as certain academics, assert that the lack of purchases of COVID-19 diagnostics and therapeutics is due to inadequate supplies at affordable prices.⁷⁴² They also advocate for measuring demand in terms of a population-based “need,” defined as “the number of people that could benefit from the treatment based on eligibility for the drug (i.e., risk status and positive tests) and epidemiological trends (e.g., emerging variants, immunity over time, and vaccination progress).”⁷⁴³

They state that governments in several LICs, LMICs, and UMICs have been deterred from launching COVID-19 test-to-treat programs because of unaffordable prices and, therefore, orders have not been

⁷³⁶ “Supply far exceeds worldwide demand and stockpiles larger than anticipated demand in 2023. If all countries increase per capita treatment to U.S. level, supply would still exceed demand.” USITC, hearing transcript, March 29, 2023, 34 (testimony of Kevin Haninger, PhRMA), 144 (testimony of Joshua Teitelbaum, Alliance for Trade Enforcement), 203, 207, 241 (testimony of Anu Osinusi, Gilead).

⁷³⁷ PhRMA, prehearing brief submission to the USITC, March 17, 2023, 39–41; industry representative, interview by USITC staff, March 10, 2023.

⁷³⁸ PhRMA, prehearing brief submission to the USITC, March 17, 2023, 6; international organization representative, interview by USITC staff, Switzerland, June 7, 2023.

⁷³⁹ USITC, hearing transcript, March 29, 2023, 54 (testimony of Patrick Kilbride, U.S. Chamber of Commerce).

⁷⁴⁰ USITC, hearing transcript, March 30, 2023, 210 (testimony of Candace DeMatteis, Partnership to Fight Infectious Disease); PhRMA, written submission to the USITC, May 5, 2023, 22.

⁷⁴¹ WTO, “TRIPS Council Discussion on COVID-19 Therapeutics and Diagnostics: Evidence and Questions on Intellectual Property Challenges Experienced by Members, Communication from Mexico and Switzerland,” November 1, 2022.

⁷⁴² USITC, hearing transcript, March 29, 2023, 40 (testimony of Peter Maybarduk, Public Citizen), 43 (testimony of Lori Wallach, Rethink Trade); USITC, hearing transcript, March 30, 2023, 181 (testimony of Tahir Amin, I-MAK), 10 (testimony of Prathibha Sivasubramanian, CAMD).

⁷⁴³ COVID GAP, “Pills to People: Accelerating Equitable Global Access to Oral Therapeutics for COVID-19,” March 3, 2022, 5.

filled to supply them.⁷⁴⁴ Furthermore, they note that low testing in many countries results in low demand for treatments.⁷⁴⁵ They also argue that purchases may reflect the lack of awareness of the availability and efficacy of these products.⁷⁴⁶ They are also concerned that when patents have been made available, such as through bilateral agreements or the MPP, a large portion of the world's population remains excluded from benefiting, owing to conditions and requirements in such agreements.⁷⁴⁷ Proponents view IP protections as limiting availability and affordability and state that issuing compulsory licenses (CLs) can play a role in increasing production, lowering prices, and thus facilitating greater access going forward.⁷⁴⁸

Estimating Need

Almost all the estimates of need have concerned COVID-19 therapeutics and not diagnostics. Using the COVID GAP definition of population-based need as the number of people that may benefit from treatment,⁷⁴⁹ estimating need is challenging, requiring assumptions about eligibility for the drug (i.e., authorized eligibility for certain treatments is only for patients infected with COVID-19 with high risk of hospitalization and death), as well as multiple epidemiological and policy uncertainties around the world. Estimates depend on many specific factors, including timely testing and tracking of COVID-19 caseloads; assumptions about the number of confirmed COVID-19 infections in high-risk patients; the health-seeking behavior of individuals; and other considerations such as regulatory guidance, country priorities, and test availability and turnaround.⁷⁵⁰ Estimating future need also depends on the trajectory of the virus in terms of infection rates and emergence of new variants. Despite the challenges, several estimates of need for therapeutics have been made and are summarized below.

Estimates of global clinical need for COVID-19 oral antiviral treatments are reported in a paper by COVID GAP.⁷⁵¹ In this paper, global clinical need is defined as how many people might benefit from COVID-19 treatments determined by the eligibility of individuals for the treatment. Because trends in infection rates are difficult to predict and depend on factors such as vaccination rates, immunity, and emergence of new variants, two scenarios are presented following different assumptions about epidemiological trends. The first scenario assumes that COVID-19 becomes endemic, with cases of COVID-19 infections

⁷⁴⁴ Wallach and Stiglitz, "The International Community Must Prioritize COVID Treatment and Test Access," November 14, 2022.

⁷⁴⁵ USITC, hearing transcript, March 30, 2023, 54 (testimony of George Poe Williams, Public Service International); USITC, hearing transcript, March 29, 2023, 137 (testimony of Lori Wallach, Rethink Trade).

⁷⁴⁶ Rethink Trade, posthearing brief submission to the USITC, April 12, 2023, 2; Public Citizen, written submission to the USITC, March 17, 2023, 7.

⁷⁴⁷ TWN, posthearing brief submission to the USITC, April 12, 2023, 3–6.

⁷⁴⁸ USITC, hearing transcript, March 30, 2023, 45 (testimony of Yoke Ling Chee, TWN Berhad).

⁷⁴⁹ COVID GAP, "Pills to People: Accelerating Equitable Global Access to Oral Therapeutics for COVID-19," March 3, 2022, 5.

⁷⁵⁰ Keller, Kaufman, and Guzman, "Oral Antiviral Treatments for COVID-19: Time to Revisit?," December 14, 2022, 7. Turnaround refers to the time between administering a test and getting the results.

⁷⁵¹ The COVID Global Accountability Platform (COVID GAP) COVID-19 is a partnership led by Duke University and COVID Collaborative. The goal of COVID GAP is to "improve and accelerate global pandemic response by serving as a source of insights and actionable recommendations, convening key stakeholders to galvanize actions and collaborations, and strengthening transparency and accountability." COVID GAP, "About COVID GAP," accessed July 2023. The referenced paper is, COVID GAP, "Pills to People: Accelerating Equitable Global Access to Oral Therapeutics for COVID-19," March 3, 2022, 5–6.

being in line with influenza infection levels. In the second scenario, infection rates are assumed to be similar to those in 2021 before the arrival of the Omicron variant. Estimates are shown in table 6.1 and indicate how many people worldwide could fall within the target population in 2022, given the eligibility to receive COVID-19 oral therapeutics.

Table 6.1 Estimate of global need for oral antivirals for COVID-19 treatment in 2022

Scenario	Courses
1: Endemic COVID-19 case rates similar to flu	175 million
2: Case rates remain on par with 2021, pre-Omicron	475 million

Source: COVID GAP, “Pills to People: Accelerating Equitable Global Access to Oral Therapeutics for COVID-19,” March 3, 2022.

Public Citizen Access to Medicine, in its written submission to the Commission, provided a method for estimating need and need-based excess demand for nirmatrelvir (+ ritonavir) by LICs and MICs in 2022.⁷⁵² The approach first calculates the market demand for nirmatrelvir (+ ritonavir), which is defined as number of courses that have been procured, either through ACT-A or directly purchased from Pfizer by a national government. Second, the population-based need is calculated as the total number of people over the age of 65 infected with COVID-19 in non-HICs.⁷⁵³ Third, need-based excess demand is calculated by the difference between market demand and population-based need. Using this approach, market demand (which includes courses procured through ACT-A and by the governments of Ukraine, Egypt, Malaysia, and Thailand) is calculated as 916,120 courses and population-based need is calculated at 9,135,953 courses, resulting in need-based excess demand of 8,219,833 courses.⁷⁵⁴

At the Commission’s public hearing, Social Watch described the following approach to estimate need, using Latin America as an example.⁷⁵⁵ According to a study indicating that nirmatrelvir (+ ritonavir) can lower the chance of infected individuals getting long COVID by 26 percent, the approach assumes that every person infected should be treated in order to prevent long COVID. According to Social Watch, Latin American countries have reportedly had more than 350,000 cases per day of individuals testing positive for COVID-19 and 68 million cases since the beginning of the pandemic.⁷⁵⁶ Therefore, this approach estimates the need for nirmatrelvir (+ ritonavir) to date is at least 68 million courses. Social Watch noted that, alternatively, need estimates can be based on the number of patients with COVID-19 in a high-risk segment of the population, such as the elderly and individuals with a comorbidity (e.g., diabetes and asthma), rather than everyone receiving treatment to prevent long COVID. According to this approach, need is estimated as the total number of infections that fall into the high-risk groups. For example, because 10 percent of the Argentine population has diabetes, 10 percent of those infected need nirmatrelvir (+ ritonavir) because of this high-risk factor.

⁷⁵² Public Citizen Access to Medicine, Written submission to the USITC, May 5, 2023, 4–8.

⁷⁵³ The over-65 criterion is a proxy for “high-risk” patients, which might include not only the over-65 age group, but also other risk factors, such as immunosuppression and chronic disease.

⁷⁵⁴ Data sources used in these calculations included World Health Organization (WHO), “ACT-A Tx Allocation Dashboard,” accessed August 11, 2023; Duke Global Health Innovation Center, “COVID-19 Therapeutics | Launch and Scale Speedometer,” accessed March 21, 2023; and Airfinity, “COVID-19,” accessed July 14, 2023 (for infection rates). Data on infection rates can also be found at Our World in Data, “Coronavirus (COVID-19) Cases,” 2020.

⁷⁵⁵ USITC, hearing transcript, March 30, 2023, 37 and 38 (testimony of Sanya Reid Smith, Social Watch).

⁷⁵⁶ USTR, “Summary of Consultations,” accessed August 9, 2023.

The Third World Network (TWN) in its post hearing brief also discussed ways to estimate need for COVID-19 diagnostics and therapeutics.⁷⁵⁷ Regarding therapeutics, TWN provided estimates of the number of people in a country who would be recommended for treatment with nirmatrelvir (+ ritonavir), following U.S. government guidelines, with an approach similar to that described by Social Watch. That is, first, determine the number of COVID-19 cases per year in a particular country. Second, identify the factors that the U.S. government recommends for administering nirmatrelvir (+ ritonavir) to those testing positive for COVID-19, such as advanced age, HIV-positive status, obesity, pregnancy, and being a smoker.⁷⁵⁸ Third, determine the percentage of the country's total population that presents with these factors,⁷⁵⁹ and fourth, multiply these percentages by the number of COVID-19 cases per year, resulting in the number of people for whom treatment is recommended. Argentina and Thailand are used as examples; both countries are excluded from Pfizer's license with the MPP and are countries where Pfizer has applied for nirmatrelvir (+ ritonavir) patents in-country.⁷⁶⁰ According to this method, Argentina, with 4.18 million COVID-19 cases and 12 percent of its population over 64 years old, has a need of about 500,000 treatments of nirmatrelvir (+ ritonavir), using the age criterion alone. Similarly, Thailand, with 2.5 million COVID-19 cases and smokers accounting for 22 percent of the population, has a need of about 552,500 treatments, using the smoker criterion alone.⁷⁶¹

Regarding COVID-19 diagnostics, no studies or reports were found that provide estimates for need. By the end of 2022, however, developing countries, excluding the least-developed countries, reportedly had performed 468,767 COVID-19 tests per million population compared to 3,340,753 tests per million population in developed countries.⁷⁶² This represents a testing rate seven times higher in developed countries assuming similar infection rates. The report by the ACT-A Facilitation Council Working Group on Therapeutics and Diagnostics also points to the disparity between testing rates in HICs and LMICs as evidence of unmet need.⁷⁶³ This disparity, however, has significantly declined since its peak in the first quarter of 2022, because testing rates across country income groups have fallen.⁷⁶⁴

Citing an analysis by the Clinton Health Access Initiative (CHAI), the COVID GAP paper discussed above also provided estimates of oral antiviral demand in LMICs for 2022.⁷⁶⁵ The method used by CHAI, which based demand on need, considers the portion of the population with risk factors as well as infection rates on a country-by-country basis. Because infection rates are challenging to predict, a range of estimates are made under three different assumptions about infection rates based on the distribution of monthly infection rates for each country during 2021 (table 6.2). The analysis also provides two scenarios based on different assumptions about the availability of diagnostic tests. First, need is estimated where unlimited (unconstrained) testing availability is assumed. Second, need is limited

⁷⁵⁷ TWN, posthearing brief submission to the USITC, April 12, 2023, 2–6.

⁷⁵⁸ HHS, "Administration for Strategic Preparedness and Response. Information Sheet – Paxlovid Eligibility and Effectiveness," accessed August 9, 2023.

⁷⁵⁹ CDC, "COVID-19 Underlying Medical Conditions," accessed August 9, 2023.

⁷⁶⁰ MPP, "The Medicines Patents and Licenses Database," accessed August 9, 2023.

⁷⁶¹ TWN, posthearing brief submission to the USITC, April 12, 2023, 4.

⁷⁶² The time period for these statistics is from March 2020 to December 2022. Our World in Data, "Coronavirus (COVID-19) Cases," 2020.

⁷⁶³ WHO, "ACT-Accelerator Facilitation Council Working Group Report," September 22, 2022, 13.

⁷⁶⁴ Our World in Data, "Coronavirus (COVID-19) Cases," 2020.

⁷⁶⁵ COVID GAP, "Pills to People: Accelerating Equitable Global Access," March 3, 2022, 5.

(constrained) to the number of tests available in the event that estimated demand is greater than the number of tests available in a country.

Table 6.2 Estimate of need for oral antivirals in LMICs, 2022

In millions of courses.

Scenario	Constrained by rapid test availability	Unconstrained by rapid test availability
Low case: 25 percentile case rates from 2021	3.1	4.4
Mid case: Average case rates from 2021	6.9	11.0
High case: 75 percentile case rates from 2021	8.2	14.8

Source: COVID GAP, “Pills to People: Accelerating Equitable Global Access to Oral Therapeutics for COVID-19,” March 3, 2022.

Note: A list of LMICs covered in this paper was not provided and may not be consistent with countries categorized as LMICs by the World Bank. The paper refers to demand, which is consistent with the definition of population-based need in this report.

The ACT-A reported estimates of need based on what clinicians would want to prescribe depending on a country’s health strategy and assuming WHO clinical guidelines are followed.⁷⁶⁶ In the report, the WHO used different approaches to provide a range of estimates based on different assumptions, such as infection rates, eligibility for prescription based on underlying health conditions, vaccination rates, prevalence of comorbidities, and health seeking behavior of the population.

One such approach, the Unconstrained Demand Model, estimates the number of people that would be treated assuming that WHO clinical guidelines are followed (i.e., a person can be prescribed a course of COVID-19 antiviral medicine if the patient (a) has symptomatic COVID-19, (b) has an underlying medical condition that gives him/her at least a 10 percent risk of hospitalization for COVID-19 and (c) is not currently taking a medication that interacts dangerously with nirmatrelvir (+ ritonavir)).⁷⁶⁷ There are no constraints based on cost and availability of diagnostics or healthcare infrastructure bottleneck. Using data for July 2022 and focusing on 138 LICs and LMICs as defined by the World Bank, need in 2022 is estimated at 224 million treatments.

Another approach, the Passive Model (also referred to as the Outpatients Model or Serviceable Achievable Demand Model) provides estimates based on need, assuming countries do nothing proactive to identify those in need.⁷⁶⁸ It assumes that only people entering outpatient healthcare facilities are assessed and prescribed antivirals if they test positive for COVID-19. Assuming all outpatient facilities in each of the 138 LICs and LMICs are used for test-to-treat, for the 24 billion patients who enter these outpatient facilities, only 33 million courses of antivirals would be prescribed. The model makes assumptions about the share of patients at “high risk” because of preexisting medical conditions, the share of patients presenting symptoms or not eligible, and the percentage of tests that return a positive

⁷⁶⁶ WHO, “Estimates for 2023. 3 Models Looking Forward,” accessed August 9, 2023.

⁷⁶⁷ WHO, “Estimates for 2023. 3 Models Looking Forward,” accessed August 9, 2023.

⁷⁶⁸ WHO, “Estimates for 2023. 3 Models Looking Forward,” accessed August 9, 2023.

result.⁷⁶⁹ The Passive Model estimates 750 million diagnostic tests are needed to treat the expected number of infected individuals that meet the high-risk criteria and have COVID-19 symptoms.⁷⁷⁰

A third approach estimated demand for therapeutics in 2022 based on the actual requested number of treatments from 41 countries that “opted-in” to receive treatments through the ACT-A system as of July 2022, extrapolated for the entire calendar year. Using this approach, 2022 demand for the 41 countries was estimated at 31 million treatment courses.⁷⁷¹

Uncertainty of Future Demand

According to a range of stakeholders, the uncertainty of demand is a significant factor in determining future production and procurement of diagnostics and therapeutics. On the production side, several originator companies and their licensees expressed caution over continued production and scaling up in light of recent epidemiological trends and uncertain future demand for their products.⁷⁷² For example, many manufacturers with licensing through the MPP are no longer pursuing WHO prequalification for nirmatrelvir (+ ritonavir) because of uncertainty of demand.⁷⁷³ Similarly, uncertainty over future demand affects decision-making over purchasing and procurement of donations. To assist governments in developing countries with procurement decisions, the WHO set up an Essential Supplies Forecasting Tool that assists at the country level in forecasting future need for COVID-19 antivirals, as well as other therapeutics, diagnostics, and consumables.⁷⁷⁴ The Center for Global Development (Center) suggests that tools could be implemented to assist in creating visibility of future demand for manufacturers and increased demand visibility could incentivize manufacturers to increase production and lower prices. According to the Center, these tools include both financial and technical measures, such as pooled purchases, volume guarantees, technology transfer, subsidies, loans, and grants.⁷⁷⁵

Prices, Purchases, Donations, and Consumption of Diagnostics and Therapeutics

A central question regarding access to COVID-19 diagnostics and therapeutics is whether, under existing IP rules, supplies are currently sufficient at affordable prices and available to anyone who could benefit from them. Answering this question is challenging owing to a lack of data. Whether estimating demand based on consumption or determining need, data on consumption are important. Data on actual consumption, defined as the number of tests taken for COVID-19 diagnostics and as the number of treatments administered to patients for COVID-19 therapeutics, are lacking. Data are available on government and private sector purchases (or announcements to purchase) and donations, which are reported in this section. With the exception of the United States, there is poor visibility of what has been

⁷⁶⁹ WHO, “Supply and Demand for COVID-19 Therapeutic Medicines,” accessed August 9, 2023.

⁷⁷⁰ This estimate is the minimum number of tests that need to be administered by only testing an individual if they are definitely eligible for a course of antiviral medicine after testing positive.

⁷⁷¹ WHO, “Estimates for 2023. 3 Models Looking Forward,” accessed August 9, 2023.

⁷⁷² IPFMA, “How Different Partnership Models Supported the Response against COVID-19,” June 7, 2023.

⁷⁷³ MPP, written submission to the USITC, May 5, 2023, 7–8.

⁷⁷⁴ WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022, 27.

⁷⁷⁵ Keller, Kaufman, and Guzman, “Oral Antiviral Treatments for COVID-19: Time to Revisit?,” December 14, 2022.

delivered, distributed within country, and administered to patients.⁷⁷⁶ Data with respect to pricing are also lacking but reported where available in this chapter. This section also discusses “access” to therapeutics, which, for the purposes of this report, refers to available potential avenues for countries to acquire products and deliver them to patients, rather than actual purchases, donations, or deliveries. Almost all countries have access to therapeutics, but many are excluded from the avenues that offer the potential for lower prices and greater affordability.

Diagnostics

Prices

The pricing of COVID-19 diagnostics diverges significantly across regions and countries because of different healthcare systems, economic conditions, and domestic regulations. Pricing also differs depending on the technology used, such as polymerase chain reaction (PCR) tests or rapid antigen tests (also known as rapid tests). The pricing and affordability of COVID-19 diagnostics vary dramatically by country, and even within country where prices differ by manufacturer, or if a test was acquired through a healthcare provider or purchased in the marketplace. This lack of uniformity and availability of data from a single source results in a collection of disparate diagnostic prices from the ACT-A pooled procurement funding mechanism (see table 6.3 below).⁷⁷⁷

Although specific data on global pricing for COVID-19 diagnostics and pricing trends are not widely available, after the initial supply constraints and surge in demand for tests in early 2020, prices began to decline as more tests became available globally. During the pandemic, diagnostics pricing was not considered to be as prohibitive as the pricing for therapeutics, with the diagnostics market likely benefitting from higher levels of competition.⁷⁷⁸ The diagnostics industry, as opposed to therapeutics, had a number of established producers able to develop and manufacture COVID-19 diagnostics, which have lower costs, are faster to make, and are easier to deploy.⁷⁷⁹ In terms of access to COVID-19 diagnostics, the development and deployment of the rapid antigen self-tests increased access for certain countries across income levels at lower prices. During the course of this investigation, the Commission received limited information on COVID-19 diagnostic prices. However, one source reported that in Mexico reagent costs for PCR tests fell by 75 percent over 18 months (from roughly \$38 to \$9).⁷⁸⁰ Additionally, some sources reported that rapid antigen test prices globally were between \$1 and \$5 by 2023.⁷⁸¹

Some pricing data are available for LMICs on diagnostics available through ACT-A after negotiated discounts. As co-convenor of the ACT-A Diagnostics Pillar, the Global Fund, a global health partnership, makes COVID-19 diagnostics available to countries through the ACT-A initiative’s pooled procurement funding mechanism, which has realized substantial cost savings for LMICs since the start of the

⁷⁷⁶ Some information on deliveries of treatments procured through multilateral programs is also available.

⁷⁷⁷ The Global Fund, *Pooled Procurement Mechanism Reference Pricing: COVID-19 Diagnostics*, April 2023.

⁷⁷⁸ USITC, hearing transcript, March 29, 2023, 127 (James Love, KEI).

⁷⁷⁹ USITC, hearing transcript, March 29, 2023, 127 (James Love, KEI); industry representative, interview by USITC staff, March 7, 2023.

⁷⁸⁰ Industry representative, interview by USITC staff, Mexico, June 21, 2023.

⁷⁸¹ Industry representative, interview by USITC staff, Malaysia, July 21, 2023; industry representative, interview by USITC staff, South Africa, June 28, 2023.

pandemic.⁷⁸² Table 6.3 lists the published prices for tests available through this mechanism. ACT-A negotiated price reductions of 30–50 percent during the course of the pandemic.⁷⁸³ As a result, PCR test prices dropped from \$20–30 per test to below \$15 for LMICs. Rapid test prices reduced by about half, from above \$3 to below \$2 per test.⁷⁸⁴

Table 6.3 Prices for COVID-19 diagnostics (rapid antigen tests and select automated PCR tests) available through the ACT-A pooled procurement mechanism, 2023

Product	Manufacturer	Price per test (\$)
SARS-CoV-2 - Rapid Antigen Diagnostic Test	n.a.	0.60–2.25
SARS-CoV-2 - Rapid Antigen Diagnostic Self-Test	n.a.	0.60–4.50
Xpert® Xpress SARS-CoV-2, 10T/Kit	Cepheid	14.90
Abbott RealTime SARS-CoV-2 RT-PCR Kit, 96T/Kit	Abbott Molecular	10.00
Aptima SARS-CoV-2 assay, 250T/Kit	Hologic	12.00
Cobas SARS-CoV-2 RT-PCR Kit	Roche	10.90
Alinity m SARS-CoV-2 AMP Kit	Abbott Molecular	12.60

Source: The Global Fund, pooled procurement reference pricing, April 2023.

Purchases

Compiling COVID-19 diagnostics data and information on purchases, donations, and consumption is challenging for a number of reasons. First, no single comprehensive source containing purchasing information currently exists. For example, Airfinity, the primary source for therapeutics purchasing data, has limited coverage for diagnostics. Second, as mentioned in chapter 4, thousands of COVID-19 diagnostic products are manufactured by more than 900 firms globally, with no requirement that firms report sales. Third, unlike COVID-19 therapeutics, diagnostics can be purchased through a variety of channels, including over-the-counter retail sales. Owing to these challenges, data in this section are from a variety of sources, such as FIND and ACT-A.⁷⁸⁵ These sources provide examples of the types of purchases made by governments, multilateral programs, and private donations rather than comprehensive coverage.

Government Purchases

Several governments have engaged in direct purchases of COVID-19 diagnostics for domestic use. For example, the United States purchased COVID-19 diagnostics for use at federal and state levels. In January 2022, the Biden Administration committed to making 1 billion at-home COVID-19 tests available to everyone in the United States for free through the government website COVIDTests.gov.⁷⁸⁶ The supply of rapid antigen self-tests was procured by the U.S. Department of Defense in partnership with

⁷⁸² WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

⁷⁸³ WHO, *ACT-Accelerator Outcomes Report*, December 14, 2022, 5. See Multilateral Programs below for information on ACT-A procurements.

⁷⁸⁴ WHO, “Emergency Global Supply Chain System (COVID-19) Catalogue,” August 20, 2022; WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

⁷⁸⁵ Information on these organizations is provided in chapter 1 of this report.

⁷⁸⁶ White House, “Fact Sheet: The Biden Administration to Begin Distributing At-Home, Rapid COVID-19 Tests,” January 14, 2022; White House, “Fact Sheet: The Biden Administration Announces Americans Can Order Additional Free At-Home, Rapid COVID-19 Tests,” May 17, 2022; Aboulenein, “U.S. Orders 100 Million COVID Tests,” September 8, 2022.

the U.S. Department of Health and Human Services.⁷⁸⁷ As of June 2023, the federal government has distributed more than 755 million free tests through its website.⁷⁸⁸ State governments also purchased COVID-19 tests for their testing initiatives. In August 2020, a bipartisan group of seven governors, in partnership with the Rockefeller Foundation, purchased 3.5 million rapid tests from two U.S. medical technology companies, Becton Dickinson and Quidel, before the existence of a national strategy.⁷⁸⁹

Other HICs also engaged in direct government purchases of COVID-19 diagnostics from private industry. In December 2020, the European Commission signed a framework contract to purchase more than 20 million rapid antigen tests from Abbott and Roche for distribution to all European Union countries.⁷⁹⁰ South Korea also made direct purchases of COVID-19 tests as part of its testing strategy to lower the financial risk of private test development.⁷⁹¹ In April 2020, Saudi Arabia signed a \$265 million agreement with China in which China would supply the country with 9 million test kits, along with 500 specialist technicians and six test laboratories.⁷⁹² Fewer examples of direct government purchases by LICs and MICs were found. Persons interviewed by the Commission, however, indicated governments in LICs and MICs did engage in the direct purchase of COVID-19 diagnostics, though the specifics of such deals were not provided or made public.⁷⁹³

Multilateral Programs

International nongovernmental organizations and intergovernmental organizations are the primary intermediaries for purchases of COVID-19 diagnostics for LICs and MICs. For example, between mid-2020 and October 2022, the Diagnostics Pillar of the WHO's ACT-A⁷⁹⁴ secured a total capacity of 314 million professional-use rapid antigen tests and 840 million rapid antigen self-tests from diagnostics manufacturers for LMICs.⁷⁹⁵ During this period, 185.5 million tests were procured for 182 countries, with 161 million of those tests delivered to LICs and MICs.⁷⁹⁶

In addition to ACT-A, WHO regional offices also engaged in direct procurement of COVID-19 tests. In August 2020, the Pan American Health Organization (PAHO), a WHO regional office, leveraged its Strategic Fund for Public Health Supplies to procure and distribute more than 10 million PCR tests for six countries in Latin America and the Caribbean.⁷⁹⁷ From the start of the pandemic through January 2022,

⁷⁸⁷ USDOD, "DOD Awards Contracts to Purchase COVID-19 Antigen Over-the-Counter Test Kits," January 13, 2022; Aboulenein, "U.S. Orders 100 Million COVID Tests," September 8, 2022, 10.

⁷⁸⁸ COVID.gov, "COVID-19 Tests," June 1, 2023.

⁷⁸⁹ The states were Louisiana, Maryland, Massachusetts, Michigan, North Carolina, Ohio, and Virginia. Kelly, "Seven Governors Join Deal in Pursuit of First Multistate Coordinated Testing Strategy," August 4, 2022.

⁷⁹⁰ European Commission, "High-Quality COVID-19 Testing," accessed June 9, 2023.

⁷⁹¹ FDA, *South Korea's Response to COVID-19*, March 3, 2020, 2.

⁷⁹² Radwan and Obaid, "Saudi Arabia and China Sign \$265m Deal to Fight Coronavirus," April 27, 2020.

⁷⁹³ Foreign government official, interview by USITC staff, Mexico, June 21, 2023; foreign government official, interview by USITC staff, Malaysia, July 25, 2023.

⁷⁹⁴ Information on the WHO's ACT-A can be found in chapter 1, table 1.1.

⁷⁹⁵ WHO, *ACT-Accelerator Outcomes Report*, December 14, 2022, 5.

⁷⁹⁶ The ACT-A diagnostics pillar is co-convened by the Global Fund, from whom \$982 million was awarded for procurement of COVID-19 diagnostics. Public health organization representative, interview by USITC staff, Switzerland, June 9, 2023; WHO, *ACT-Accelerator Outcomes Report*, December 14, 2022, 5.

⁷⁹⁷ PAHO, "PAHO Helped Procure 10 Million PCR Diagnostic Tests," August 6, 2020.

the PAHO acquired more than 42 million PCR tests and rapid antigen tests for 36 different countries.⁷⁹⁸ The Southeast Asian regional office also supported procurement and distribution of tests. For example, in June 2020, it delivered 2,178 PCR test kits to Indonesia in collaboration with the Indonesian Ministry of Health.⁷⁹⁹

The United Nations Children’s Fund (UNICEF)⁸⁰⁰ also operates a program of pooled procurement and distribution of diagnostics to developing countries. Shortly after the WHO officially declared COVID-19 a pandemic in March 2020, UNICEF issued a tender for COVID-19 diagnostics.⁸⁰¹ By mid-April 2020, UNICEF had already procured 280,000 tests for distribution in 22 countries around the world. By the end of the year, UNICEF had distributed 3.7 million tests to 63 countries, with the largest recipients being LICs and MICs, such as Nigeria, India, Uganda, Iran, and Zimbabwe. Of these tests, 2.2 million were manual PCR tests, 1.1 million were automated PCR tests, and about 360,000 were rapid antigen tests.⁸⁰² In 2021, UNICEF’s Supply Division delivered a total of 12.4 million tests worldwide. This included 5.4 million PCR tests and 7 million rapid antigen tests, as well as PCR equipment and sample collection kits.⁸⁰³ UNICEF entered into long-term arrangements with 19 diagnostics manufacturers globally, enabling these procurements.⁸⁰⁴ Some of its largest suppliers included Abbott (United States), SD Biosensor (South Korea), Cepheid (United States), Roche (Switzerland), and Life Technologies (United States).⁸⁰⁵

Donations

Financial and in-kind donations of COVID-19 diagnostics have been made through a variety of channels, including donations from manufacturers, governments, and philanthropic foundations. Comprehensive data for these types of donations are not available; however, several examples of donations were identified. For instance, in 2020, a direct donation from Becton Dickinson of \$350,000 in cash and product was made to China for COVID-19 relief efforts and an additional \$750,000 to U.S. and international response efforts.⁸⁰⁶ In March 2021, Germany-based Siemens Group donated 25,000 antibody tests to the Malaysian Ministry of Health.⁸⁰⁷ In December 2021, U.S.-based Quidel donated 10,000 rapid antigen self-tests to the United Way of New Jersey in partnership with a U.S. football team, the New York Jets.⁸⁰⁸ In April 2022, Optum Rx, a U.S.-based prescription drug benefit provider, donated

⁷⁹⁸ PAHO, “PAHO Calls for Countries to Prioritize Rapid Tests,” January 19, 2022.

⁷⁹⁹ WHO, “WHO and Ministry of Health Distribute COVID-19 Test Kits,” July 7, 2020.

⁸⁰⁰ Information on UNICEF can be found in chapter 1, table 1.1.

⁸⁰¹ UNICEF Supply Division, “Getting COVID-19 Tests into the Hands of Health Workers,” March 29, 2021.

⁸⁰² UNICEF Supply Division, “Getting COVID-19 Tests into the Hands of Health Workers,” March 29, 2021.

⁸⁰³ UNICEF, “Boosting the Availability,” March 31, 2022.

⁸⁰⁴ UNICEF Supply Division, *COVID-19 In Vitro Diagnostics Supply Assessment and Outlook Update*, October 2021, 9–10.

⁸⁰⁵ Life Technologies was acquired by Thermo Fisher in 2014. UNICEF Supply Division, *COVID-19 In Vitro Diagnostics Supply Assessment and Outlook Update*, October 2021, 6–7; Thermo Fisher Scientific, “Life Technologies,” accessed June 11, 2023.

⁸⁰⁶ Products may include test kits, supplies, and medical equipment. BD, “BD Commits \$1.1 Million to Global COVID-19 Response Efforts,” March 23, 2020.

⁸⁰⁷ Siemens, “Siemens Group of Companies in Malaysia Donate COVID-19 Test Kits,” March 16, 2021.

⁸⁰⁸ United Way of Northern New Jersey, “New York Jets and Quidel Donate At-Home COVID-19 Test Kits,” accessed June 9, 2023.

5,000 rapid antigen self-tests to underserved communities in Chicago through the Chicago Department of Public Health.⁸⁰⁹

Certain philanthropic foundations also reported donations of COVID-19 diagnostics. For example, in March 2020, two foundations in China, the Jack Ma Foundation and the Alibaba Foundation donated more than 1.5 million laboratory diagnostic test kits to the Africa Centres for Disease Control and Prevention and the Government of Ethiopia to be distributed among African Union member states.⁸¹⁰ In the same month, the two foundations also donated 500,000 test kits to the United States.⁸¹¹ Since January 2020, the Bill & Melinda Gates Foundation⁸¹² has provided \$100 million in guarantees to Abbott and SD Biosensor to make rapid antigen tests available at no more than \$5 per test in LICs and MICs.⁸¹³ The foundation also directed funding toward UK-based diagnostics firm, Lumira Dx, for the roll out of COVID-19 diagnostic platforms and rapid antigen tests in Africa.

Government-to-government donations of COVID-19 diagnostics also occurred. For example, in July 2021, the United States donated 500,000 rapid tests to Sri Lanka for early detection and 100,000 tests to the Maldives.⁸¹⁴ In addition to test kits themselves, the United States donated PCR machines to Bulgaria and laboratory equipment to Namibia to bolster laboratory capacity for PCR testing.⁸¹⁵ In 2021, the European Union provided medical supplies, including COVID-19 tests, to Tunisia and Nepal.⁸¹⁶

Consumption

Data are not available on global consumption of COVID-19 diagnostics. Trends in consumption can be inferred by observing trends in testing rates (figure 6.1), although consumption of a large portion of tests (such as rapid antigen self-tests) is not reported to authorities. Testing rates are lower at lower income levels, and, apart from an uptick in testing by UMICs in early 2023, the overall trend in daily testing rates steadily declined since the beginning of 2022. By the second quarter of 2023, testing appears to have mostly stopped in LMICs and UMICs and data are no longer reported for LICs. In HICs, testing fell to less than one test per 1,000 people in the first half of 2023.

⁸⁰⁹ UnitedHealth Group, “Optum Rx Donates COVID-19 Test Kits to Increase Access to Free Testing Among Underserved Communities in Chicago,” April 28, 2022.

⁸¹⁰ The Jack Ma Foundation was founded by Alibaba founder Jack Ma. Africa Union, “Jack Ma and Alibaba Foundations Donate COVID-19 Medical Equipment,” March 22, 2020.

⁸¹¹ O’Kane, “Chinese Billionaire Jack Ma Is Shipping Coronavirus Test Kits and Masks to the U.S.,” March 16, 2020.

⁸¹² Information on the Bill & Melinda Gates Foundation can be found in chapter 1, table 1.1.

⁸¹³ Bill & Melinda Gates Foundation, “Funding Commitments to Fight COVID-19,” January 12, 2022.

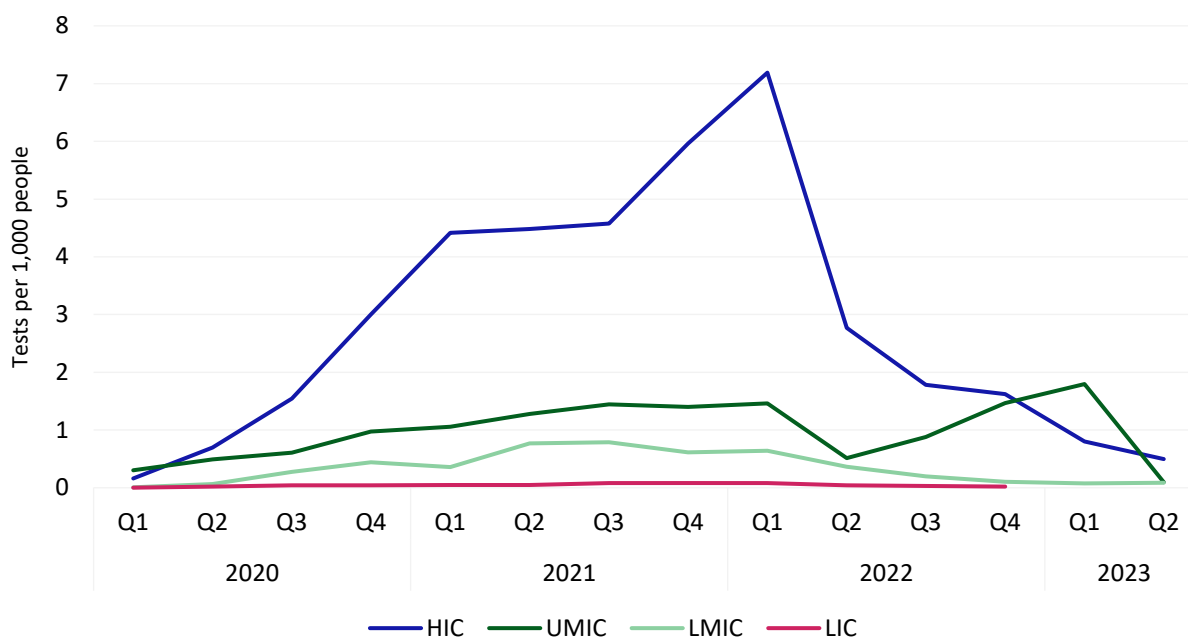
⁸¹⁴ USAID, “U.S. Donates 500,000 Rapid Diagnostic Tests to Sri Lanka,” accessed April 3, 2023; U.S. Mission to Maldives, “U.S. Donates 100,000 Rapid Diagnostic Tests to Maldives for Early COVID-19 Detection,” July 15, 2021.

⁸¹⁵ U.S. Embassy in Bulgaria, “U.S. Donates Fastest, Most Reliable COVID-19 Test Machine to Bulgaria,” April 30, 2020; U.S. Embassy in Namibia, “U.S. Donates Laboratory Equipment to Test for COVID-19,” April 13, 2021.

⁸¹⁶ European Parliament, “Coronavirus: A Timeline of EU Action in 2021,” January 31, 2022.

Figure 6.1 COVID-19 average daily testing rates, quarterly by country income class

In tests per 1,000 people. HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries; Q1 = January–March; Q2 = April–June; Q3 = July–September; Q4 = October–December. Underlying data for this figure can be found in appendix J, [table J.19](#).



Source: FIND, “COVID-19 Test Tracker.” FIND also has data on average daily testing rate per 1,000 people broken out by income group for countries. Data stopped being updated in April 2023.

Notes: Data presented in this figure do not include rapid antigen self-tests. There were no testing rate data for LICs after Q4 2022.

Therapeutics

Prices

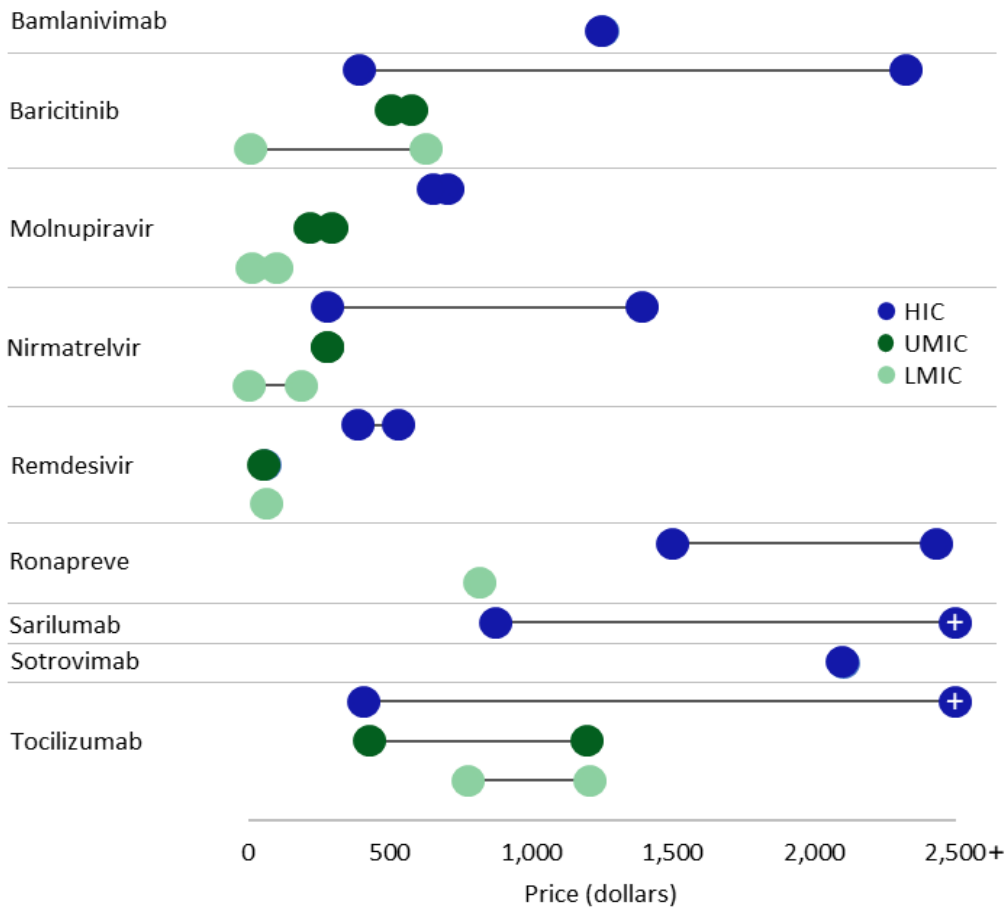
Price transparency for COVID-19 therapeutics is lacking.⁸¹⁷ Pharmaceutical companies often negotiate prices with governments, health systems, insurance providers, and multilateral organizations. These negotiations are typically conducted in private, resulting in confidential supply agreements that prevent public disclosure of pricing details.⁸¹⁸ This lack of transparency is challenging when trying to evaluate cross-country comparisons of prices for COVID-19 drugs. Additionally, pricing can vary significantly between countries as a result of differences in healthcare systems, economies, and purchasing power. As explained below, pharmaceutical companies often use different pricing strategies depending on the market conditions of each country. This contributes to a lack of uniformity in drug pricing worldwide. The limited data available are retrieved from ad hoc data points from negotiated supply deals and press releases from generic manufacturers. Examples of these data points, which might not be representative of global drug prices, are reported in figure 6.2.

⁸¹⁷ For example, see USITC, hearing transcript, March 29, 2023, 40 (testimony of Peter Maybarduk, Public Citizen), 357 (testimony of Brook Baker, Health Global Access Project, Inc.); WHO, “WHO Recommends Highly Successful COVID-19 Therapy,” April 22, 2022.

⁸¹⁸ For more information on pricing disclosure in voluntary licensing agreements, see chapter 5.

Figure 6.2 Select price ranges for COVID-19 therapeutics by country income groups

Pricing in dollars per dose/treatment. HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = low and lower-middle-income countries. Underlying data for this figure can be found in appendix J, [figure J.20](#).



Source: Airfinity, “COVID-19,” accessed August 9, 2023.

Notes: For presentation purposes, any maximum price exceeding \$2,500 was truncated, and is denoted by a “+”. For sarilumab (HIC) the maximum price was \$3,827 and for tocilizumab (HIC) it was \$5,304. Baricitinib excludes data for a dosage of 2 mg and Tocilizumab excludes dosages of 162 mg subcutaneous and 400 mg infusions. Ronapreve pricing is based on 2 different dosages – LMICs received a dosage of 1200 mg infusion, while HICs received 2400 mg infusion doses. Price data presented are from public announcements of negotiated supply deals and press releases from generic manufacturers. Price negotiations are typically private, however, and prices are not released publicly. It is unclear how representative these prices are because the data points are limited.

Several pharmaceutical originator companies, including Pfizer, Merck, and Gilead, employ tiered-pricing strategies in which different countries or regions pay different prices for the same medication. Prices are calculated using various factors such as local market conditions, volume, purchasing power, and healthcare infrastructure.⁸¹⁹ These strategies are employed by drug makers to optimize their revenue and market reach.⁸²⁰ Prices tend to be higher in developed countries with higher income levels and are often lower in developing nations with lower purchasing power. The first tier of the pricing system is set

⁸¹⁹ For more information on tiered-pricing schemes, see the section below on Price as factor affecting purchases and procurement. Refer to chapter 4 for a list of therapeutics and associated manufacturers covered in this report.

⁸²⁰ Rethink Trade, written submission to the USITC, May 5, 2023, 5; Pfizer, “Pfizer to Supply Global Fund Up to 6 Million PAXLOVID™ Treatment Courses,” accessed April 3, 2023; Merck, “Merck Provides Update on Phase 3 MOVE-AHEAD Trial,” accessed August 4, 2023.

for HICs such as the United States, the United Kingdom, and member states of the European Union.⁸²¹ The price range for HICs is \$280–1393 per treatment course for nirmatrelvir (+ ritonavir) and \$653–705 per treatment course for molnupiravir (figure 6.2).⁸²²

The second pricing tier includes UMICs, such as Brazil, Mexico, and Thailand, that are often excluded from purchasing less expensive, licensed versions of products made under VLs.⁸²³ Unless the price has been reported by country officials, little transparency exists for these negotiated prices. It has been reported, however, that the treatment course price for nirmatrelvir (+ ritonavir) in Thailand and countries with similar per capita income is over \$250.⁸²⁴ The third tier is for LICs and LMICs and is sometimes referred to as the “best access price” or “not-for-profit price” by manufacturers.⁸²⁵ Therapeutic manufacturers keep this “best access price” confidential. One participant at the Commission’s hearing put the price at \$80–90 per treatment course for nirmatrelvir (+ ritonavir).⁸²⁶

As discussed in chapter 5, Pfizer, Merck, Gilead, and Shionogi entered into VLs with licensed manufacturers (via the MPP or bilateral agreements) to facilitate access to LICs and LMICs.⁸²⁷ In these agreements, pricing is set by the licensed manufacturer, with a certain royalty percentage paid to the originator.⁸²⁸ For example, under the licensing agreements involving Pfizer, the MPP, and sublicensees, for sales outside of LICs, Pfizer receives 5 percent of net sales from all public purchases and 10 percent of net sales from all private purchases to the extent (i) a valid patent claim exists in the country of manufacture or sale or (ii) regulatory exclusivities exist in the country of sale.⁸²⁹ Royalty payments were suspended until the end of May 2023, when the WHO declared the end of the Public Health Emergency of International Concern, and purchases by LICs remain royalty-free.⁸³⁰ Currently, there is only one licensed and approved generic manufacturer (Hetero in India) for Pfizer’s nirmatrelvir (+ ritonavir). The per treatment course of generic nirmatrelvir (+ ritonavir) made by Hetero, is about \$60. Lower per course treatment costs are anticipated, however, if more manufacturers are approved and more production comes online.⁸³¹ Other companies such as Gilead do not take a royalty from their VLs serving LICs and LMICs for the manufacture of remdesivir.⁸³²

⁸²¹ Pfizer, “Ensuring Broad and Affordable Access to Paxlovid,” accessed September 7, 2023; Merck, “Merck Provides Update on Phase 3 MOVE-AHEAD Trial,” accessed August 4, 2023.

⁸²² The price range for HICs for nirmatrelvir (+ ritonavir) includes Panama (\$280), which the World Bank classifies as a HIC. Other international organizations, such as the IMF, consider it a UMIC.

⁸²³ Pfizer, “Ensuring Broad and Affordable Access to Paxlovid,” accessed September 7, 2023; Merck, “Merck Provides Update on Phase 3 MOVE-AHEAD Trial,” accessed August 4, 2023. For more information about the geographic coverage of bilateral agreements and the MPP, see chapter 5.

⁸²⁴ Airfinity, “COVID-19,” accessed July 14, 2023; USITC, hearing transcript, March 29, 2023, 40 (testimony of Peter Maybarduk, Public Citizen); USITC, hearing transcript, March 30, 2023, 85 (testimony of Jennifer Reid, Oxfam America), 297 (testimony of Susana Van der Ploeg, Brazilian AIDS Interdisciplinary Association).

⁸²⁵ Merck, “Merck Provides Update on Phase 3 MOVE-AHEAD Trial,” accessed August 4, 2023; Pfizer, “Pfizer to Supply Global Fund Up to 6 Million PAXLOVID™ Treatment Courses,” accessed April 3, 2023.

⁸²⁶ USITC, hearing transcript, March 29, 2023, 354 (testimony of Brook Baker, Health Global Access Project, Inc.).

⁸²⁷ For more information about the MPP, see Chapter 5.

⁸²⁸ In the MPP agreements for COVID-19 therapeutics, specific pricing is not included.

⁸²⁹ MPP, “NIRMATRELVIR,” Sublicense Agreement – Form, par. 7.2, accessed August 15, 2023.

⁸³⁰ USITC, hearing transcript, March 29, 2023, 166 (testimony of Jayashree K. Iyer, Access to Medicine Foundation); MPP, “NIRMATRELVIR,” Sublicense Agreement – Form, pars. 7.2 and 7.3, accessed August 15, 2023.

⁸³¹ WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

⁸³² Industry representative, interview by USITC staff, May 25, 2023.

For LMICs and LICs, CHAI⁸³³ has an arrangement with many of the licensed manufacturers under the MPP to offer courses of nirmatrelvir (+ ritonavir) for \$25 per treatment. The \$25 price will apply only if volume requirements are met: any single order must meet a minimum of 50,000 treatment courses and orders across all 95 countries must meet or exceed 1 million treatment courses.⁸³⁴ Developing countries can also procure a limited number of courses through UNICEF and the Global Fund.⁸³⁵ As noted below, procurement agencies purchased stocks of therapeutics at the originators' "best access price," which was made available to countries to procure using their allotted COVID-19 funds.

Access to Therapeutics

COVID-19 therapeutics are potentially accessible to countries of all income categories, but the avenues through which countries can obtain access differ significantly among HICs, UMICs, LMICs, and LICs. Broadly, the six potential access avenues are: (1) direct purchase of branded product from originator, (2) purchase of licensed versions of product from a manufacturer operating under a bilateral license agreement with an originator, as discussed in chapter 5, (3) purchase of licensed versions of product from manufacturer operating under a sublicense agreement with the MPP, as discussed in chapter 5, (4) procurement of branded product through a multilateral organization, such as UNICEF and the Global Fund, (5) purchase of generic versions of product from manufacturers operating under a Least Developed Country exemption (for example, Bangladesh) or under a compulsory license (for example, Hungary), as discussed in chapter 5, and (6) donations. The price of drugs in a particular country depends upon the avenues of access that are available to it. Although pricing is not very transparent, countries able to access drugs via multilateral organizations and donations are likely to pay significantly less than countries with sole access through direct purchase from the originator. Prices under bilateral and MPP licenses and LDC exemption are generally lower than branded prices. Therefore, the avenues of access available to a particular country are important in determining its purchases and consumption.

As noted earlier, concern has been raised about certain countries having limited access through voluntary licenses (VL) and multilateral programs. In particular, some stakeholders view UMICs as countries with limited or unaffordable access to products, or only via direct procurement from originator firms. Figure 6.3 identifies UMICs that are not included in any VL and multilateral program agreements for COVID-19 therapeutics according to the MPP's or Gilead's access partnerships. These countries purchased (or made agreements to purchase) products from originators. For example, Mexico and Brazil contracted for 300,000 and 100,000 treatment courses of nirmatrelvir (+ ritonavir), respectively, in late 2022.⁸³⁶ None of the financial details of these transactions, including prices paid and actual quantities delivered, are publicly available.

⁸³³ Information on CHAI can be found in chapter 1, table 1.1.

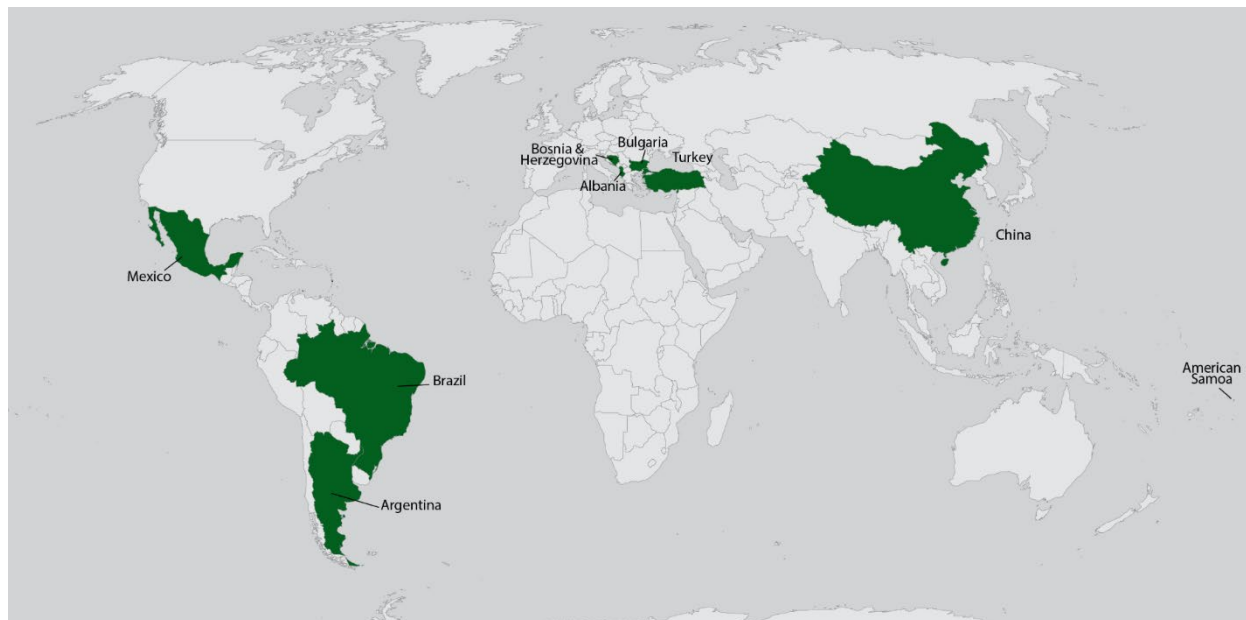
⁸³⁴ CHAI, "FAQ," May 12, 2022. As of publication, no licensed manufacturers party to the CHAI arrangement are producing nirmatrelvir (+ ritonavir).

⁸³⁵ For detailed information, see the section on purchases below.

⁸³⁶ Airfinity, "COVID-19," accessed August 29, 2023.

Figure 6.3 UMICs where COVID-19 therapeutics cannot be offered for sale under voluntary license agreements or procured through multilateral programs according to MPP or Gilead’s access partnerships

Underlying data for this figure can be found in appendix J, [table J.21](#).



Sources: MPP, Nirmatrelvir, “Country List,” <https://medicinespatentpool.org/licence-post/pf-07321332>, accessed June 26, 2023; MPP, Molnupiravir, “Country List,” <https://medicinespatentpool.org/licence-post/molnupiravir-mol>, accessed June 26, 2023; MPP, Ensitrelvir Fumaric Acid, “Country List,” <https://medicinespatentpool.org/licence-post/ensitrelvir>, accessed June 26, 2023; Gilead, Access Partnerships, “2020 Original COVID-19 Voluntary License Agreement,” <https://www.gilead.com/-/media/files/pdfs/other/original-covid-19-voluntary-license-agreement.pdf>, accessed June 26, 2023; Source: Airfinity, “COVID-19,” accessed August 9, 2023.

Note: COVID-19 therapeutics for this figure comprise those that are part of the MPP’s or Gilead’s access partnerships—ensitrelvir, molnupiravir, nirmatrelvir (+ ritonavir), and remdesivir.

Purchases

Government Purchases

Governments are by far the largest purchasers of COVID-19 therapeutics.⁸³⁷ Between March 2020 and April 2023, government purchase agreements were announced for about 77 million courses globally (table 6.4). Of these, about 85 percent were antivirals (small molecule), and 15 percent were monoclonal antibodies (mABs). HICs accounted for about 81 percent of these purchases (62.4 million), UMICs accounted for 14 percent (11 million courses), and LMICs accounted for 5 percent (3.6 million courses). There are no reported government purchases by LICs.

⁸³⁷ Airfinity provides data on purchase agreements and procurements, which in their database, are described as “purchases.” They include government purchases, private sector purchases (including by multilateral organizations), and donations. The data provided by Airfinity reflect public statements from news releases and other sources concerning such agreements and procurements. Visibility is poor with respect to amounts that have actually been delivered, distributed within country, and administered to patients.

Table 6.4 COVID-19 therapeutics: Announced government purchase agreements between March 2020 and December 2022, by treatment and country income level

In number of courses. INN = International Nonproprietary Name; Lilly = Eli Lilly and Company; Vir = Vir Biotechnology; GSK= GlaxoSmithKline; Regeneron = Regeneron Pharmaceuticals; Shionogi = Shionogi & Co.; Syngene = Syngene International Ltd; — = not applicable; n.a. = not available; HIC = High-income countries; UMIC = Upper-middle-income countries; LMIC = Lower-middle-income countries.

Manufacturer	Drug (INN)	Category	HIC	UMIC	LMIC	Total
AstraZeneca	Tixagevimab and cilgavimab	biologic	2,414,540	261,000	70,000	2,745,540
Aurobindo Pharma	Molnupiravir	small-molecule	n.a.	n.a.	300,000	300,000
Celltrion	Regdanvimab	biologic	295,000	n.a.	100,000	395,000
Lilly	Bamlanivimab	biologic	1,126,000	n.a.	n.a.	1,126,000
Lilly	Bamlanivimab and etesevimab	biologic	934,000	n.a.	n.a.	934,000
Lilly	Bebtelovimab	biologic	810,000	n.a.	n.a.	810,000
Lilly	Etesevimab	biologic	388,000	n.a.	n.a.	388,000
Eva Pharma	Remdesivir	small-molecule	n.a.	n.a.	50,000	50,000
Roche	Casirivimab and imdevimab	biologic	801,300	n.a.	n.a.	801,300
Roche	Tocilizumab	biologic	14,551	n.a.	240,000	254,551
Gilead	Remdesivir	small-molecule	1,556,491	n.a.	n.a.	1,556,491
GSK	Sotrovimab	biologic	1,526,579	n.a.	n.a.	1,526,579
Merck	Molnupiravir	small-molecule	8,590,402	215,000	420,000	9,225,402
Pfizer	Nirmatrelvir (+ ritonavir)	small-molecule	39,020,517	584,166	333,333	39,938,016
Regeneron	Casirivimab and imdevimab	biologic	2,950,000	n.a.	n.a.	2,950,000
Sanofi	Sarilumab	biologic	1,000	n.a.	n.a.	1,000
Shionogi	Ensitrelvir	small-molecule	2,000,000	n.a.	n.a.	2,000,000
Syngene	Remdesivir	small-molecule	n.a.	n.a.	83,333	83,333
Unidentified	2-Deoxy-D-Glucose	small-molecule	n.a.	n.a.	10,000	10,000
Unidentified	Favipiravir	small-molecule	n.a.	9,936,170	2,000,000	11,936,170
Unidentified	Remdesivir	small-molecule	n.a.	33,333	n.a.	33,333
Total	—	—	62,428,380	11,029,669	3,606,666	77,064,715

Source: Airfinity, "COVID-19," accessed July 14, 2023.

Notes: For more information on types on therapeutics, see chapter 3. Number of courses is the number of patients that could be treated with the volume of supply procured. Favipiravir is a repurposed antiviral drug developed for the flu and not SARS-CoV-2 but has been authorized by many countries for treating COVID-19. The table provides data on announced government purchase agreements as reported by Airfinity. However, it is unknown whether treatment courses were actually delivered, distributed within a country, or administered to patients.

According to the most recent Airfinity data, the drugs most purchased to treat COVID-19 are antivirals—nirmatrelvir (+ ritonavir), favipiravir, and molnupiravir. A little more than one-half of government purchase agreements were for Pfizer's nirmatrelvir (+ ritonavir) (39 million courses), almost all by HICs. The United States purchased about 23.7 million nirmatrelvir (+ ritonavir) courses (60 percent). Other major purchasers were the United Kingdom, Japan, several European governments, as well as the

European Commission. For UMICs, Brazil, Malaysia, and Mexico accounted for most of the nirmatrelvir (+ ritonavir) purchases. Ukraine accounted for almost all purchases by LMICs. About 15 percent of government therapeutic purchases were of favipiravir, an antiviral drug developed and manufactured in Japan, that is approved for use against COVID-19 in several countries. Thailand accounted for 9 million of the close to 12 million courses of favipiravir purchased by governments. The only other government purchases of favipiravir were made by Indonesia and Venezuela with 2 million and 1 million courses, respectively. Governments purchased more than 9.5 million courses of Merck’s molnupiravir, of which about one-third was by the United States (3.1 million courses) followed by the United Kingdom with 2.3 million courses and Japan with 1.6 million courses. Among LMICs, Ukraine and the Philippines were the major purchases of molnupiravir. In the case of the Philippines, purchases were made from the Indian pharmaceutical manufacturer, Aurobindo Pharma, which had a bilateral license agreement with Merck.⁸³⁸

Private Sector Purchases

According to Airfinity, certain private sector purchases (or purchase agreements) of COVID-19 therapeutics have occurred, although only by companies in LMICs and in small volumes (table 6.5). Most of these purchases were by My Med Rx Plus Corporation, a major pharmaceutical products importer and distributor organization located in Manila, the Philippines. DB Investment and Vingroup JSC also purchased small volumes of Gilead’s remdesivir for distribution in Vietnam.

Table 6.5 COVID-19 therapeutics: Announced private sector purchase agreements between March 2020 and December 2022, by treatment and country income level.

In number of courses. INN = International Nonproprietary Name; mAb = monoclonal antibody; n.a. = not available; LMIC = lower-middle-income countries.

Purchasing organization	Drug (INN)	Category	Type	Manufacturer	Recipient income level	Number of courses
DB Investment	Remdesivir	small-molecule	Antiviral	Mylan	LMIC	30,000
Vingroup JSC	Remdesivir	small-molecule	Antiviral	Cipla	LMIC	83,333
Cipla	Casirivimab and imdevimab	biologic	mAb	Roche	LMIC	200,000
My Med Rx Plus Corp.	Favipiravir	small-molecule	Antiviral	n.a.	LMIC	1,000,000
My Med Rx Plus Corp.	Umifenovir	small-molecule	Antiviral	n.a.	LMIC	3,000,000

Source: Airfinity, “COVID-19,” accessed July 14, 2023.

Notes: Number of full courses is the number of patients that could be treated with the volume of supply procured. Favipiravir is a repurposed antiviral drug developed for the flu and not SARS-CoV-2 but has been authorized by many countries for treating COVID-19. In this instance, antiviral is referring to small-molecule antivirals. Some of the mAbs listed are antiviral (biologics); for more information types of therapeutics see chapter 3. The table provides data on announced private sector purchase agreements (excluding those by multilateral organizations) as reported by Airfinity. However, it is unknown whether treatment courses were actually delivered, distributed within country, or administered to patients.

Multilateral Programs

As stated earlier in the chapter, by 2022, therapeutics for COVID-19 were made available through pooled procurement programs of multilateral organizations (see table 1.1). The main procurements

⁸³⁸ Airfinity, “COVID-19,” accessed July 14, 2023.

were of nirmatrelvir (+ ritonavir) by the Global Fund and of nirmatrelvir (+ ritonavir) and molnupiravir by UNICEF (table 6.6).⁸³⁹ These agreements limit access to these pooled procurement purchases to certain LICs and MICs, as shown in figure 6.4. In late 2020, the Bill & Melinda Gates Foundation announced an agreement with Eli Lilly and Company (Lilly) to potentially supply its experimental antibody treatment for COVID-19 to LICs and MICs through ACT-A.⁸⁴⁰ It has stated that prices for its drugs will be tiered according to the World Bank’s GNI per capita, with the lowest-income countries paying only “marginal costs.”⁸⁴¹ The quantities of the procurements of bamlanivimab through the Bill & Melinda Gates Foundation are undisclosed.⁸⁴²

Table 6.6 COVID-19 therapeutics: Announced multilateral organization purchase agreements between March 2020 and December 2022, by treatment and country income level

In number of courses. INN = International Nonproprietary Name; Lilly = Eli Lilly and Company; n.a. = not available; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries.

Purchasing organization	Drug (INN)	Category	Manufacturer	Recipient income level	Number of courses
UNICEF	Molnupiravir	small-molecule	Merck	LMIC, LIC	3,000,000
UNICEF	Nirmatrelvir (+ ritonavir)	small-molecule	Pfizer	UMIC, LMIC, LIC	4,000,000
Global Fund	Nirmatrelvir (+ ritonavir)	small-molecule	Pfizer	UMIC, LMIC, LIC	6,000,000
Gates Foundation	Bamlanivimab	biologic	Lilly	LMIC, LIC	n.a.

Source: Airfinity, “COVID-19,” accessed July 14, 2023.

Notes: For more information on types of therapeutics, see chapter 3. Number of courses is the number of patients that could be treated with the volume of supply procured. The table provides data on announced purchase agreements by multilateral organizations as reported by Airfinity. However, it is unknown whether treatment courses were actually delivered, distributed within country, or administered to patients.

⁸³⁹ Real-time data on shipments under multilateral programs can be found at the UNICEF COVID-19 Market Dashboard: UNICEF, “COVID-19 Market Dashboard,” accessed August 11, 2023. WHO, “ACT-A Tx Allocation Dashboard,” accessed August 11, 2023.

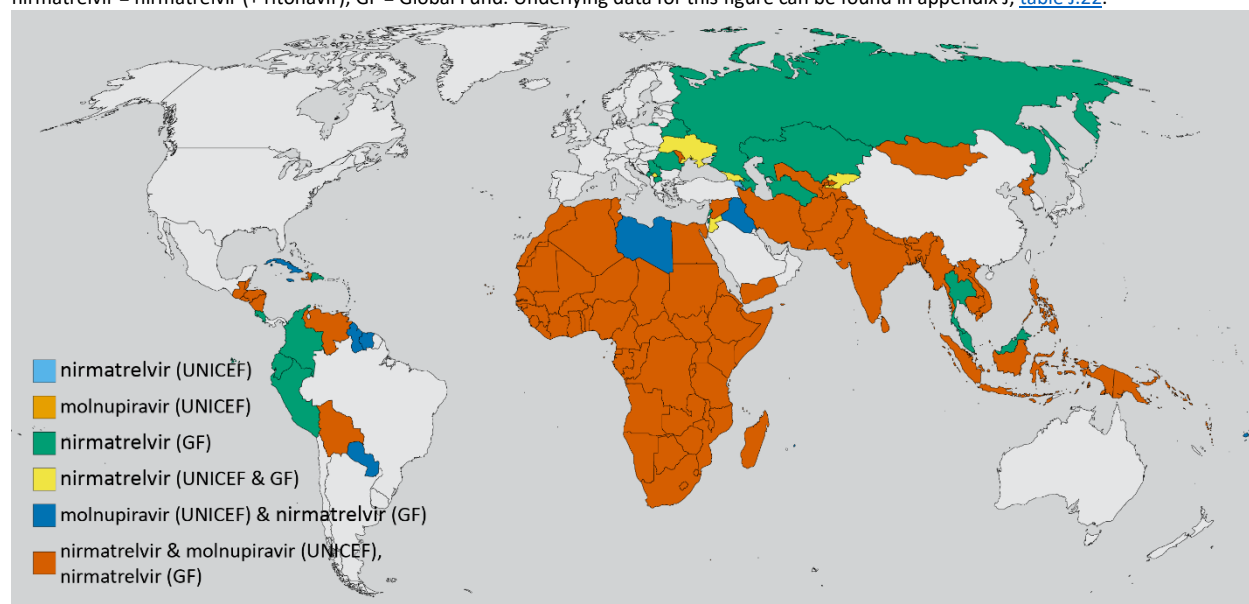
⁸⁴⁰ Lilly, “Lilly Announces Arrangement for Supply of Potential COVID-19 Antibody Therapy,” October 8, 2020.

⁸⁴¹ Ricks, “Dave Ricks Shares Lilly’s Principles of COVID-19 Antibody Therapy Pricing and Access,” October 28, 2020.

⁸⁴² The FDA rescinded authorization of bamlanivimab as a solo treatment, but subsequently authorized bamlanivimab and etesevimab as a combination treatment. Lilly donated this combination treatment to Direct Relief, see the Donations section to see how many courses were donated under this agreement. Lilly, “Lilly Announces Arrangement for Supply of Potential COVID-19 Antibody Therapy,” October 8, 2020; Lilly, “EMA issues advice on Lilly’s bamlanivimab (LY-CoV555) alone,” March 5, 2021.

Figure 6.4 Countries where COVID-19 therapeutics were offered through multilateral programs, as of 2022

nirmatrelvir = nirmatrelvir (+ ritonavir); GF = Global Fund. Underlying data for this figure can be found in appendix J, [table J.22](#).



Source: Airfinity, “COVID-19,” accessed August 9, 2023.

Note: Global fund signed a letter of intent with Pfizer for nirmatrelvir (+ ritonavir) on May 20, 2022. UNICEF announced its agreement with Pfizer for nirmatrelvir (+ ritonavir) on March 22, 2022. UNICEF announced its agreement with Merck for molnupiravir on January 12, 2022.

By May 2022, three main agreements had been reached to make certain antiviral treatments available to LICs and LMICs. The agreements required that supply be made available only to those countries where the necessary regulatory authorizations and approvals had been put in place.⁸⁴³ In January 2022, Merck announced that it had signed a long-term agreement with UNICEF to supply up to 3 million courses of molnupiravir to more than 100 LICs and MICs.⁸⁴⁴ At that time, this volume represented about 30 percent of Merck’s total supply. In March 2022, it was announced that Pfizer had reached an agreement with UNICEF to provide up to 4 million treatment courses of nirmatrelvir (+ ritonavir) in 2022, covering 95 potential recipient countries including all LICs and LMICs, and some UMICs in Sub-Saharan Africa.⁸⁴⁵ In May 2022, the Global Fund announced that it had signed a letter of intent with Pfizer for the procurement of up to 6 million treatment courses of nirmatrelvir (+ ritonavir) to be made available in 2022–23 to 132 countries that are eligible for Global Fund grants.⁸⁴⁶ The Global Fund’s coverage is much wider than UNICEF, and includes Russia, Kazakhstan, and Turkmenistan. It also includes Colombia, Ecuador, and Peru, countries without access via VLs or through UNICEF.

⁸⁴³ Merck also offered 2 million courses to the U.S. Agency for International Development (USAID), also at its “best price,” although this agreement was never finalized. Merck, written testimony to the USITC, March 22, 2023, 4, 201. For more information on regulatory approval, see chapter 2.

⁸⁴⁴ Reuters, “Merck Signs Supply Deal with UNICEF,” January 18, 2022; Merck, “Merck and Ridgeback Announce Supply Agreement with UNICEF,” January 18, 2022.

⁸⁴⁵ UNICEF, “UNICEF Signs Supply Agreement with Pfizer for Oral COVID-19 Treatment,” March 22, 2022.

⁸⁴⁶ The Global Fund, “Global Fund Signs Letter of Intent with Pfizer for Oral COVID-19 Treatment,” May 20, 2022.

Contract negotiations for the agreements between multilateral organizations and originators were prolonged and at times reportedly difficult, leading to delays in delivery.⁸⁴⁷ Agreement was particularly difficult to reach on contract clauses dealing with disclosure and confidentiality, as well as liability and indemnity.⁸⁴⁸ Confidentiality of pricing information was of particular concern to many eligible countries in making the funding requests to donors necessary to pay for the treatments procured (see box 6.1). Ultimately confidentiality clauses resulted in few financial details of the procurement agreements, including prices, being made available to the public.⁸⁴⁹

Box 6.1 Funding of COVID-19 Therapeutics Through Multilateral Organizations

Many countries are eligible for healthcare funding from international donors through multilateral organizations such as UNICEF and the Global Fund based primarily on income level. The specific amount of funds multilateral organizations allocate to eligible countries is determined by several factors, including the total amount of funds received by multilateral organizations, countries' funding requests, and overall health status of the population. To receive funds from their allocation, countries must submit funding requests for financing the procurement of medical goods, such as drugs, oxygen, and personal protective equipment, and for investments in healthcare infrastructure. Because of financial accountability requirements of funders, country requests for such procurements must contain information on costs, prices, and quantities, as well as delivery costs information. Requests then go through a technical review panel to assess the proposed funding request and once approved a grant agreement is drawn up.

To follow this process, countries requesting funds to procure COVID-19 therapeutics are required to disclose fully prices and costs. However, originators were reportedly concerned over making prices publicly availability and wanted a set of confidentiality agreements on pricing and quantities across funding agencies and countries. This demand created challenges for many countries, including LMICs, some of which have legislation that requires price transparency, regardless of the source of financing. For example, South Africa reportedly declined to participate in procurement through this means based on concerns over a lack of price transparency. Ultimately an agreement was reached in which reference prices are made available on the procurement portal that allows orders to be placed. However, this portal is only open to those that are procuring and is not publicly accessible. Although WHO was not a signatory to the supply agreements with Pfizer, prices were posted by WHO on a closed platform, where prices were shared on a "need to know" basis."

Source: International organization, interview by USITC staff, Switzerland, June 9, 2023; Government agency, interview by USITC staff, April 24, 2023.

Negotiations over liability and indemnification issues were also protracted. While manufacturers of COVID-19 therapeutics are indemnified in the United States under The Public Readiness and Emergency Preparedness Act (PREP Act), that protection against liability did not extend to other jurisdictions and

⁸⁴⁷ International organization, interview by USITC staff, Switzerland, June 8, 2023.

⁸⁴⁸ International organization, interview by USITC staff, May 25, 2023.

⁸⁴⁹ According to Pfizer, treatment courses are available to low- and lower-middle-income countries at the "not-for-profit price" and to upper-middle-income countries at "the price defined in Pfizer's tiered pricing approach." International organization, interview by USITC staff, Switzerland, June 8, 2023; Pfizer, "Pfizer to Supply UNICEF up to 4 Million Treatment Courses," March 22, 2022. A Merck representative noted that supplies to UNICEF are available at Merck's "best access price." Merck, prehearing brief submission to the USITC, March 22, 2023, 3.

required contract negotiations to secure it.⁸⁵⁰ The time taken in negotiations delayed final agreement until well into 2022, when the infection rates were declining sharply and demand falling.⁸⁵¹

Treatments are offered to eligible countries through ACT-A.⁸⁵² In 2022, 2.22 million and 2.17 million courses of molnupiravir and nirmatrelvir (+ ritonavir), respectively, were offered to countries that opted in.⁸⁵³ Merck reported slow progress in distributing these supplies, noting that the first shipment was 20,000 courses to Cambodia in August 2022.⁸⁵⁴ As of August 2023, 43 eligible countries out of a possible 103 had opted-in to be allocated molnupiravir, and 149,393 courses were confirmed to have been delivered.⁸⁵⁵ For nirmatrelvir (+ ritonavir), as of August 2023, 59 out of 138 countries had opted-in and 140,084 treatments were delivered. In Q1 2023 an additional round for the allocation of treatments took place with only 7 countries opting-in for confirmed delivery of 3,785 treatment courses of molnupiravir, and for nirmatrelvir (+ ritonavir), 8 countries opted-in for 4,964 treatment courses. Merck attributes this slow uptake to governments not giving a high priority to procuring COVID-19 antivirals in their efforts to fight the pandemic.⁸⁵⁶ Other stakeholders contend that procurements by LICs and LMICs from multilateral organizations would have been much higher if agreements between the originator firms and multilateral organizations had been reached much sooner in the pandemic.⁸⁵⁷

Donations

A few originators, such as Pfizer, Lilly, Merck, and Gilead, have made or committed to donations of COVID-19 therapeutics to certain LICs and LMICs, as reported by Airfinity (table 6.7), although information on delivery is minimal. As of April 2023, no government-to-government donations had been identified. Since late 2021, Pfizer has donated 100,000 courses of nirmatrelvir (+ ritonavir) to the COVID Treatment Quick Start Consortium.⁸⁵⁸ The consortium is working to support test-to-treat demonstration programs, as well as to introduce and scale up access to COVID-19 oral antiviral therapies in high-risk populations in 10 LICs and LMICs. Partner countries include nine African countries (Ghana, Kenya, Malawi, Nigeria, Rwanda, South Africa, Uganda, Zambia, and Zimbabwe) and one in Asia (Laos). In December 2022, Zambia became the first country to receive a donation, with 1,000 courses distributed and made available through the Ministry of Health in Lusaka.⁸⁵⁹ A second shipment was received by

⁸⁵⁰ See The Public Readiness and Emergency Preparedness Act (PREP Act), Pub. L. No. 109-148, Division C § 2, 119 Stat. 2680 (2005) (codified at 42 U.S.C § 247d–6d); but see also Taylor, “In Vaccine Contracts, Pfizer Took Hard Line,” October 19, 2021.

⁸⁵¹ Negotiations began in early 2021 and were not completed until well into 2022. International organization, interview by USITC staff, Switzerland, June 9, 2023.

⁸⁵² It is not clear if ACT-A is the exclusive channel through which these supplies are distributed to countries.

⁸⁵³ Under the system countries may ‘opt-in’ each quarter to be allocated and receive COVID-19 treatments.

⁸⁵⁴ Merck, prehearing submission to the USITC, March 22, 2023, 4; USITC, hearing transcript, March 29, 2023, 201 (testimony of Gregg Szabo, Merck).

⁸⁵⁵ Real time data on procurements under multilateral programs can be found at WHO, “ACT-A Tx Allocation Dashboard,” accessed August 11, 2023, and UNICEF, “COVID-19 Market Dashboard,” accessed August 11, 2023.

⁸⁵⁶ Merck, prehearing submission to the USITC, March 22, 2023, 5.

⁸⁵⁷ Government official, interview by USITC staff, April 24, 2023; international organization, interview by USITC staff, Switzerland, June 8, 2023.

⁸⁵⁸ Information on COVID Treatment Quick Start Consortium can be found in table 1.1. COVID Treatment Quick Start Consortium, “10-Country Partnership in Africa and Southeast Asia,” September 7, 2022.

⁸⁵⁹ Foreign government official, interview by USITC staff, Zambia, June 7, 2023; COVID Treatment Quick Start Consortium, “Zambia Becomes First Country to Receive Paxlovid,” December 22, 2022.

Zambia in early March 2023. In mid-March 2023, the consortium announced that Laos, Malawi, and Rwanda had received shipments of nirmatrelvir (+ ritonavir).⁸⁶⁰

Table 6.7 COVID-19 Therapeutics: Certain private sector donations between March 2020 and December 2022, by treatment and recipient country income level

In number of courses. INN = International Nonproprietary Name; Lilly = Eli Lilly and Company; LMIC = lower-middle-income countries; MIC = middle-income countries; LIC = low-income countries.

Recipient	Drug (INN)	Category	Donating Manufacturer	Country income level	Number of courses
COVID Treatment Quick Start Consortium	Nirmatrelvir (+ ritonavir)	small-molecule	Pfizer	LIC	100,000
Government of India	Favipiravir	small-molecule	n.a.	LMIC	300,000
Government of India	Remdesivir	small-molecule	n.a.	LMIC	5,500
Direct Relief	Bamlanivimab and etesevimab	biologic	Lilly	LMIC, LIC	n.a.
Direct Relief	Baricitinib	small-molecule	Lilly	LMIC, LIC	n.a.
Government of India	Baricitinib	small-molecule	Lilly	LMIC	400,000
Indian manufacturers	Remdesivir	small-molecule	Gilead	LMIC	75,000
Direct Relief	Molnupiravir	small-molecule	Merck	LMIC	50,000
Direct Relief	Molnupiravir	small-molecule	Merck	MIC, LIC	50,000
Direct Relief	Nirmatrelvir (+ ritonavir)	small-molecule	Pfizer	LMIC	200,000

Source: Airfinity, "COVID-19," accessed July 14, 2023.

Notes: COVID Treatment Quick Start Consortium consists of implementing partners: Duke University, AmeriCare, the Clinton Health Access Initiative (CHAI), and COVID Collaborative, with support from the Open Society Foundations, Pfizer, and the Conrad N. Hilton Foundation. Baricitinib is not a virus-directed drug; it is host-directed (i.e., not specific for SARS-CoV-2). For more information on types of therapeutics, see chapter 3. Favipiravir is a repurposed antiviral drug developed for the flu and not SARS-CoV-2 but has been authorized by many countries for treating COVID-19. Number of courses is the number of patients that could be treated with the volume of supply procured. The table provides donations reported by Airfinity. However, it is unknown whether treatment courses were actually delivered, distributed within country, and administered to patients. The table does not include certain donations reported in testimony provided to the USITC in connection with this investigation.

Lilly donated its antiviral monoclonal antibody drugs bamlanivimab and etesevimab, bebtelovimab, and baricitinib, working with Direct Relief⁸⁶¹ to be distributed to LICs and LMICs.⁸⁶² Donations were first shipped in February 2021 and were made available to such countries at no cost.⁸⁶³ Lilly will increase manufacturing of baricitinib and supply 400,000 tablets to the Indian government through Direct Relief.⁸⁶⁴

⁸⁶⁰ COVID Treatment Quick Start Consortium, "Laos, Malawi, Rwanda and Zambia Have Received Oral Antiviral Treatments for High-Risk Patients," March 16, 2023.

⁸⁶¹ Information on Direct Relief can be found in chapter 1, table 1.1.

⁸⁶² Lilly, prehearing brief submission to the USITC, March 17, 2023, 2.

⁸⁶³ USITC, hearing transcript, March 29, 2023, 204 (testimony of Cynthia Cardona, Lilly).

⁸⁶⁴ Airfinity, "COVID-19," accessed July 14, 2023.

Gilead has stated that it has donated more than 2 million vials of remdesivir since the beginning of the pandemic.⁸⁶⁵ Donations include 450,000 vials to India in April 2021 and more than 100,000 vials to Armenia and Indonesia in October 2022.⁸⁶⁶ Merck, in a press release on April 1, 2022, announced a commitment to donate 100,000 courses of molnupiravir to Direct Relief to be distributed to refugees in LICs and LMICs.⁸⁶⁷ The donation included 50,000 courses specifically targeted to people affected by the conflict in Ukraine.

Consumption

Data on COVID-19 therapeutics consumption, as defined as the number of full treatment courses administered (i.e., number of patients treated), are limited to a few HICs and only for nirmatrelvir (+ ritonavir) and molnupiravir, according to Airfinity. No data are available for any MICs and LICs, representing a significant data gap for analyzing global trends in consumption. In 2022, about 7.3 million courses of nirmatrelvir (+ ritonavir) were administered, rising quickly during the second and third quarters, and then declining sharply in the fourth quarter and first quarter of 2023 (table 6.8). About 94 percent of the courses administered to these HICs were administered to patients in the United States.

Table 6.8: Number of courses of nirmatrelvir (+ ritonavir) administered by certain high-income countries (HIC), quarterly, 2022–23.

In number of full treatments. n.a. = not available; Q1 = January–March; Q2 = April–June; Q3 = July–September; Q4 = October–December.

HIC	2022 (Q1)	2022 (Q2)	2022 (Q3)	2022 (Q4)	2023 (Q1)
Australia	n.a.	9,076	50,845	96,977	58,953
Germany	3,286	8,850	32,372	n.a.	n.a.
Italy	5,343	19,174	41,166	39,351	15,449
Japan	2,400	7,501	34,801	28,101	29,000
United Kingdom	5,265	10,174	10,217	8,179	7,914
United States	163,852	1,793,344	3,075,430	1,862,659	1,867,238
Total	180,146	1,848,119	3,244,831	2,035,267	1,978,554

Source: Airfinity, “COVID-19,” accessed July 14, 2023. Airfinity reports data on courses of nirmatrelvir (+ ritonavir) only for the countries listed in the table above.

Note: Number of courses is the number of patients that could be treated with the volume of supply procured.

For molnupiravir, more than 3.0 million courses were reported as consumed by a subset of HICs (table 6.9). Like nirmatrelvir (+ ritonavir), consumption increased during 2022, reaching a peak in the third quarter, declining sharply in the fourth quarter and even further in the first quarter of 2023. The United States and Japan each accounted for about 40 percent of consumption.

⁸⁶⁵ Gilead, prehearing brief submission to the USITC, March 17, 2023, exhibit A. USITC, hearing transcript, March 29, 2023, 202 (testimony of Anu Osinusi, Gilead).

⁸⁶⁶ Gilead, prehearing brief submission to the USITC, March 17, 2023, exhibit D.

⁸⁶⁷ Merck, “Merck and Ridgeback Announce Supply Agreement with UNICEF,” January 18, 2022.

Table 6.9 Number of courses of molnupiravir administered by certain high-income countries (HIC), quarterly, 2022–23.

In number of full treatments. n.a. = not available; Q1 = January–March; Q2 = April–June; Q3 = July–September; Q4 = October–December.

HIC	2022 (Q1)	2022 (Q2)	2022 (Q3)	2022 (Q4)	2023 (Q1)
Australia	2,350	53,096	178,753	200,049	81,575
Germany	7,630	5,798	8,004	n.a.	n.a.
Italy	12,796	18,706	13,043	13,253	4,955
Japan	122,300	78,299	419,000	314,318	222,938
United Kingdom	7,257	3,116	3,222	4,188	4,833
United States	91,854	259,195	385,730	215,226	301,754
Total	244,187	418,210	1,007,752	747,034	616,055

Source: Airfinity, “COVID-19,” accessed July 14, 2023. Airfinity reports data on courses of nirmatrelvir (+ ritonavir) only for the countries listed in the table above.

Note: Number of courses is the number of patients that could be treated with the volume of supply procured.

Factors Affecting Demand and Availability of Diagnostics and Therapeutics

Numerous stakeholders and interested persons provided information to explain demand, procurement, and consumption trends and the reasons for market segmentation and barriers to a more diverse geographical distribution of COVID-19 diagnostics and therapeutics. Among the many factors they highlighted, the most pervasive were pricing, regulations and approvals, competing healthcare priorities, testing availability, and last mile delivery. Other factors include trade policy, product awareness, and evidence of cost-effectiveness. The relative importance of each of these factors differs among country income groups. For example, prices and regulatory approvals appear to have been significant barriers to access in MICs; while last mile delivery and healthcare infrastructure are more pertinent barriers to access in LICs. Common across many countries is the impact of the epidemiological trends of the disease and reevaluation of healthcare priorities away from COVID-19 diagnostics and therapeutics. As a result, many of the factors that may have previously constrained a more diverse distribution may become increasingly less relevant as the severity of COVID-19 infections wanes.

Price

The affordability of COVID-19 therapeutics has been noted as a significant barrier to access for many LICs and MICs, especially where generic manufacturers for a given product are not authorized under VLS, CLs, or the LDC exception to the TRIPS Agreement.⁸⁶⁸ Of greatest concern were interrelated barriers related to pricing: the use of tiered-pricing schemes for direct purchase by countries and the exclusion of many UMICs from MPP sublicensing agreements.

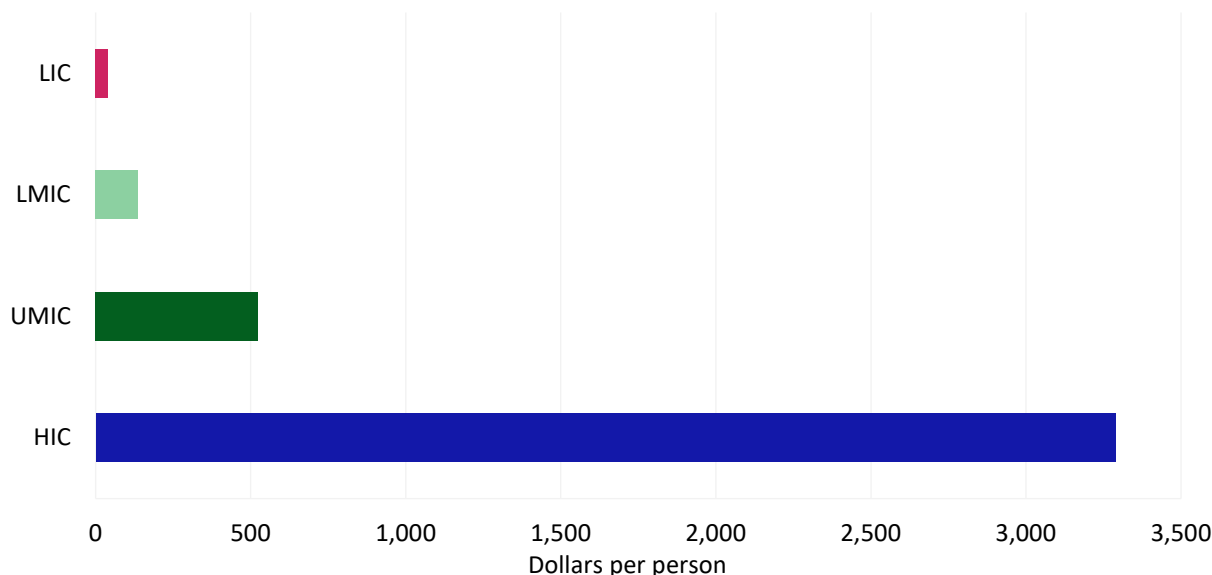
As noted above, several pharmaceutical companies employ a tiered-pricing scheme for direct country sales. For example, for Pfizer’s nirmatrelvir (+ ritonavir), these tiers range from up to \$740 per treatment course in HICs to \$250 in UMICs, to a reported \$80–90 for LICs and LMICs. Even though the middle and lowest “best access” prices are well below the highest price points paid by HICs, they may still be

⁸⁶⁸ Health Advocacy International, prehearing brief submission to the USITC, March 16, 2023, 1; TWN, posthearing brief submission to the USITC, April 12, 2023, 5; WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

untenably high for LICs, LMICs, and UMICs.⁸⁶⁹ Indeed, for many countries, the “best access price” exceeds the average annual health care expenditure for LICs (\$39 per capita) and is more than half the price of the average annual per capita health care expenditure of LMICs (\$137) (figure 6.5).⁸⁷⁰

Figure 6.5 Per capita annual health care expenditure, by income group, 2021

In U.S. dollars. HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries. Underlying data for this figure can be found in appendix J, [table J.23](#).



Source: World Health Organization, current health care expenditure, per capita, accessed May 31, 2023

As discussed in chapter 5 and highlighted in the pricing discussion above, COVID-19 therapeutics manufacturers Merck, Pfizer, and Gilead have entered into VLs with licensed manufacturers, either through bilateral agreements or via the MPP.⁸⁷¹ An intention of MPP agreements is to facilitate competition between manufacturers with the goal of producing lower-cost versions of these therapeutics.⁸⁷² Additionally, as noted above, CHAI arranged with several manufacturers sublicensed under the MPP to provide licensed nirmatrelvir (+ ritonavir) to LICs and MICs for \$25 per treatment course,⁸⁷³ representing a significant cost savings for many of these countries compared to the “best access price” available through originators. As of publication, however, no licensed manufacturers party to the CHAI arrangement are producing nirmatrelvir (+ ritonavir). First, for many drugs, but especially for nirmatrelvir (+ ritonavir), generics have been slow to become available. Only one licensed manufacturer,

⁸⁶⁹ Health Advocacy International, prehearing brief submission to the USITC, March 16, 2023, 1; TWN, posthearing brief submission to the USITC, April 12, 2023, 5; Keller, Kaufman, and Guzman, “Oral Antiviral Treatments for COVID-19: Time to Revisit?,” December 14, 2022.

⁸⁷⁰ Certain stakeholders have questioned whether comparing price with per capita healthcare expenditure is an appropriate measure of affordability. Industry representative, interview by USITC staff, Switzerland, June 7, 2023.

⁸⁷¹ In October 2022, Shionogi signed an agreement with the MPP for Shionogi’s antiviral candidate ensitrelvir fumaric acid. MPP, “ENSITRELVIR FUMARIC ACID,” October 2022.

⁸⁷² MPP, written submission to the USITC, May 5, 2023, 2; Ravelo, “35 Companies in 12 Nations to Manufacture Pfizer’s Oral COVID-19 Drug | Devex,” March 17, 2022; FDA, “Generic Competition and Drug Prices,” September 12, 2022.

⁸⁷³ CHAI, “FAQ,” May 12, 2022.

who is not part of the CHAI arrangement, has received WHO prequalification for nirmatrelvir (+ ritonavir)—a pre-condition of the MPP sublicensing agreement—and the firm has had little demand for its products priced at \$60 per treatment course.⁸⁷⁴ Additionally, the potential \$25 per treatment course price under the CHAI agreement would only be available once a minimum purchase threshold is reached, which may be difficult given declining demand.⁸⁷⁵ Several sources stated that, without more manufacturers coming on board with generic versions of nirmatrelvir (+ ritonavir) and further lowering the price, the pricing for LICs and LMICs may be untenable.⁸⁷⁶

One of the main concerns expressed by several stakeholders about affordability and access is centered on the tiered prices for many MICs and UMICs that are offered high per treatment prices and are generally excluded from the MPP and CHAI agreements.⁸⁷⁷ This includes countries like Brazil, Panama, and Thailand. The tiered price for these UMICs is about \$250 per treatment course for nirmatrelvir (+ ritonavir), which is about half of the average per capita annual health care expenditure (\$524) (figure 6.5).⁸⁷⁸ Many UMICs excluded from certain MPP agreements have average annual per capita health expenditures that are even less than that. For example, a \$250 treatment course price would comprise almost 70 percent of the \$354 annual per capita health expenditure in the Dominican Republic.⁸⁷⁹

While products are available through international organizations using each country’s allocated funds, uptake has been minimal. These products are essentially “free” because the allocated funds are donated, but the countries must prioritize what to purchase with these funds. At \$80–90 per course (the “best access price” for nirmatrelvir (+ ritonavir)), many courses may not be affordable, given the total amount of funding dollars, and other priorities for limited national healthcare budgets may be competing.⁸⁸⁰ Having the funds to purchase COVID-19 diagnostics may now be less of a concern, however. Many of the COVID-19 therapeutics covered in this report became available only at the end of 2022, when negotiations with international procurement agencies were complete and, for certain products, received WHO prequalification.⁸⁸¹ At that time, reported COVID-19 cases started to decline in most countries.⁸⁸² As a result, global demand for novel antivirals is low and declining as of this writing.⁸⁸³

⁸⁷⁴ Industry representative, interview by USITC staff, June 13, 2023.

⁸⁷⁵ CHAI, “FAQ,” May 12, 2022.

⁸⁷⁶ Public Citizen, written submission to the USITC, May 5, 2023, 8–9; WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

⁸⁷⁷ Rethink Trade, written submission to the USITC, May 5, 2023, 5; Public Citizen, written submission to the USITC, May 5, 2023, 8–9; USITC, hearing transcript, March 29, 2023, 360 (testimony of Brook Baker, Health Global Access Project, Inc.); USITC, hearing transcript, March 30, 2023, 85 (testimony of Jennifer Reid, Oxfam America).

⁸⁷⁸ Airfinity, “COVID-19,” accessed July 14, 2023; USITC, hearing transcript, March 29, 2023, 40 (testimony of Peter Maybarduk, Public Citizen); USITC, hearing transcript, March 30, 2023, 85 (testimony of Jennifer Reid, Oxfam America), 297 (testimony of Susana Van der Ploeg, Brazilian AIDS Interdisciplinary Association).

⁸⁷⁹ World Health Organization (WHO), “Current Health Care Expenditure, Per Capita,” accessed May 31, 2023. Applications have been filed for a CL of nirmatrelvir (+ ritonavir) in the Dominican Republic. The Dominican Republic is home to 1 of the 35 sublicensees for nirmatrelvir under the MPP, but it cannot sell the product domestically. Wallach, “The International Community Must Prioritize COVID Treatment and Test Access,” accessed February 21, 2023.

⁸⁸⁰ See the section Competing Healthcare Priorities below.

⁸⁸¹ See chapter 2 for more information about WHO prequalification.

⁸⁸² Airfinity, “COVID-19,” accessed July 14, 2023. International organization, interview by USITC staff, Switzerland, June 12, 2023.

⁸⁸³ WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

While LICs and LMICs can access COVID-19 therapeutics using their allocated donated funds, many countries have not used the majority of their COVID-19-designated funds. In response, the Global Fund is reallocating a portion of those funds back to the general fund because of a lack of demand for COVID-specific donations.⁸⁸⁴ For these countries, several other factors described below may be more significant hurdles for access, including regulatory barriers, lack of knowledge of the product, and waning focus on the COVID-19 pandemic now that cases have ebbed. For LICs and LMICs, other health concerns may now be more pressing, including HIV/AIDS and malaria.⁸⁸⁵ This may not be the case for some UMICs, where these allocated funds may not be available. They may also be excluded from the MPP and bilateral license agreements' country coverage, and tiered-pricing schemes may remain unaffordable, particularly if demand increases.⁸⁸⁶

Regarding COVID-19 diagnostics, prices declined substantially during the course of the pandemic, partially as a result of pooled-procurement mechanisms organized under the ACT-A diagnostics pillar.⁸⁸⁷ One industry expert noted that the diagnostics market functioned better than the therapeutics market and that pricing was not as aggressive for diagnostics because there was greater competition.⁸⁸⁸

Others have noted that the current price point for diagnostics for consumers is still not optimal given existing differentials between the procured price and the prices available to the final consumer, indicating that affordability may still be a barrier to access in some locations.⁸⁸⁹ Additionally, affordability of COVID-19 diagnostics may be more of a barrier for countries where a large share of laboratory testing capacity is reliant on closed-system automated PCR machines. Often, consumables in these closed-system machines, such as reagent cartridges, can only be sourced from one supplier.⁸⁹⁰ The cartridges used in Cepheid's GeneXpert COVID-19 diagnostic test, for example, are currently priced at \$14.90 as part of the pooled procurement mechanism in developing countries.⁸⁹¹

Regulations and Approvals

WHO prequalification and guidance and national regulatory approval are essential for safeguarding public health but can also pose a barrier to access in developing countries. Specific, yet interrelated barriers include the length of approval processes, limited resources and expertise within regulatory authorities, and lack of regulatory harmonization between countries. As detailed below, these barriers are prevalent for approval via national regulatory authorities as well as WHO prequalification and guidance. Various aid groups and company suppliers have suggested that because of regulatory

⁸⁸⁴ International organization, interview by USITC staff, Switzerland, June 9, 2023.

⁸⁸⁵ WHO, "ACT-Accelerator Facilitation Council Working Group Report," September 22, 2022; government representative, interview by USITC staff, Bangladesh, July 17, 2023; government representative, interview by USITC staff, Malaysia, July 25, 2023.

⁸⁸⁶ International organization, interview by USITC staff, August 25, 2023.

⁸⁸⁷ PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023.

⁸⁸⁸ USITC, hearing transcript, March 29, 2023, 127 (testimony of James Love, KEI).

⁸⁸⁹ PVA, *Study on the Availability and Affordability of Diagnostics*, January 2023; CAMD, prehearing brief submission to the USITC, March 22, 2023, 2; Public Citizen, written submission to the USITC, May 5, 2023, 3.

⁸⁹⁰ For more information on closed system PCR tests, see chapters 3 and 4.

⁸⁹¹ TWN, prehearing brief submission to the USITC, March 17, 2023, 8.

approval delays, product availability ultimately coincided with the waning of the COVID-19 pandemic in late 2022 and early 2023, which subsequently impacted demand for the products.⁸⁹²

The process of regulatory approval can be time-consuming, often involving extensive clinical trials and comprehensive data submissions, analysis, and review. Although important, these processes can delay the availability of COVID-19 drugs.

As mentioned above, many LMICs relied on donated funds to procure diagnostics and therapeutics through international procurement agencies, such as the Global Fund and UNICEF.⁸⁹³ These procurement agencies, however, rely on WHO prequalification (or emergency use listing) and guidance issuance for all tests and treatments, which were reported to have caused delays.⁸⁹⁴ In the case of some therapeutics, such as remdesivir, WHO recommendation and prequalification came a full two years after U.S. authorization and the first VLs were signed. This means that although treatments were available, many countries were not immediately able to access them.⁸⁹⁵ WHO prequalification, which is also required for certain MPP sublicensing agreements, requires significant effort by manufacturers in order to complete the application requirements and address data standards, which may be challenging for some manufacturers.⁸⁹⁶ It can also be costly. As noted in chapter 2, a one-time application fee of \$25,000 is required in addition to a \$20,000 annual fee for a full product assessment. Industry representatives have noted that these fees may be too expensive for smaller manufacturers in many LMICs.⁸⁹⁷

In the case of diagnostics, WHO Emergency Use Listing Procedure (EUL) and official guidance delays were a significant factor for access to rapid antigen tests.⁸⁹⁸ The WHO issued its first two EULs for rapid antigen tests in September and November 2020, but the initial guidance did not recommend their use.⁸⁹⁹ The guidance in late December 2020 only recommended the use of rapid antigen tests in limited circumstances where molecular testing was unavailable. Even when use of rapid antigen tests was finally recommended for primary detection in October 2021, self-testing was explicitly not recommended. Only two rapid antigen self-tests have received WHO EULs. They occurred in July and September 2022, more than a year after the U.S. Food and Drug Administration (FDA) issued Emergency Use Authorizations.

⁸⁹² Government representative, interview by USITC staff, April 24, 2023; industry representatives, interviews by USITC staff, May 25, June 6, and June 13, 2023; WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

⁸⁹³ USITC, hearing transcript, March 29, 2023, 226–7 (testimony of Anu Osinusi, Gilead).

⁸⁹⁴ USITC, hearing transcript, March 29, 2023, 226–7 (testimony of Anu Osinusi, Gilead); international organization, interview by USITC staff, March 7, 2023; industry representative, interview by USITC staff, Bangladesh, June 19, 2023.

⁸⁹⁵ USITC, hearing transcript, March 29, 2023, 224 and 226–7 (testimony of Anu Osinusi, Gilead); industry representative, interview by USITC staff, May 17, 2023. It should be noted that not all therapeutic manufacturers experienced what they thought were lengthy delays with the WHO prequalification process. Industry representative, interview by USITC staff, June 5, 2023.

⁸⁹⁶ WHO prequalification does provide technical assistance to complete dossiers and include relevant data and evidence standards. Hodges et al., *Navigating Complexity to Improve Global Access*, August 20, 2022.

⁸⁹⁷ Several industry representatives have questioned whether the annual prequalification fees are worth paying when demand for the product is so low. Industry representative, interview by USITC staff, South Africa, June 29, 2023; industry representative, interview by USITC staff, Bangladesh, July 19, 2023.

⁸⁹⁸ PVA, *Study on the Availability and Affordability of Diagnostics*, January 31, 2023.

⁸⁹⁹ Advamed, prehearing brief submission to the USITC, March 17, 2023, 12.

The delays in EULs and guidance from the WHO likely reduced demand for rapid antigen tests in LMIC markets, despite the ample supply.⁹⁰⁰

WHO prequalification can help facilitate LICs' and LMICs' access to tests and treatment through global procurement agencies. Prequalification, however, does not automatically translate to marketing authorization in-country. As a result, delays between prequalification and national approval can exist.⁹⁰¹ Although some countries automatically approve or authorize certain therapeutics after they have received WHO prequalification, industry representatives have noted that every national regulatory authority has a different timeline that can vary from months to years.⁹⁰²

Additionally, regulatory authorities in developing countries may have limited access to advanced laboratories, clinical research facilities, and skilled personnel needed to conduct the necessary reviews to expedite the regulatory approval process when domestic review is required.⁹⁰³ Indeed, as noted in chapter 2, about 70 percent of WHO member countries (144 of 190) have suboptimal regulatory systems, and about 50 percent are operating at the lowest level.⁹⁰⁴ This scarcity of resources has led to delays in obtaining regulatory approval. According to Airfinity, only 16 LICs and LMICs, including five countries in Africa, have approved or authorized COVID-19 therapeutics for their own markets, even though several therapeutics have received WHO prequalification (see figure 6.6).⁹⁰⁵ Thus, many LICs and LMICs have been limited in their ability to accept existing COVID-19 treatments from nongovernmental organizations, manufacturers, and governments even though the treatments were offered at no cost.⁹⁰⁶ In the case of diagnostics, many LICs and LMICs do not have regulatory pathways available for medical

⁹⁰⁰ Industry representative, interview by USITC staff, March 7, 2023.

⁹⁰¹ WHO, "ACT-Accelerator Facilitation Council Working Group Report," September 22, 2022; international organization, interview by USITC staff, June 5, 2023; industry representative, interview by USITC staff, July 6, 2023. Approval by national regulatory authorities after WHO prequalification is reported to take up to five months on average. Hodges et al., *Navigating Complexity to Improve Global Access*, August 20, 2022.

⁹⁰² Industry representative, interview by USITC staff, May 25, 2023; government representatives, interview by USITC staff, Zambia, June 21, 2023; industry representative, interview by USITC staff, South Africa, June 28, 2023. Additionally, some countries may rely on prequalification (which the WHO recommends for national regulatory authorities below maturity level 3) but others may also require access to the assessment reports in order to review before approval. This information would come from the manufacturers and the WHO prequalification team tries to facilitate this process. International organization, interview by USITC staff, June 5, 2023. Additionally, many national regulatory authorities, including those of many countries in sub-Saharan Africa, the Middle East, and Latin America, require a Certificate of Pharmaceutical Product from a manufacturer to facilitate domestic registration, which can lead to further delays. For example, the certificate for Pfizer's nirmatrelvir (+ ritonavir) was not issued until the company received full market approval from the FDA on May 25, 2023, meaning that the company was not able to move forward with full approval in many countries before that date. Industry representative, interview by USITC staff, June 5, 2023. The WHO also aims to accelerate national approval for medicines, in vitro diagnostics, and vaccines through its Collaborative Registration Procedure by sharing confidential application material from the prequalification process with national regulatory authorities for countries that commit to participating in the procedure and approving products within 90 days. Hodges et al., *Navigating Complexity to Improve Global Access*, August 20, 2022.

⁹⁰³ Industry representative, interview by USITC staff, June 5, 2023; USITC, hearing transcript, March 30, 2023, 158–9 (testimony of Sanya Reid Smith, Social Watch).

⁹⁰⁴ International organization, interview by USITC staff, Switzerland, June 5, 2023; Khadem Broojerdi et al., "The World Health Organization Global Benchmarking Tool," August 19, 2020.

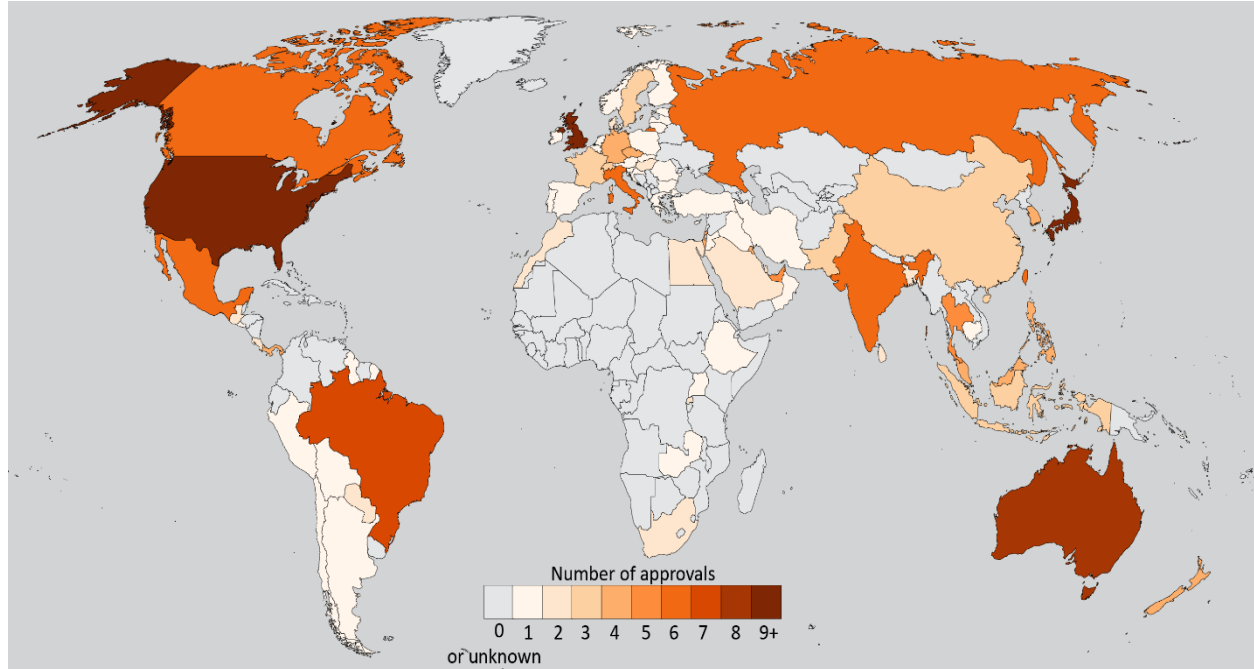
⁹⁰⁵ Airfinity, "Regulatory Overview by Country," July 11, 2023.

⁹⁰⁶ PhRMA, prehearing brief submission to the USITC, March 17, 2023, 6.

devices.⁹⁰⁷ Many of these countries rely instead on WHO EULs and guidance. The discrepancy can be sizeable between the number of tests approved in the Americas and Europe compared to the number approved in sub-Saharan Africa, as shown in chapter 2.

Figure 6.6 Regulatory approvals by country for relevant COVID-19 therapeutics

In number of approvals. Underlying data for this figure can be found in appendix J, [table J.24](#).



Source: Airfinity, "COVID-19," accessed August 9, 2023.

Stakeholders have also noted that the lack of regulatory harmonization has presented significant challenges to access. National regulatory authorities can vary significantly in submission, technical, clinical, and quality requirements for the same diagnostic or therapeutic.⁹⁰⁸ Industry representatives note that the variety of processes, including translating hundreds of pages of documents and repeated site inspections, are time-consuming and burdensome.⁹⁰⁹ Additionally, the myriad of approval processes can require significant financial investments, including costs associated with clinical trials, data generation, analysis, and dossier submissions.⁹¹⁰ Industry representatives noted that a harmonized regulatory process, perhaps at the regional level, could simplify the process and increase access.⁹¹¹

⁹⁰⁷ USITC, hearing transcript, March 29, 2023, 138–9 (testimony of Ashley Miller, AdvaMed).

⁹⁰⁸ AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 11; industry representative, interview by USITC staff, May 16, 2023; USITC, hearing transcript, March 29, 2023, 116 (testimony of Zachary Rothstein, AdvaMed).

⁹⁰⁹ Industry representative, interview by USITC staff, May 16, 2023; industry representative, interview by USITC staff, May 25, 2023; Hodges et al., *Navigating Complexity to Improve Global Access*, August 20, 2022.

⁹¹⁰ USITC, hearing transcript, March 29, 2023, 198 (testimony of George Scangos, Vir Biotechnology); international organization, interview by USITC staff, Switzerland, June 5, 2023.

⁹¹¹ USITC, hearing transcript, March 29, 2023, 198 (testimony of George Scangos, Vir Biotechnology). Currently there are efforts underway in sub-Saharan Africa to implement uniform regulatory qualifications. To date, 28

Competing Healthcare Priorities

The vast majority of COVID-19 diagnostics and therapeutics are purchased and distributed by governments, typically through entities responsible for providing public health services and delivering care to their populations. These entities must allocate their budgets among competing priorities within the healthcare delivery system targeting disease prevention and treatment. In many LICs with access to treatments through multilateral programs, government health departments must balance their response to COVID-19 with efforts to combat other diseases, including other infectious diseases. According to the WHO, the major causes of death in such countries include other infectious diseases (e.g., HIV/AIDS and tuberculosis); parasitic diseases (e.g., malaria); and maternal, perinatal, and nutritional conditions.⁹¹² Even in response to COVID-19, governments must weigh the cost-effectiveness of diagnostics and therapeutics against vaccines, including boosters, that may provide greater health impact per amount spent.⁹¹³ Among the key factors in setting healthcare priorities are the epidemiological trends in disease among the population, such as rates of infection, hospitalizations, and deaths. As noted in chapter 1, infection rates and deaths from COVID-19 have steadily declined since early 2022, to the extent that by early May 2023, the WHO declared that COVID-19 would no longer be classified as a public health emergency of international concern, and the U.S. government ended the U.S. public health emergency status for the pandemic.⁹¹⁴

Representatives of foreign governments and multilateral organizations noted that government agencies are now placing a lower priority on their response to COVID-19, and many countries with competing healthcare priorities, such as childhood vaccination programs, have chosen to allocate their limited health budgets to other areas. Stakeholders interviewed by the Commission pointed to a sharp decline in testing to the point that testing in some countries no longer exists.⁹¹⁵ For example, Brazil's focus is on continuation of its COVID-19 vaccination program, including campaigns for boosters, rather than testing and treating those presenting with mild symptoms.⁹¹⁶ In Mexico, testing programs have disappeared and treatment is limited to severely ill patients.⁹¹⁷ In Zambia, HIV/AIDS, polio, and malaria are among the major public healthcare issues, which were made worse by COVID-19. As a result, early in the pandemic, addressing COVID-19 was a top healthcare priority. However, as the pandemic ebbed, the effects of COVID-19 on other healthcare priorities diminished.⁹¹⁸ In South Africa, it is reported that testing for COVID-19 has almost come to a standstill, and no data on testing are being published. In many LICs, addressing HIV/AIDS and tuberculosis, as well as improving healthcare infrastructure, are prioritized over COVID-19.⁹¹⁹ Other evidence that healthcare priorities have moved away from COVID-19

countries have signed on to participate. Industry representative, interview by USITC staff, May 25, 2023; industry representatives, interviews by USITC staff, South Africa, June 29 and June 30, 2023.

⁹¹² World Health Organization (WHO), "The Top 10 Causes of Death," December 9, 2020; government representative, interview by USITC staff, Zambia, June 21, 2023.

⁹¹³ Our World in Data, "COVID-19 Vaccination," accessed August 11, 2023.

⁹¹⁴ United Nations. "WHO chief declares end to COVID-19 as a global health emergency." UN News. May 5, 2023.

⁹¹⁵ Nonprofit representative, interview by USITC staff, Switzerland, June 9, 2023.

⁹¹⁶ Government representative, interview by USITC staff, Brazil, June 30, 2023.

⁹¹⁷ Industry representative, interview by USITC staff, Mexico, June 21, 2023.

⁹¹⁸ Government representative, interview by USITC staff, Zambia, June 21, 2023.

⁹¹⁹ Nonprofit organization representative, interview by USITC staff, South Africa, June 28, 2023.

towards other diseases is reflected in the Global Fund, the lead ACT-A procurement partner, recently reallocating over \$500 million of its remaining COVID-19 funds to other programs.⁹²⁰

Testing and Demand for Treatment

The demand for COVID-19 therapeutics is dependent on the availability of diagnostics tests and testing facilities. More specifically, most COVID-19 treatments are approved for use for patients that have tested positive for mild or moderate disease, have been diagnosed within a short window from the onset of symptoms, and are at high risk for hospitalization, owing to such factors as age, obesity, or underlying health conditions. In turn, for patients to test positive for COVID-19 and receive treatment, not only must tests be available at testing sites and results accurately reported, but also the population presenting with COVID-19 symptoms must seek care. The relationship between COVID-19 testing and demand for treatment is highly complex, involving supportive healthcare infrastructure, adequate funding, affordable products, and regulatory guidance, as well as the behavior and attitudes of patients in response to the disease. To address this complexity, so-called test-to-treat (also called test-and-treat) programs, designed to coordinate patient care so that treatment can begin quickly following an affirmative diagnosis, have been established in many countries.

A successful test-to-treat program was established in the United States. It offers services free of charge and is designed to initiate antiviral treatment within five days of the onset of symptoms, as this is the timeframe recommended for some COVID-19 therapeutics.⁹²¹ It established sites offering access to testing and oral antiviral treatment (or prescriptions for antivirals) that are conveniently located at a variety of institutions, such as pharmacy clinics, federally funded health centers, long-term care facilities, and other community sites. In addition to sites established under the U.S. COVID-19 test-to-treat program, those seeking COVID-19 testing and treatment may also visit traditional healthcare providers to receive these services.

Establishment of these programs, such as that in the United States, has largely been limited to HICs. As of 2023, there have been attempts to establish test-to-treat programs in LICs, LMICs, and UMICs.⁹²² However, LICs and LMICs have faced many challenges in establishing such programs, with success varying according to the public health circumstances of each country and the general epidemiology of COVID-19.⁹²³ For example, representatives of organizations such as Rethink Trade, Oxfam America, and the Initiative for Medicines, Access, and Knowledge are among those that cite insufficient supplies of affordable diagnostics and therapeutics (as discussed earlier in this chapter) as factors that hindered

⁹²⁰ International organization, interview by USITC staff, Switzerland, June 9, 2023.

⁹²¹ ASPR, “Fact Sheet: Federally-Supported Test to Treat Sites,” May 2022; Merck, posthearing brief submission to the USITC, May 5, 2023, 13.

⁹²² Test-to-treat programs in many countries were a lower priority. USITC, hearing transcript, March 29, 2023, 30 (Jennifer Reid, Oxfam America), 181 (Tahir Amin, Initiative for Medicines, Access & Knowledge), and 135 (Lori Wallach, Rethink Trade); Connor et al., “Access to COVID-19 Testing,” October 27, 2021.

⁹²³ For example, in countries where chronic conditions (such as diabetes) may be widely undiagnosed, a test-to-treat program may lower the age threshold for risk of severe COVID-19 from 65 to 50 years old, hoping to capture individuals with undiagnosed chronic pathologies. Public health organization representative, interview by USITC staff, August 25, 2023; multilateral organization representative, interview by USITC staff, August 8, 2023.

development of test-to-treat programs.⁹²⁴ Limitations in health system capacity also reportedly inhibited development of test-to-treat programs in LICs and LMICs.⁹²⁵ An external evaluation of ACT-A noted that diagnostics were often difficult to access and isolated from primary health care systems.⁹²⁶ ACT-A reported an “insufficient awareness among government officials, health workers, and communities” in many LICs and LMICs of the importance of test-to-treat programs.⁹²⁷ Additionally, healthcare workers experienced “pandemic fatigue” and had difficulty focusing on COVID-19 in the face of other health and humanitarian concerns.⁹²⁸

To assist LICs and LMICs in establishing test-to-treat programs, several NGOs and national governments have initiated substantial efforts to support test-to-treat efforts in LICs and LMICs. In 2021, ACT-A announced a \$50 million pilot program to support test-to-treat pilot initiatives in 22 countries.⁹²⁹ On May 12, 2022, the U.S. Agency for International Development (USAID) announced a test-to-treat program, and the COVID Treatment QuickStart Consortium (QuickStart) announced one on September 27, 2022.⁹³⁰ These organizations share broadly consistent goals that help define the scope of current test-to-treat efforts in LMICs: working with governments and communities to support the consistent availability of affordable COVID-19 testing, the availability of timely and affordable treatment for those most at risk of developing serious disease, and the identification and sharing of best practices.⁹³¹ These programs coordinate efforts, notably through a therapeutics coordination group that includes member organizations such as ACT-A and QuickStart as well as through USAID’s coordination with ACT-A

⁹²⁴ USITC, hearing transcript, March 29, 2023, 30 (Jennifer Reid, Oxfam America), 135 (Lori Wallach, Rethink Trade), 181 (Tahir Amin, Initiative for Medicines, Access & Knowledge); Connor et al., “Access to COVID-19 Testing,” October 27, 2021.

⁹²⁵ In many LICs and LMICs, the limited diagnostic infrastructure and shortage of qualified staff constrained PCR test capacity early in the response to COVID-19. In some rural settings, testing facilities can be distant and difficult to reach, increasing indirect costs, or even making treatment impractical to seek. Matahari Global, “Cost, Distance, and Complexity: Results from a Rapid Diagnostics Assessment in Rural and Semi-Rural Communities in Madagascar,” July 2023, 8.

⁹²⁶ This evaluation also identified low treatment availability as a “disincentive” to pursue testing, notably when a positive test resulted in restrictions on the patient’s activities due to lack of access to effective treatments. Open Consultants, “External Evaluation of ACT-A,” October 10, 2022, 57.

⁹²⁷ WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

⁹²⁸ UNICEF, “Access-to-COVID-19-Tools-Accelerator (ACT-A)-SitRep-No-4,” December 31, 2022, 7.

⁹²⁹ ACT-A lists its co-convening groups as: the Coalition for Epidemic Preparedness Initiatives (CEPI), FIND, Gavi, The Global Fund, UNICEF, Unitaid, Wellcome, WHO, the World Bank and The Bill & Melinda Gates Foundation. ACT-Accelerator, “About ACT-A,” accessed June 14, 2023; WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022, 29. In May 2022, ACT-A partners Unitaid, the Global Fund, and USAID expanded funding for test-to-treat programs with the commitment of an additional \$125 million. WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022, 30.

⁹³⁰ The USAID program is coordinated with The United States President’s Emergency Plan for AIDS Relief (commonly known as PEPFAR), other U.S. government programs, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria to procure oral antivirals and rapid tests. The USAID program works with Unitaid to support new treatments through Unitaid/FIND test-to-treat programs. USAID, “USAID Announces \$220 Million Test and Treat,” June 14, 2023. Implementing partners for the COVID Treatment QuickStart Consortium are Duke University, Americares, the Clinton Health Access Initiative (CHAI), and COVID Collaborative. The Open Society Foundations, Pfizer and the Conrad N. Hilton Foundation provide support. Partner countries include Ghana, Kenya, Laos, Malawi, Nigeria, Rwanda, South Africa, Uganda, Zambia, and Zimbabwe. Duke Global Health Innovation Center, “COVID Treatment QuickStart Consortium,” accessed June 14, 2023.

⁹³¹ WHO, “ACT-Accelerator Facilitation Council Working Group Report,” September 22, 2022.

co-convening groups Unitaid and FIND.⁹³² These three programs are pilot efforts and, therefore, working in a limited number of countries. It is unclear if funding is adequate to implement more global test-to-treat programs.⁹³³

Last Mile Delivery

For diagnostics and therapeutics, last mile delivery describes the logistics of delivering items to hospitals, clinics, or directly to patients in their homes.⁹³⁴ This stage involves the transportation of smaller aggregations of items to a variety of locations, usually from a supplier at a central warehouse where the items were originally delivered in bulk.⁹³⁵ Last mile delivery requires more coordination and is usually more time- and labor-intensive than earlier stages in the logistics chain because of the larger number of delivery locations over a wide geography.

In hearing testimony and written submissions, disagreement on the impacts of last mile delivery on access was significant. Opponents of the extension of the 2022 Ministerial Decision made general claims about challenges with last mile delivery, including claiming that non-IP issues, such as last mile delivery, are among the reasons for the lack of patient access to COVID-19-related diagnostics and therapeutics in developing countries.⁹³⁶ At the Commission's hearing, the Pharmaceutical Research and Manufacturers of America (PhRMA) stated that it is widely acknowledged that last mile delivery is a problem in developing countries.⁹³⁷ PhRMA also argued that although programs for treating HIV invested in last mile delivery, no similar effort has been made for the COVID-19 pandemic.⁹³⁸ In addition, citing a communication submitted to the WTO TRIPS Council, the Bayh-Dole Coalition stated in a written submission that logistics and distribution issues led to a surplus of COVID-19 diagnostic products.⁹³⁹

Supporters of extending the 2022 Ministerial Decision, however, stated that any last mile delivery challenges, to the extent they are a constraint on access, can be overcome and that pricing remains a key constraint. Hearing witnesses stated that developing countries have prior experience with infectious

⁹³² WHO, "ACT-Accelerator Facilitation Council Working Group Report," September 22, 2022. USAID, "USAID Announces Countries for Test-To-Treat," September 23, 2022. USAID, "USAID Announces \$220 Million Test and Treat," accessed June 14, 2023. Duke Global Health Innovation Center, "COVID Treatment QuickStart Consortium," accessed June 14, 2023. USAID, "USAID Announces \$220 Million Test and Treat," June 14, 2023.

⁹³³ USITC, hearing transcript, March 29, 2023, 104 and 149 (testimony of Peter Maybarduk, Public Citizen).

⁹³⁴ Dolan, "The Challenges of Last Mile Delivery Logistics," January 9, 2023; Onfleet, Inc., "Last Mile Delivery," January 21, 2023.

⁹³⁵ Industry representative, interview by USITC staff, March 7, 2023; AAM, "Generics and Biosimilars Industry Response to COVID-19," July 2, 2020.

⁹³⁶ AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 14; USITC, hearing transcript, March 29, 2023, 37 (testimony of Kevin Haninger, PhRMA); USITC, hearing transcript, March 30, 2023, 210 (testimony of Candace DeMatteis, PFID), 218 (testimony of Natalie Buford-Young, Springboard Enterprises); AFTE, prehearing brief submission to the USITC, March 12, 2023, 4; USTR, "Summary of Consultations," December 2022.

⁹³⁷ PhRMA additionally stated that challenges in last mile delivery can also extend to pills and specifically noted that challenges in delivering products to people in rural areas have led to products expiring before delivery. USITC, hearing transcript, March 29, 2023, 133–134 (testimony of Kevin Haninger, PhRMA); independent consultant, interview by USITC staff, March 10, 2023.

⁹³⁸ USITC, hearing transcript, March 29, 2023, 134 (testimony of Kevin Haninger, PhRMA).

⁹³⁹ Bayh-Dole Coalition, written submission to the USITC, April 25, 2023, 7; see also WTO TRIPS Council, "TRIPS Council Discussions on COVID-19 Therapeutics and Diagnostics: Evidence and Questions on Intellectual Property Challenges Experienced by Members," IP/C/W/693, November 1, 2022.

diseases, such as HIV/AIDS, hepatitis C, and Ebola, and have healthcare systems that can deliver diagnostics and therapeutics when prices and IP are not barriers.⁹⁴⁰ Multiple hearing witnesses also argued that, after countries have access to affordable diagnostics and therapeutics, where necessary, they would invest in last mile delivery.⁹⁴¹ Two government officials, one in the United States and one in Zambia, reported that last mile delivery and logistics did not hamper their efforts to distribute therapeutics.⁹⁴²

Last mile delivery tends to vary among countries by income level.⁹⁴³ It does not tend to be an issue in HICs, but in LICs, it can be more challenging, particularly for rural areas.⁹⁴⁴ In LICs, the transportation networks and cold chain storage required for some therapeutics may be inadequate.⁹⁴⁵ One study found that up to 20 percent of vaccination centers and healthcare facilities lacked refrigerators and a significant share of facilities had nonfunctional refrigerators.⁹⁴⁶ Also, logistical issues are more difficult in the poorest parts of countries and may inhibit the delivery of medical treatments.⁹⁴⁷ A review of literature covering “stock-outs” in community health centers (situations where an item was out of stock) in LICs and LMICs found that transportation delays from a district distribution point to a local health center was often listed as a reason an item was out of stock.⁹⁴⁸

For some diagnostics such as PCR tests, last mile delivery can be complicated because of the need to collect samples from patients and transport those samples to a lab for processing, which can delay the time between the onset of symptoms and the confirmation of diagnosis.⁹⁴⁹ A study of turnaround times for PCR tests in a group of 13 countries, which included LICs, LMICs, and UMICs, found that the time required to receive results varied significantly, ranging from 8–12 hours in urban Bangladesh to two weeks in rural parts of the Democratic Republic of the Congo.⁹⁵⁰ Many therapeutics are effective only when administered during the first few days of the illness, meaning that delays in diagnosis may cause patients to miss the opportunity for treatment.⁹⁵¹ Rapid antigen tests—which are inexpensive, simple to

⁹⁴⁰ USITC, hearing transcript, March 30, 2023, 62–64 (testimony of Yoke Ling Chee, TWN Berhad), 106–108 (testimony of Sanya Reid Smith, Social Watch), 215–216 (testimony of Mogha Kamal-Yanni, People’s Vaccine Alliance); see also, TWN, posthearing brief submission to the USITC, April 12, 2023, 7.

⁹⁴¹ USITC, hearing transcript, March 29, 2023, 135–136 (testimony of Lori Wallach, Rethink Trade); USITC, hearing transcript, March 30, 2023, 60–62 (testimony of Fatima Hassan, Health Justice Initiative), 72–73 (testimony of Rajnia Rodrigues, Development Alternatives with Women for a New Era), 108–109 (testimony of Gopakumar Madhavan, TWN TRUST).

⁹⁴² Government representative, interview by USITC staff, April 24, 2023; government representative, interview by USITC staff, Zambia, June 21, 2023.

⁹⁴³ Baumeister, Kauschke, and Tipping, “Convenience Is Key,” November 26, 2018.

⁹⁴⁴ Multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023; public health organization representative, interview by USITC staff, August 25, 2023.

⁹⁴⁵ Council for Innovation Promotion, posthearing brief submission to the USITC, April 10, 2023, 3; industry representative, interview by USITC staff, March 24, 2023.

⁹⁴⁶ Fleming, Okebukola, Skiba, “Port to Patient,” September 14, 2021.

⁹⁴⁷ Industry representative, interview by USITC staff, April 4, 2023.

⁹⁴⁸ Olaniran et al., “Stock-Outs of Essential Medicines,” July 15, 2022.

⁹⁴⁹ For examples of challenges with sample transportation for measuring viral load in patients receiving HIV/AIDS treatment, see Nichols et al., “Monitoring Viral Load for the Last Mile,” September 1, 2019.

⁹⁵⁰ Rahman et al., “Mapping COVID-19 Access Gaps,” August 25, 2022, 4. Turnaround time is defined as the time from collection of the sample to time of communication of results to the individual. The study included Bangladesh, Democratic Republic of the Congo, Haiti, Jamaica, Liberia, Madagascar, Nepal, Nigeria, Peru, Senegal, Somalia, Uganda, and Ukraine. See also, PSI, posthearing brief submission to the USITC, April 11, 2023, 2.

⁹⁵¹ Think tank representative, interview by USITC staff, March 1, 2023.

use, and can be performed at the point of care—can help overcome the cost and challenges associated with PCR tests.⁹⁵² Access to rapid antigen tests was not equitable across country income categories, with substantially lower adoption in low- and middle-income regions.⁹⁵³

Timely delivery and proper handling of COVID-19 therapeutics are necessary to ensure the safety, quality, and purity of the product. The delivery of injectables, which may need cold storage, faces some difficulty particularly for LICs that are more likely to lack cold chain storage.⁹⁵⁴ For COVID-19 vaccines, improper handling reportedly led to spoilage of donated doses, in some cases.⁹⁵⁵ The WHO guidelines for medicine donations state that donations of medicines just before expiry should be avoided because in most cases they will expire before delivery.⁹⁵⁶ The WHO recommends that donated medicines have a remaining shelf-life of at least one year.⁹⁵⁷ Zambia, as an example, requires that donated medicines have at least 80 percent of the original shelf life remaining.⁹⁵⁸

National governments, multilateral organizations, the private sector, and nonprofit organizations have worked to improve last mile delivery, including USAID’s Global Health Supply Chain program operating in multiple countries.⁹⁵⁹ The systems created by these efforts before and during the pandemic were often used to distribute COVID-19 diagnostics and therapeutics. In Zambia, the U.S. government funded the use of a private logistics provider to distribute vaccines, tests, and treatments (box 6.2).⁹⁶⁰ Another example is Project Last Mile, a collaboration between the Global Fund and Coca-Cola, which worked in 12 African countries to deliver medicines to 35 million people.⁹⁶¹ Ventilator manufacturers formed the Ventilator Training Alliance and developed an application (app) for mobile devices to enable frontline medical providers to access ventilator training.⁹⁶² Direct Relief, a nonprofit organization, has worked toward improving last mile delivery in LICs, particularly in improving the cold chain.⁹⁶³ Many of these

⁹⁵² Hannay, Fernández-Suárez, and Duneton, “COVID-19 Diagnostics: Preserving Manufacturing Capacity for Future Pandemics,” February 1, 2022, 1; FIND, written submission to the USITC, May 16, 2023, 4.

⁹⁵³ Budd et al., “Lateral Flow Test Engineering and Lessons Learned from COVID-19,” January 1, 2023, 17; FIND, written submission to the USITC, May 16, 2023, 4; nonprofit organization representative, interview by USITC staff, March 9, 2023. See also, Rahman et al., “Mapping COVID-19 Access Gaps,” August 25, 2022, 4, which found that eight countries studied had little or no access to rapid antigen test for COVID-19. The eight countries studied were LICs (Liberia, Somalia, and Uganda), LMICs (Bangladesh, Nepal, Nigeria, and Ukraine), and a UMIC (Peru).

⁹⁵⁴ USITC, hearing transcript, March 30, 2023, 107 (testimony of Sanya Reid Smith, Social Watch).

⁹⁵⁵ Multilateral organization representative, interview by USITC staff, Switzerland, June 13, 2023; government representative, interview by USITC staff, Zambia, June 21, 2023.

⁹⁵⁶ WHO, “Guidelines for Medicine Donations,” 2011, 10; independent consultant, interview by USITC staff, March 10, 2023.

⁹⁵⁷ WHO, “Guidelines for Medicine Donations,” 2011, 10.

⁹⁵⁸ Government representative, interview by USITC staff, Zambia, June 21, 2023.

⁹⁵⁹ USAID GHSC, “Last Mile Delivery to 320 PEPFAR-Supported Health Facilities,” January 7, 2022; Westley and Moro Martin, “Driving Last-Mile Solutions,” September 2022.

⁹⁶⁰ Government representative, interview by USITC staff, Zambia, June 21, 2023.

⁹⁶¹ World Economic Forum, “Project Last Mile,” May 23, 2022.

⁹⁶² Willden, “Ventilator Manufacturers Form Ventilator Training Alliance,” April 15, 2020.

⁹⁶³ Direct Relief, “Donations of Emergency Use Authorization Covid-19 Medical Products,” January 23, 2023; Direct Relief, “COVID-19 Relief,” accessed April 14, 2023; Hovey, “Strengthening Cold Chain Capacity in Nepal,” November 16, 2022.

projects predate the COVID-19 pandemic and helped create systems that continue to be used in response to COVID-19 and other health issues.⁹⁶⁴

Box 6.2 Last Mile Distribution in Zambia

Zambia is a low-income country in central southern Africa with a population of nearly 20 million people.^a The population relies on donations and imports to supply tests and treatments for its most prominent public health concerns, including HIV/AIDS, tuberculosis, malaria, and COVID-19.^b

In Zambia, the need for decentralized testing and organized delivery systems was a high priority during the COVID-19 pandemic. Storage and distribution are centralized in the Zambian Medicines and Medical Supplies Agency (ZAMMSA), a government organization based in the capital of Lusaka that stores all COVID-19-related donations.^c Because ZAMMSA stores and distributes COVID-19 tests and treatments, it can monitor the supply of COVID-19 commodities that enter the country.^d

In order to decentralize testing and organize delivery systems, Zambia uses provincial medical hubs that distribute supplies to smaller medical centers throughout each of its 10 provinces.^e Each provincial hub receives information on vaccine, testing, and treatment needs from local clinics and sends the data to ZAMMSA.^f ZAMMSA then distributes medical supplies to provincial hubs every two to three months, using a fleet of vehicles.^g The Centers for Disease Control and Prevention (CDC) and USAID play active roles in addressing distribution challenges.^h In 2021, when vehicles supplied by ZAMMSA occasionally broke down and caused a delivery backlogs, the CDC and USAID assisted ZAMMSA by procuring and supplying a third-party logistics company to deliver medical supplies to provincial hubs; this service remains in use today.ⁱ

^a This report uses the World Bank Group's country classification by income level from 2022. Zambia was reclassified as a lower-middle-income country in 2023. ZamStats, "2022 Census," August 2, 2023.

^b Government representative, interview by USITC staff, Zambia, June 21, 2023.

^c Government of Zambia, National Assembly of Zambia, "The Zambia Medicines and Medical Supplies Agency Act," 2019.

^d Government representative, interview by USITC staff, Zambia, June 21, 2023.

^e Government representative, interview by USITC staff, Zambia, June 21, 2023.

^f Government representative, interview by USITC staff, Zambia, June 21, 2023.

^g Government representative, interview by USITC staff, Zambia, June 21, 2023; public health organization representative, interview by USITC staff, Zambia, June 22, 2023.

^h Government representative, interview by USITC staff, Zambia, June 21, 2023.

ⁱ Government representative, interview by USITC staff, Zambia, June 21, 2023.

Other Factors Reported

Other factors that may have affected the availability of COVID-19 diagnostics and therapeutics in certain situations were mentioned during the investigation. For example, trade barriers, such as tariffs, export restrictions, and bottlenecks in customs and border inspections, were reported to impede access to COVID-19 medicines.⁹⁶⁵ For example, in April 2021, when a sharp rise in COVID-19 cases sent demand

⁹⁶⁴ Nonprofit organization representative, interview by USITC staff, Switzerland, June 7, 2023; USITC, hearing transcript, March 29, 2023, 139–140 (testimony of Ashley Miller, AdvaMed); USITC, hearing transcript, March 30, 2023, 62–64 (testimony of Yoke Ling Chee, TWN Berhad), 106–108 (testimony of Sanya Reid Smith, Social Watch), 215–216 (testimony of Mogha Kamal-Yanni, People's Vaccine Alliance).

⁹⁶⁵ Industry representative, interview by USITC staff, Switzerland, June 5, 2023. Note that the tariffs specifically cited during the hearing were on inputs for vaccines. USITC, hearing transcript, March 30, 2023, 298 (testimony of Mark L. Busch), 347 (testimony Stephen Ezell, ITIF).

surging, the government of India imposed by export ban on remdesivir and its API in response.⁹⁶⁶ In addition to finished pharmaceutical products, exports of APIs were restricted in certain countries that had access to the necessary IP and technical capacity.⁹⁶⁷ It was also reported that materials required for testing and approvals also need to move through customs, which can potentially present additional barriers to final access.⁹⁶⁸

The Center for Global Development identified several challenges that may help explain the low demand for oral antiviral treatments in MICs and LICs. Among these factors are limited data on the clinical efficacy against dominant variants and a lack of economic data on cost-effectiveness that may have contributed to low demand by LICs and MICs. For example, the Center notes that the data for nirmatrelvir (+ ritonavir) are available only from HICs in clinical trials performed before the Omicron variant emerged in November 2021.⁹⁶⁹ According to one study, efficacy data are available only for at-risk unvaccinated people who received treatment within five days of showing symptoms.⁹⁷⁰ For LICs and MICs, these data may not provide useful information on how the drug may perform against the Omicron variant, in settings where medication may not be received within the five-day window of opportunity and where the population may have some existing immunity as a result of vaccinations or prior infection.⁹⁷¹ The Center notes that data on COVID-19 testing are limited. Overall, there is little evidence available to policymakers in LICs and MICs to assess the relative costs and health benefits associated with purchasing antiviral treatments as a response to COVID-19.⁹⁷² Other analysis by the Center suggests that expenditures on COVID-19 therapeutics may not provide good value for money, given other health care priorities.⁹⁷³

Another factor that has been noted to impact the demand for antivirals currently available relates to medical scenarios that render the use of certain products inadvisable, excluding some patients from treatment.⁹⁷⁴ For example, nirmatrelvir (+ ritonavir) should not be used when patients take a number of common drugs, and molnupiravir is not recommended for pregnant or breastfeeding patients.⁹⁷⁵ Because some common medications for non-COVID-19 ailments must be suspended during treatment for COVID-19 and reinitiated after treatment is complete, patients might be less inclined to take COVID-19 treatments.

⁹⁶⁶ Reuters, “India Bans Exports of Anti-Viral Drug Remdesivir as COVID-19 Cases Surge,” April 11, 2021.

⁹⁶⁷ Foreign government official, interview by USITC staff, Brazil, June 26, 2023.

⁹⁶⁸ International organization, interview by USITC staff, Switzerland, June 8, 2023.

⁹⁶⁹ Keller, Kaufman, and Guzman, “Oral Antiviral Treatments for COVID-19: Time to Revisit?,” December 2022.

⁹⁷⁰ Reis et al., “Is the Combination Nirmatrelvir plus Ritonavir Effective for Treating or Preventing COVID-19?,” September 20, 2022.

⁹⁷¹ Reis et al., “Is the Combination Nirmatrelvir plus Ritonavir Effective for Treating or Preventing COVID-19?,” September 20, 2022.

⁹⁷² The Health Economics Program at the Africa Centres for Disease Control and Prevention (Africa CDC), in collaboration with the International Decision Support Initiative and the Center for Global Development, is undertaking a project on the cost-effectiveness of COVID-19 oral antivirals. Bristol, “Africa CDC Models Data to Aid Oral Antiviral Roll Out Decisions in Africa,” October 13, 2022.

⁹⁷³ Regan et al., “Do COVID-19 Oral Antivirals Represent Good Value for Money for African Countries?,” December 14, 2022.

⁹⁷⁴ Keller, Kaufman, and Guzman, “Oral Antiviral Treatments for COVID-19: Time to Revisit?,” December 2022.

⁹⁷⁵ Raglow, et al., “Outpatient Treatment for Covid-19,” August 16, 2023; NIH, “Pregnancy, Lactation, and Covid-19 Therapeutics,” April 20, 2023.

Finally, as with any new treatment, lack of awareness of the products in some communities also has an impact on demand (i.e., demand cannot exist without at least medical professionals having knowledge of the products). A report by the global health consulting firm Matahari Group Solutions surveyed 14 LICs and found that many doctors in rural communities had not heard of the existence of novel antivirals as possible treatment for COVID-19.⁹⁷⁶ Moreover, if the potential recipients are not aware of the existence of COVID-19 antivirals, they will not know to request them. In May 2022, a survey of New York City residents with COVID-19 found that 55.9 percent were not aware of nirmatrelvir (+ ritonavir).⁹⁷⁷

⁹⁷⁶ Matahari Global Solutions, “Mapping Access Gaps in COVID-19: Results from 14 Countries and Territories,” August 2022.

⁹⁷⁷ Qasmieh, et al., “The Prevalence of SARS-CoV-2,” June 30, 2023.

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Chapter 7

Views of Interested Persons

Introduction

In her request letter, the U.S. Trade Representative stated that public input would be particularly salient for eight topics listed in the letter. This chapter summarizes public input provided at the U.S. International Trade Commission’s (Commission’s) March 29–30, 2023 hearing and through written submissions on these eight topics. The hearing included testimony from 56 participants. The Commission also received 145 prehearing briefs, 22 posthearing briefs, and 168 other written submissions. In total, 195 individuals and organizations submitted documents to the Commission for this investigation.

The summaries of public views provided in this chapter do not attempt to assess, analyze, or draw conclusions about these views.⁹⁷⁸ In addition, this chapter often uses language as provided by participants to avoid changing the meaning of their submitted views. Therefore, some wording used in this chapter may not match wording used in other chapters of this report.⁹⁷⁹ ⁹⁸⁰ Also, the coverage of the topics addressed by the views ranges from narrower discussions of COVID-19-related diagnostics and therapeutics to broader discussions of the pharmaceutical and diagnostics industries. Although the views presented are attributed to many organizations—and given the volume of submissions and because many of the views were similar in nature—this chapter does not include references to each individual submission or participant who expressed views on each of the eight topics. Some participants provided 500-word summaries of their submissions. These summaries, which are presented in appendix D, may contain information about the eight topics addressed in this chapter.⁹⁸¹ In addition,

⁹⁷⁸ This chapter consists of information compiled by the USITC to address the topics for which the U.S. Trade Representative stated that public input would be particularly salient. Appendix D contains unedited versions of the optional 500-word written summaries provided on the record by some participants in this investigation.

⁹⁷⁹ Some examples of retaining wording as provided by participants include (1) Country income-level categories are listed in this chapter as they were provided in the submissions. For example, an acronym such as “LIC” may be used elsewhere in the report to refer to a low-income country, but this chapter will spell out “low-income country” if that is the language used by the participant because definitions for those terms were not provided in the submissions. (2) Participants used varying language to refer to the action being considered by the WTO. For example, some participants referred to this action as an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics, but others referred to it as a waiver of intellectual property (IP) rights or a TRIPS Agreement waiver. This chapter retains the participants’ language to refer to the action being considered by the WTO. (3) Specific comments on “costs” have not been evaluated by the USITC against a common definition and therefore references to costs in the text are only within the context provided by the witnesses or submissions. Therefore, all discussions of costs and cost estimates provided by witnesses may not be directly comparable. (4) The concept of demand as used by participants in this chapter may not be consistent with the methods for measuring demand in chapter 6 or other chapters of this report.

⁹⁸⁰ Organizations and individuals are generally described as they describe themselves; no attempt is made to describe them further, e.g., with respect to affiliations or external financial support.

⁹⁸¹ All submissions and summaries are also available on the USITC Electronic Document Information System (EDIS) at <https://edis.usitc.gov/external/>.

some of the views provided in this chapter have been discussed in other sections of this report where relevant.

To keep related information together, the eight topics listed in the request letter are organized into three sections: (1) intellectual property (IP) protection, research and development (R&D), and jobs; (2) the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and access to medicine; and (3) the TRIPS Agreement and COVID-19 diagnostics and therapeutics. The eight topics listed in the request letter are shown below, divided into the three sections.

IP protection, R&D, and jobs

- The relationship between IP protection and corporate R&D expenditures, taking into account other expenditures, such as share buybacks, dividends, and marketing
- The location of jobs associated with the manufacturing of diagnostics and therapeutics, including in the United States

The TRIPS Agreement and access to medicine

- Whether and how existing TRIPS rules and flexibilities can be deployed to improve access to medicines
- Successes and challenges in using existing TRIPS flexibilities
- To what extent further clarifications of existing TRIPS flexibilities would be useful in improving access to medicines

The TRIPS Agreement and COVID-19 diagnostics and therapeutics

- How the TRIPS Agreement promotes innovation in and/or limits access to COVID-19 diagnostics and therapeutics
- The extent to which products not yet on the market, or new uses for existing products, could be affected by an extension of the Ministerial Decision to COVID-19 diagnostics and therapeutics
- The relevance, if any, of the fact that diagnostic and therapeutic products used with respect to COVID-19 may also have application to other diseases

Intellectual Property Protection, R&D, and Jobs

The Relationship between Intellectual Property Protection and Corporate R&D Expenditures, Taking into Account Other Expenditures, such as Share Buybacks, Dividends, and Marketing

Some participants noted the necessity of IP protections for the development of new products and the repurposing of existing products, R&D partnerships, and R&D to prepare for future public health crises. These participants stated that IP protections are necessary to incentivize corporate R&D expenditures,

including investments that made possible the development of COVID-19 diagnostics and therapeutics.⁹⁸² In addition, it was stated that through the global IP system and patents, companies are afforded a period of market exclusivity, providing companies the opportunity to earn returns on investments and cover the cost of R&D expenditures.⁹⁸³

Some participants stated that IP protections were particularly important to attracting investment for R&D in industry sectors that are high risk and capital intensive, such as the diagnostics and therapeutics industries.⁹⁸⁴ Development of a new drug was reported to take about 10 to 15 years,⁹⁸⁵ with about 90 percent of medicines in development never receiving U.S. Food and Drug Administration (FDA) approval.⁹⁸⁶ The Advanced Medical Technology Association (AdvaMed), a trade association of medical technology companies, stated that R&D for a molecular testing platform can take five to seven years or more.⁹⁸⁷ The cost to develop an FDA-approved drug was said to require investments of \$2.0–3.0 billion to cover costs, including R&D, clinical trials, and regulatory approval.⁹⁸⁸ The Pacific Research Institute for Public Policy, a think tank, stated that IP protections are particularly important for the pharmaceutical industry, which it claims spends more than 25 percent of its revenues on R&D.⁹⁸⁹ Novartis AG (Novartis), a healthcare company based in Switzerland, quoted a study that found only 2 of every 10 new medicines see revenues that equal or exceed R&D costs.⁹⁹⁰

Multiple pharmaceutical companies discussed how IP protections enabled investments that resulted in the production of COVID-19 therapeutics. Anu Osinusi of Gilead Sciences, Inc. (Gilead), a biopharmaceutical company, testified about the unique challenges of investing in therapeutics for future pandemics. Osinusi added that very few companies work on the development of medicines for viral threats because the viral threat may never turn into a public health pandemic and, for such high-risk investments, IP protections are what drive R&D.⁹⁹¹ In its prehearing brief, Gilead stated that the TRIPS Agreement establishes global minimum IP standards that allow companies to make risky, long-term R&D investments, and that the global IP system allowed the company to make the investments that resulted in the production of remdesivir.⁹⁹² Pfizer Inc. (Pfizer), a biopharmaceutical company, stated that the

⁹⁸² For example, see USITC, hearing transcript, March 29, 2023, 18–19 (testimony of Joshua Teitelbaum, AFTE); USITC, hearing transcript, March 30, 2023, 178–180 (testimony of Adam Mossoff); AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 4–5.

⁹⁸³ Gilead, prehearing brief submission to the USITC, March 17, 2023, 7–8; C4IP, written submission to the USITC, April 26, 2023, 5, 9; 60 Plus Association, written submission to the USITC, May 1, 2023, 3.

⁹⁸⁴ For example, see EFPIA, written submission to the USITC, May 4, 2023, 1–2; USITC, hearing transcript, March 29, 2023, 190–191 (testimony of Gregg Szabo, Merck); U.S. Chamber of Commerce, written submission to the USITC, May 5, 2023, 5.

⁹⁸⁵ EFPIA, written submission to the USITC, May 4, 2023, 1; Novartis, written submission to the USITC, May 5, 2023, 5.

⁹⁸⁶ USITC, hearing transcript, March 29, 2023, 255 (testimony of Anu Osinusi, Gilead); USITC, hearing transcript, March 30, 2023, 183 (testimony of Peter J. Pitts, CMPI), 301 (testimony of Andrew Spiegel, Global Colon Cancer Association).

⁹⁸⁷ AdvaMed, prehearing brief submission to the USITC, March 17, 2023, 5.

⁹⁸⁸ USITC, hearing transcript, March 29, 2023, 24 (testimony of John Murphy, BIO); Parrish, written submission to the USITC, April 24, 2023, 3; PRI, written submission to the USITC, May 2, 2023, 3.

⁹⁸⁹ PRI, written submission to the USITC, May 2, 2023, 3–4.

⁹⁹⁰ Novartis, written submission to the USITC, May 5, 2023, 5.

⁹⁹¹ USITC, hearing transcript, March 29, 2023, 250–251 (testimony of Anu Osinusi, Gilead).

⁹⁹² Gilead, prehearing brief submission to the USITC, March 17, 2023, 3–8.

global IP system enabled the long-term risk-taking, collaboration, and investments necessary to develop Paxlovid, a combination of nirmatrelvir (+ ritonavir) tablets.⁹⁹³

Investments in R&D also apply to repurposing of existing drugs for new uses. In a research paper submitted to the Commission, the Geneva Network, a research and advocacy organization based in the United Kingdom, stated that differing industry participation rates in drug repurposing trials for COVID-19 uses could be explained by IP protections. According to data cited by the Geneva Network, private companies had greater participation rates in drug repurposing trials for COVID-19 uses involving patented drugs and repurposing studies for drugs without patent protections were mainly conducted by academia. The Geneva Network theorized that private companies participated at a lower rate in the repurposing of drugs without patent protections because of the difficulties in covering the cost of R&D for repurposing drugs that faced generic competition.⁹⁹⁴

According to some participants, IP protections such as those ensured by the TRIPS Agreement also enable R&D partnerships. Patrick Kilbride of the U.S. Chamber of Commerce, an organization that advocates for American businesses, stated that IP protections clarify each partner's initial contribution to a collaboration, thus enabling various organizations conducting biotechnology R&D, such as governments, universities, small businesses, large companies, and investors, to work together.⁹⁹⁵ Novartis stated that IP protections distinguish the IP each organization brings into a partnership from the IP created within the partnership and determine how each partner's IP can be used. This gives companies like Novartis the confidence to enter partnerships, knowing that their proprietary assets are secure.⁹⁹⁶

Gregg Szabo of Merck & Co., Inc. (Merck), a biopharmaceutical company, testified that partnerships enabled by IP protections led to the development of the COVID-19 therapeutic molnupiravir. Szabo described how Ridgeback Biotherapeutics first received a license for research done by Emory University, which led to Ridgeback Biotherapeutics partnering with Merck for the development and eventual production of molnupiravir.⁹⁹⁷ The Association of American Universities, an organization of 65 U.S. and Canadian public and private research universities, and the Bayh-Dole Coalition, an organization dedicated to protecting the Bayh-Dole Act of 1980, each contended that private companies would not invest to develop and commercialize discoveries made during underlying research at universities if the IP rights were not secure.⁹⁹⁸

⁹⁹³ Pfizer, written submission to the USITC, May 5, 2023, 3.

⁹⁹⁴ The Geneva Network cites the study Greenblatt, Gupta, and Kao, "Drug Repurposing During The COVID-19 Pandemic: Lessons for Expediting Drug Development and Access," March 2023, which states that for drugs with generic competition, academia conducted 126 repurposing trials for COVID-19 uses, compared with 35 conducted by private companies (with an additional 12 trials that were partnerships with industry and government). In repurposing trials for COVID-19 uses of patented drugs, private companies participated in 34 of 65 trials (19 alone, 13 in partnership with academia, and 2 in partnership with government). Geneva Network, written submission to the USITC, April 25, 2023, 8–9.

⁹⁹⁵ USITC, hearing transcript, March 29, 2023, 53–54 (testimony of Patrick Kilbride, U.S. Chamber of Commerce).

⁹⁹⁶ Novartis, written submission to the USITC, May 5, 2023, 13.

⁹⁹⁷ USITC, hearing transcript, March 29, 2023, 256–257 (testimony of Gregg Szabo, Merck).

⁹⁹⁸ AAU, written submission to the USITC, May 5, 2023, 1; Bayh-Dole Coalition, written submission to the USITC, April 25, 2023, 4–6.

Some participants also asserted that expanding a TRIPS Agreement waiver to or weakening IP protections on COVID-19 diagnostics and therapeutics could impede the response to any future public health crisis by reducing investment in the R&D of new diagnostics and therapeutics.⁹⁹⁹ The European Federation of Pharmaceutical Industries and Associations (EFPIA), an association based in Brussels that represents the biopharmaceutical industry operating in Europe, noted that successful COVID-19 therapeutics were based on platform technologies developed before the pandemic began. The EFPIA also contended that long-term IP protections in the United States and the EU allowed for the R&D that achieved those innovations.¹⁰⁰⁰

It was noted that IP protections were particularly important for investment in R&D at SMEs. The Biotechnology Innovation Organization, a biotechnology industry trade association, stated that a waiver of IP rights would particularly disrupt investment and research at such enterprises, which accounted for more than 50 percent of COVID-19 R&D programs globally and 87 percent in the United States.¹⁰⁰¹ Eli Lilly and Company (Lilly), a biopharmaceutical company, stated that, although waivers of IP rights could make it difficult for well-funded and diversified companies like Lilly to make investments, small companies may choose not to invest in innovation if they fear they could lose IP protections on successful products.¹⁰⁰²

Other participants asserted that extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would not have a substantial effect on corporate R&D expenditures. Brook K. Baker of Health GAP, an international organization that advocates for access to HIV treatment, care, and prevention, testified that more than 87 percent of branded pharmaceutical sales are made in developed-country markets where the extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would not apply. Baker stated that pharmaceutical companies would continue to have the same incentives to develop therapeutics to sell in their primary markets in developed countries.¹⁰⁰³

Sarah Gabriele, a Master of Bioethics candidate at Harvard Medical School, stated that IP protections contained in the TRIPS Agreement are not incentivizing R&D for pharmaceuticals mostly needed in low- and middle-income countries. The burden of incentivizing innovations is shared by all countries because all countries are required to have patents. Although all countries share this burden, the benefits of innovations are often realized by only wealthier countries that can afford them. In addition, Gabriele noted that the distribution of the benefits of R&D innovations is further imbalanced because some therapeutics are tested in some countries where those same drugs are not made available after they are approved.¹⁰⁰⁴

Some information was provided by participants about the effect of other expenditures, such as share buybacks, dividends, and marketing on R&D expenditures. Sanya Reid Smith of Social Watch, an

⁹⁹⁹ For example, see Novartis, written submission to the USITC, May 5, 2023, 10–11, 16–17; USITC, hearing transcript, March 29, 2023, 324–325 (testimony of Stephen Ezell, ITIF), 190–191 (testimony of Gregg Szabo, Merck); LES, written submission to the USITC, May 1, 2023, 4–5.

¹⁰⁰⁰ EFPIA, written submission to the USITC, May 4, 2023, 2.

¹⁰⁰¹ BIO, written submission to the USITC, May 5, 2023, 1–2.

¹⁰⁰² Lilly, prehearing brief submission to the USITC, March 17, 2023, 3–4.

¹⁰⁰³ USITC, hearing transcript, March 29, 2023, 286–287 (testimony of Brook K. Baker, Health GAP).

¹⁰⁰⁴ Gabriele, written submission to the USITC, May 5, 2023, 4.

international network of citizens’ organizations based in Uruguay, stated that a U.S. Senate committee found that the pharmaceutical industry inflates its R&D costs by including the costs of administration and marketing.¹⁰⁰⁵ Rethink Trade, a program of the American Economic Liberties Project, a nonprofit research and advocacy organization, asserted that limited pharmaceutical profits go into R&D relative to the portion used for dividends and share buybacks.¹⁰⁰⁶ In contrast, Merck stated that it prioritizes investments in its business and pipeline of products. This includes investing in R&D, launching new products, and expanding manufacturing capacity. Merck also stated that share repurchases do not affect how it prices its medicines.¹⁰⁰⁷ Novartis stated that other expenditures such as share buybacks, dividends, and marketing are normal for publicly traded companies and did not agree that they impact or are relevant to the relationship between IP rights and R&D investment. Novartis asserted that the relationship between IP rights and R&D investment should be assessed comparatively to “other IP-intensive and knowledge-based industries.”¹⁰⁰⁸

The Location of Jobs Associated with the Manufacturing of Diagnostics and Therapeutics, including in the United States

This section contains information provided by participants on the location of jobs associated with the manufacturing of diagnostics and therapeutics. It is not a comprehensive collection but rather a summary of public information provided on the record for this investigation.

Reported employment figures vary and often include jobs not directly related to the manufacturing of diagnostics and therapeutics. For example, AdvaMed noted that employment data for the diagnostics industry are often reported at the company level and are difficult to disaggregate by business units (e.g., at the COVID-19 product level).¹⁰⁰⁹ Also, terminology and industry categories used by participants were not always consistent. For example, participants used “pharmaceutical industry,” “biopharmaceutical industry,” “biotechnology industry,” “life sciences industry,” and so on, but did not provide definitions for these terms.

The information below is reported using the participants’ own language and does not attempt to interpret the information submitted. Furthermore, discussion in this section of global production facilities is used as an indicator of employment when employment figures were not provided.

Global Jobs

Diagnostics and therapeutics production sites outside the United States were discussed by participants, but country-specific employment figures were not usually provided. The countries where participants noted production sites or production capacity for therapeutics (not including diagnostics), implying production-related employment, were Argentina, Bangladesh, Brazil, Canada, China, Denmark, Egypt, France, Germany, Hungary, India, Indonesia, Ireland, Italy, Japan, Kenya, Malaysia, Mexico, Pakistan,

¹⁰⁰⁵ USITC, hearing transcript, March 30, 2023, 113 (testimony of Sanya Reid Smith, Social Watch).

¹⁰⁰⁶ Rethink Trade, written submission to the USITC, May 5, 2023, 5.

¹⁰⁰⁷ Merck, written submission to the USITC, May 5, 2023, A-6.

¹⁰⁰⁸ Novartis, written submission to the USITC, May 5, 2023, 5.

¹⁰⁰⁹ AdvaMed, posthearing brief submission to the USITC, April 12, 2023, 1.

Paraguay, Portugal, Russia, Singapore, South Africa, and Thailand. The information submitted about jobs in each of these countries is provided below.

Jamie Love of Knowledge Economy International (KEI), a nonprofit research organization, testified that Canada and Europe had capacity to produce therapeutics.¹⁰¹⁰ Verband Forschender Arzneimittelhersteller e.V. (VFA), a trade association of the research-based biopharmaceutical industry in Germany, stated that it represents 46 international pharmaceutical companies that, together, have close to 100,000 employees in Germany alone. This includes VFA members with approved therapeutics for the treatment of COVID-19.¹⁰¹¹ The Japan Pharmaceutical Manufacturers Association, an association of pharmaceutical companies in Japan, noted that it is composed of 72 R&D-oriented pharmaceutical companies.¹⁰¹² Giorgio Franyuti of Medical IMPACT, a nonprofit organization based in Mexico, testified that Mexico has experience in producing viral therapeutics.¹⁰¹³

The Information Technology and Innovation Foundation stated that, through voluntary licenses (VLs) alone, more than 200 production sites for COVID-19 treatments were established in more than 30 countries, including Bangladesh, Brazil, Egypt, India, Indonesia, Kenya, Pakistan, Paraguay, Singapore, and South Africa.¹⁰¹⁴ Kevin Haninger of Pharmaceutical Research and Manufacturers of America (PhRMA) testified that more than 140 manufacturing partnerships for COVID-19 treatments spanned more than 30 countries, including Brazil, India, Indonesia, Kenya, Singapore, and South Africa.¹⁰¹⁵ Gilead stated that it had formed manufacturing partnerships for remdesivir in China, Denmark, France, Germany, Hungary, Ireland, Italy, Japan, and Portugal.¹⁰¹⁶

Sanya Reid Smith of Social Watch testified that generic therapeutic manufacturing capacity exists in Argentina, Brazil, other Latin American countries, India, Indonesia, South Africa, and Thailand.¹⁰¹⁷ Karina Yong of the Consumers' Association of Penang, a nonprofit organization based in Malaysia, testified that Malaysia has some generic therapeutic manufacturing capacity.¹⁰¹⁸ Médecins Sans Frontières (Doctors Without Borders) (MSF), a nonprofit organization based in Switzerland, noted that Hungary and Russia issued compulsory licenses (CLs) for domestic production of COVID-19 therapeutics.¹⁰¹⁹

Ashley Miller of AdvaMed testified that China and India have significant production capacity for diagnostics.¹⁰²⁰ The Foundation for Innovative New Diagnostics (FIND), a nonprofit organization based in Switzerland, noted that production of diagnostics primarily takes place in high-income countries, with the United States being the leading manufacturer, followed by Europe and the Asia-Pacific region.¹⁰²¹ In its posthearing brief submission, the People's Vaccine Alliance (PVA), a coalition of more than 100

¹⁰¹⁰ USITC, hearing transcript, March 29, 2023, 153 (testimony of James Love, KEI).

¹⁰¹¹ VFA, written submission to the USITC, May 5, 2023, 1–2.

¹⁰¹² JPMA, written submission to the USITC, May 5, 2023, 1.

¹⁰¹³ USITC, hearing transcript, March 30, 2023, 338 (testimony of Giorgio Franyuti, Medical IMPACT).

¹⁰¹⁴ ITIF, prehearing brief submission to the USITC, March 17, 2023, 8. See chapter 5 for a discussion of voluntary licenses.

¹⁰¹⁵ USITC, hearing transcript, March 29, 2023, 35 (testimony of Kevin Haninger, PhRMA).

¹⁰¹⁶ Gilead, prehearing brief submission to the USITC, March 17, 2023, Exhibit B.

¹⁰¹⁷ USITC, hearing transcript, March 30, 2023, 88 (testimony of Sanya Reid Smith, Social Watch).

¹⁰¹⁸ USITC, hearing transcript, March 30, 2023, 19 (testimony of Karina Yong, CAP).

¹⁰¹⁹ MSF, written submission to the USITC, May 17, 2023, 6.

¹⁰²⁰ USITC, hearing transcript, March 29, 2023, 154 (testimony of Ashley Miller, AdvaMed).

¹⁰²¹ FIND, written submission to the USITC, May 16, 2023, 4.

organizations and networks focusing on equitable access to medical technologies that help to prevent and respond to COVID-19 and future pandemics, provided an MSF report that identified diagnostic manufacturing capacity in Argentina, Brazil, Kenya, Morocco, Peru, Senegal, South Africa, and Uganda.¹⁰²²

Jobs in the United States

Some participants asserted that the diagnostics and therapeutics industries (which include but are not limited to COVID-19 diagnostics and therapeutics) provide a significant number of jobs in the United States.¹⁰²³ Kevin Haninger of PhRMA, a biopharmaceutical trade association, testified that the biopharmaceutical industry is one of the top five manufacturing employers in the United States and that PhRMA members directly employ 900,000 people in the United States.¹⁰²⁴ The Information Technology and Innovation Foundation, a think tank, cited Bureau of Labor Statistics data showing that the U.S. pharmaceutical industry directly employs 314,000 people in the United States.¹⁰²⁵ The Biotechnology Innovation Organization stated that its members directly employ 2.14 million people in the United States in early-stage startup biotech firms, pre-commercial SMEs, and larger multinational biotechnology companies.¹⁰²⁶ The Business Council of New York State, an association representing businesses in the state of New York, maintained that the U.S. biotechnology industry supports almost 1.7 million jobs in the United States.¹⁰²⁷ AdvaMed stated that the medical technology industry directly supports 400,000 jobs in the United States at more than 15,000 facilities throughout all 50 states.¹⁰²⁸

Two pharmaceutical companies provided information on their employment figures. Pfizer stated that it has nearly 10,000 U.S. employees at 11 manufacturing and distribution sites in Kansas, Massachusetts, Michigan, New York, North Carolina, Ohio, Tennessee, and Wisconsin.¹⁰²⁹ Gilead noted that it employs 17,000 people worldwide, with more than 60 percent (>10,200 people) of its workforce located in the United States and more than 60 percent of its workforce engaged in manufacturing and R&D activities.¹⁰³⁰ The Association of the British Pharmaceutical Industry, an association representing the biopharmaceutical industry based in the United Kingdom, stated that the pharmaceutical company GSK (formerly GlaxoSmithKline), biopharmaceutical company based in the United Kingdom, employs about 15,000 people in the United States across commercial, R&D, manufacturing, and corporate functions. In addition, the association stated that AstraZeneca, a biopharmaceutical company based in the United Kingdom, employs 16,700 people with R&D, manufacturing, and commercial locations in 12 U.S. states.¹⁰³¹

¹⁰²² PVA, posthearing brief submission to the USITC, April 12, 2023, 4.

¹⁰²³ For data related to U.S. jobs in the pharmaceuticals sector based on North American Industry Classification System (NAICS) see appendix I.

¹⁰²⁴ USITC, hearing transcript, March 29, 2023, 33, 56 (testimony of Kevin Haninger, PhRMA).

¹⁰²⁵ ITIF, prehearing brief submission to the USITC, March 17, 2023, 19.

¹⁰²⁶ BIO, written submission to the USITC, May 5, 2023, 2.

¹⁰²⁷ The Business Council of New York State, written submission to the USITC, April 27, 2023, 1.

¹⁰²⁸ AdvaMed, posthearing brief submission to the USITC, April 12, 2023, 1.

¹⁰²⁹ Pfizer, written submission to the USITC, May 5, 2023, 2–3.

¹⁰³⁰ Gilead, prehearing brief submission to the USITC, March 17, 2023, 15.

¹⁰³¹ ABPI, written submission to the USITC, May 17, 2023, 5.

Several participants stated that the diagnostics and therapeutics industries also create a significant amount of indirect employment in the United States. The Biotechnology Innovation Organization asserted that each job in the biopharmaceutical industry supports an additional 3.92 jobs indirectly and that its member companies indirectly support 10.3 million jobs.¹⁰³² Howard Dean, a former governor of Vermont, stated that the biopharmaceutical industry indirectly supports 3.5 million jobs.¹⁰³³ AdvaMed stated that the medical technology industry supports about 2 million direct and indirect jobs.¹⁰³⁴

Some information was provided about the location of jobs at the state level. According to the Biotechnology Innovation Organization, in 2020, 40 states had five or more facilities manufacturing FDA-approved medicines, led by New Jersey (180 facilities), California (174), and Pennsylvania (104).¹⁰³⁵ Debbie Hart of BioNJ, the life sciences trade association of New Jersey, testified that 3,200 life sciences establishments are located in New Jersey, which has 8 of the top 10 biopharmaceutical companies, 12 of the top 20 medical device companies, and 9 of the top 10 R&D organizations with a presence in the state.¹⁰³⁶

The Maryland Public Policy Institute, a policy research organization in Maryland, stated that Maryland has 2,700 life sciences businesses and the life sciences industry directly employs 28,000 people and indirectly supports more than 100,000 jobs.¹⁰³⁷ The Massachusetts Biotechnology Council, a representative of the life sciences industry in Massachusetts, stated that during the pandemic, more than 80 Massachusetts life sciences companies worked to develop COVID-19 diagnostics, therapeutics, and vaccines.¹⁰³⁸ The Associated Industries of Massachusetts, a trade association of businesses in Massachusetts, cited a PhRMA report that said the biopharmaceutical sector supported more than 72,000 direct jobs and 216,000 indirect jobs in Massachusetts in 2020.¹⁰³⁹ The Freedom Foundation of Minnesota, a think tank, stated that biopharmaceutical companies employ nearly 12,000 people in the state and support another 62,000 jobs indirectly.¹⁰⁴⁰ Market Access Solutions, a life-sciences consulting firm, stated that the pharmaceuticals, biotechnology, and medical devices industries employ 76,000 people in New Jersey, accounting for 2.4 percent of private sector employment.¹⁰⁴¹ NewYorkBIO, an organization for the life science industry in the state of New York, noted that the state of New York directly employs 110,000 in bioscience jobs,¹⁰⁴² and The Business Council of New York State, a business association for the state of New York, stated that the New York City metro area has approximately 47,000 biotechnology jobs.¹⁰⁴³ The North Carolina Biosciences Organization, a trade association for North Carolina's life sciences industry, stated that North Carolina's life sciences industry (including early

¹⁰³² BIO, written submission to the USITC, May 5, 2023, 4.

¹⁰³³ Dean, written submission to the USITC, May 1, 2023, 4.

¹⁰³⁴ AdvaMed identified 400,000 direct jobs and about 2 million U.S. jobs when including indirect employment, thus implying about 1.6 million indirect jobs. AdvaMed, posthearing brief submission to the USITC, April 12, 2023, 1.

¹⁰³⁵ BIO, written submission to the USITC, May 5, 2023, 4.

¹⁰³⁶ USITC, hearing transcript, March 30, 2023, 290 (testimony of Debbie Hart, BioNJ).

¹⁰³⁷ Maryland Public Policy Institute, written submission to the USITC, May 4, 2023, 4.

¹⁰³⁸ MassBIO, written submission to the USITC, May 1, 2023, 2.

¹⁰³⁹ AIM, written submission to the USITC, May 5, 2023, 1.

¹⁰⁴⁰ Freedom Foundation of Minnesota, written submission to the USITC, May 5, 2023, 2.

¹⁰⁴¹ Market Access Solutions, written submission to the USITC, May 5, 2023, 5.

¹⁰⁴² NewYorkBIO, written submission to the USITC, April 24, 2023, 1.

¹⁰⁴³ The Business Council of New York State, written submission to the USITC, April 27, 2023, 1.

R&D, contract research, and manufacturing across pharmaceuticals, biologics, medical devices, diagnostics, agricultural technologies, and environmental products) employs nearly 75,000 people.¹⁰⁴⁴ The Nashville Area Chamber of Commerce, member organization that represents the business community in Nashville and Middle Tennessee, noted that Tennessee has at least three pharmaceutical manufacturing facilities.¹⁰⁴⁵ Lori Otto Punke of the Washington Council on International Trade, an advocacy group for trade and investment policies in the state of Washington, testified that the life sciences sector in Washington State supports 100,000 union jobs, including researchers, scientists, plumbers, electricians, and sheet metal workers.¹⁰⁴⁶ In addition, the National Puerto Rican Chamber of Commerce, a nonprofit that supports business in Puerto Rico and the U.S. mainland, stated that Puerto Rico, an unincorporated territory of the United States, has 52 FDA-approved pharmaceutical-production plants and the island's biopharmaceutical industry is responsible for 153,997 jobs.¹⁰⁴⁷

The TRIPS Agreement and Access to Medicine

Whether and How Existing TRIPS Rules and Flexibilities Can Be Deployed to Improve Access to Medicines

As presented in chapter 2, the TRIPS Agreement incorporated a number of IP protections into the multilateral rules-based trading system but also included certain flexibilities such as allowing for CLs. This section first covers perceptions of existing TRIPS Agreement IP protections, followed by general perceptions of TRIPS Agreement flexibilities. A later section covers more specifically how stakeholders view the successes and challenges in using existing TRIPS flexibilities. For the purposes of this section, existing flexibilities do not include any provided by the 2022 Ministerial Decision. Participants tended to emphasize either the need for strong IP protections to encourage innovation or the need to interpret flexibilities in ways that increase access to medicine.

TRIPS Agreement IP Protections and Access to Medicines

Some participants stated that IP protections such as those established in the TRIPS Agreement increase access to medicine by incentivizing investment in the R&D of new medicines or in finding new uses for existing medicines. These participants maintained that because R&D for medicines is long term, capital intensive, and high risk, companies need IP protections to attract investment to develop new medicines.¹⁰⁴⁸ In addition, Rafael Fonseca, the Chief Innovation Officer at the Mayo Clinic in Arizona speaking in his personal capacity, asserted that without IP protections, research would not be conducted to find new uses for existing drugs.¹⁰⁴⁹ Novartis stated that investments incentivized by IP protections

¹⁰⁴⁴ NCBio, written submission to the USITC, May 2, 2023, 1.

¹⁰⁴⁵ Nashville Area Chamber of Commerce, written submission to the USITC, May 4, 2023, 3.

¹⁰⁴⁶ USITC, hearing transcript, March 30, 2023, 317 (testimony of Lori Otto Punke, WCIT).

¹⁰⁴⁷ National Puerto Rican Chamber of Commerce, written submission to the USITC, May 4, 2023, 5–6.

¹⁰⁴⁸ For example, see USITC, hearing transcript, March 29, 2023, 106–107 (testimony of Patrick Kilbride, U.S. Chamber of Commerce); EFPIA, written submission to the USITC, May 4, 2023, 1–2; USITC, hearing transcript, March 29, 2023, 190–191 (testimony of Gregg Szabo, Merck).

¹⁰⁴⁹ Fonseca, written submission to the USITC, May 4, 2023, 3–4.

also fund activities that facilitate access at the local level such as “seeking local regulatory approvals, building local supply and distribution chains, building or strengthening local medical infrastructure, and educating doctors and patients about the existence and proper use of a new medicine.”¹⁰⁵⁰

John Stanford of Incubate Coalition, an organization that represents life science venture capitalists, testified that if IP protections for malaria, AIDS, neglected diseases, or pandemic therapeutics appear to be less reliable than protections for products to be sold only in developed countries, it could have a harmful effect on investment in those therapeutics.¹⁰⁵¹ Brook K. Baker of Health GAP, however, said that extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would not have a negative effect on the development and marketing of products in high-income countries. Baker asserted that profits are made in high-income, developed countries, which would not be affected by an extension of the 2022 Ministerial Decision.¹⁰⁵²

Some participants asserted that, without IP protections, access to certain medicines would not be possible because those medicines would not be available to begin with.¹⁰⁵³ Several participants discussed messenger RNA (mRNA) technology, which was the basis for certain COVID-19 vaccines, as an example of a medical innovation that was available as a result of investments incentivized by IP protections.¹⁰⁵⁴ John A. Fraser, the founder of the Burnside Development consulting firm, noted that although mRNA technology was developed over decades in publicly funded National Institutes of Health (NIH) labs, that technology was licensed to pharmaceutical companies for the development, manufacturing, and distribution of COVID-19 vaccines.¹⁰⁵⁵

It was also noted that, IP protections enable access to medicines through VLs and other partnerships, because clearly defined IP ownership gives companies the confidence to share their knowledge.¹⁰⁵⁶ INTERPAT, a global think tank focused on IP management and innovation policymaking, noted that collaborations fostered by IP allowed companies to quickly scale up manufacturing of COVID-19 vaccines and therapeutics.¹⁰⁵⁷ Kevin Haninger of PhRMA testified that IP protections provided the predictability that enabled more than 140 manufacturing partnerships across more than 30 countries, including Brazil, India, Indonesia, Kenya, Singapore, and South Africa.¹⁰⁵⁸

Several companies described their efforts to use VLs and partnerships to increase access to COVID-19 therapeutics. Anu Osinusi of Gilead testified that it has VLs with generic manufacturers in India, Pakistan, and Egypt to supply remdesivir to 127 low- and lower-middle-income countries and certain

¹⁰⁵⁰ Novartis, written submission to the USITC, May 5, 2023, 7.

¹⁰⁵¹ USITC, hearing transcript, March 30, 2023, 281–282 (testimony of John Stanford, Incubate Coalition).

¹⁰⁵² USITC, hearing transcript, March 29, 2023, 321–322 (testimony of Brook K. Baker, Health GAP).

¹⁰⁵³ For example, see USITC, hearing transcript, March 29, 2023, 360–361 (testimony of Marc Busch); Geneva Network, written submission to the USITC, April 25, 2023, 11–12; IFPMA, written submission to the USITC, May 5, 2023, 8–9.

¹⁰⁵⁴ USITC, hearing transcript, March 30, 2023, 178–181 (testimony of Adam Mossoff), 183–184 (testimony of Peter Pitts, Center for Medicine in the Public Interest).

¹⁰⁵⁵ Fraser, written submission to the USITC, May 3, 2023, 5.

¹⁰⁵⁶ C4IP, written submission to the USITC, April 26, 2023, 3–4; LES, written submission to the USITC, May 1, 2023, 3; EFPIA, written submission to the USITC, May 4, 2023, 2.

¹⁰⁵⁷ INTERPAT, written submission to the USITC, May 4, 2023, 4–5.

¹⁰⁵⁸ USITC, hearing transcript, March 29, 2023, 34–35 (testimony of Kevin Haninger, PhRMA).

upper-middle-income countries.¹⁰⁵⁹ Osinusi also testified that VLs allow for technology transfer, including transfer of various information, including manufacturing processes, specifications, and methods. Osinusi contrasted this with CLs, which she stated do not involve collaboration between patent-holding companies and the companies producing under a CL.¹⁰⁶⁰

Merck stated that it has both bilateral VLs and an agreement with the Medicines Patent Pool (MPP), which allows the MPP to issue sublicenses for the manufacturing of the raw ingredients for molnupiravir or the finished drug itself in 106 low- and middle-income countries. In addition, Merck stated that it entered manufacturing and supply partnerships with companies in Brazil and China. Merck contended that the countries included in those licensing arrangements and local partnerships cover approximately 90 percent of the population in low- and middle-income countries.¹⁰⁶¹ Pfizer noted that it entered a voluntary license agreement with the MPP, which resulted in 35 generic manufacturers of Paxlovid supplying 95 low-, lower-middle-, and upper-middle-income countries, which account for up to 53 percent of the world's population.¹⁰⁶²

Some participants also noted that IP protections increase access to safe medicines. The Information Technology and Innovation Foundation stated that the legal certainty that IP rights confer facilitates sharing of knowledge and technology that allows partners to produce therapeutics safely and reliably.¹⁰⁶³ The EFPIA stated that production under a VL must meet certain quality standards and pharmacovigilance obligations, increasing patient safety.¹⁰⁶⁴

Other participants asserted, however, that voluntary programs do not do enough to increase access to medicines. Oxfam America, a nonprofit organization, cited an analysis by MSF that said certain characteristics of VLs limit access to medicines. These characteristics included a “lack of transparency, geographic limitations, product usage restrictions, segmentation of public and private health systems, active pharmaceutical ingredient source restrictions, restrictive technology transfer conditions, anti-diversion clauses, unfair grant-back terms, research restrictions, and more.”¹⁰⁶⁵

These participants stated that under voluntary tiered-pricing programs, medicines were often still only available at unaffordable prices, especially when compared to prices for generic medicines. Public Citizen, a nonprofit consumer advocacy organization, stated that the lack of full usage of programs offering tiered-pricing options indicated that the prices offered were too high to induce demand that met need.¹⁰⁶⁶ Rethink Trade noted that tiered pricing has not provided therapeutics that are affordable in developing countries and that prices for generic medicines are usually significantly lower than prices under tiered-pricing options.¹⁰⁶⁷ Sanya Reid Smith of Social Watch testified that tiered pricing can still be unaffordable and that not-for-profit prices for molnupiravir and Paxlovid were significantly higher than prices for generic versions.¹⁰⁶⁸ Mohga Kamal-Yanni of PVA testified that tiered pricing is high for many

¹⁰⁵⁹ USITC, hearing transcript, March 29, 2023, 175 (testimony of Anu Osinusi, Gilead).

¹⁰⁶⁰ USITC, hearing transcript, March 29, 2023, 212–213 (testimony of Anu Osinusi, Gilead).

¹⁰⁶¹ Merck, written submission to the USITC, May 5, 2023, 4–7.

¹⁰⁶² Pfizer, written submission to the USITC, May 5, 2023, 17.

¹⁰⁶³ ITIF, written submission to the USITC, May 5, 2023, 7.

¹⁰⁶⁴ EFPIA, written submission to the USITC, May 4, 2023, 4.

¹⁰⁶⁵ Oxfam America, written submission to the USITC, May 5, 2023, 10.

¹⁰⁶⁶ Public Citizen, written submission to the USITC, May 5, 2023, 16–17.

¹⁰⁶⁷ Rethink Trade, written submission to the USITC, May 5, 2023, 5.

¹⁰⁶⁸ USITC, hearing transcript, March 30, 2023, 85 (testimony of Sanya Reid Smith, Social Watch).

developing countries and the price of Paxlovid was multiple times higher than the estimated price of generic versions.¹⁰⁶⁹

It was also stated that many countries are often left out of voluntary access programs. Oxfam America stated that MPP voluntary license agreements for WHO-recommended oral antiviral treatments had excluded nearly half the world’s population, including more than four dozen low- and middle-income countries. Mohga Kamal-Yanni of PVA testified that more than 50 developing countries were excluded from MPP voluntary license agreements. Rethink Trade noted that MPP and other voluntary license agreements exclude many countries with large populations that suffered some of the highest COVID-19 infection rates.¹⁰⁷⁰

Cámara Industrial de Laboratorios Farmacéuticos Argentinos (Industrial Chamber of Argentinian Pharmaceutical Laboratories) (CILFA), an association of manufacturers of generic and biosimilar medicines in Argentina, asserted that IP is one instrument among many others to promote development and public welfare, but strict and uniform IP regulations may not necessarily benefit society as a whole. CILFA noted that while countries are obligated to follow the minimum standards of the TRIPS Agreement, flexibilities contained in the TRIPS Agreement allow a margin of freedom and regulatory discretion to establish appropriate rules within each country’s legal system. The ability to use flexibilities allows for a balance between IP and the public good according to the different characteristics of each country.¹⁰⁷¹

TRIPS Agreement Flexibilities and Access to Medicines

Some participants noted that CLs allowed under TRIPS Agreement flexibilities permit production of and access to affordable generic medicines. Oxfam America asserted that CLs enable access to affordable generic medicines. Public Citizen stated that CLs can provide access to medicines when pharmaceutical companies choose not to enact voluntary measures and that CLs can be a useful bargaining tool when negotiating access deals with pharmaceutical companies.¹⁰⁷²

James Love of KEI testified that CLs can be used as leverage to obtain either a VL or a price reduction on medicines.¹⁰⁷³ Medicines Law & Policy (ML&P), a nonprofit research organization, stated that, although CLs may not be necessary when VLs are available, it is prudent to have nonvoluntary measures in place for cases where IP holders are reluctant or slow to enter into voluntary agreements.¹⁰⁷⁴ The PVA stated that CLs are the only way that countries excluded from VLs can access certain generic medicines.¹⁰⁷⁵ Jayashree Watal, a professor who formerly worked in the Intellectual Property, Government Procurement and Competition Division of the World Trade Organization (WTO), asserted that

¹⁰⁶⁹ USITC, hearing transcript, March 30, 2023, 215 (testimony of Mohga Kamal-Yanni, PVA).

¹⁰⁷⁰ Oxfam America, written submission to the USITC, May 5, 2023, 10; Rethink Trade written submission to the USITC, May 5, 2023, 6; USITC, hearing transcript, March 30, 2023, 214–215 (testimony of Mohga Kamal-Yanni, PVA).

¹⁰⁷¹ CILFA, written submission to the USITC, May 5, 2023, 14–17.

¹⁰⁷² Oxfam America, written submission to the USITC, May 5, 2023, 12–13; Public Citizen, written submission to the USITC, May 5, 2023, 17–18.

¹⁰⁷³ USITC, hearing transcript, March 29, 2023, 111–112 (testimony of James Love, KEI).

¹⁰⁷⁴ ML&P, written submission to the USITC, May 2, 2023, 4.

¹⁰⁷⁵ PVA, written submission to the USITC, May 4, 2023, 8.

pharmaceutical companies would likely not have entered into access programs for COVID-19 treatments voluntarily if not for the threat of CLs provided for in the TRIPS Agreement flexibilities.¹⁰⁷⁶

AdvaMed contended that IP protections were not a barrier to access for diagnostics; therefore, it did not see any evidence that CLs would increase access to diagnostics. Other factors, such as obtaining regulatory approval, are bigger barriers, according to AdvaMed. Because of these barriers, voluntary partnerships are the most effective way to increase access.¹⁰⁷⁷ FIND noted that individual patents are rarely a primary barrier to access for diagnostics and stated that neither CLs nor VLs would have helped increase local production in middle-income countries. FIND also stated that trade secrets and technology transfers are more important barriers in terms of access to diagnostics; but it also noted that the TRIPS Agreement provides limited tools to address them.¹⁰⁷⁸

Successes and Challenges in Using Existing TRIPS Flexibilities

Although the TRIPS Agreement contains several flexibilities, for this topic, participants focused their comments on the use of CLs. Some participants gave examples of successes in using TRIPS Agreement flexibilities, but more focused on the challenges.¹⁰⁷⁹

Successes in Using TRIPS Agreement Flexibilities

Development Alternatives with Women for a New Era (DAWN), a Fiji-based network of feminist scholars, researchers and activists, and the Brazilian Interdisciplinary AIDS Association (ABIA), a nongovernmental organization based in Brazil, provided an example of Brazil using a CL to lower the price of efavirenz, an antiretroviral for the treatment of HIV. DAWN stated that the government of Brazil attempted first to negotiate a price reduction with the manufacturer, Merck, for efavirenz. When the government of Brazil did not receive a price that it thought was acceptable, it issued CLs to import efavirenz from India and to produce domestically. According to DAWN, efavirenz was produced in Brazil under a CL beginning in January 2009, reducing the price by 45 percent.¹⁰⁸⁰

The Bangladesh Ministry of Commerce stated that, in November 2020, the government of Argentina authorized importation of a generic version of remdesivir from Bangladesh under the legal mechanism known as parallel importation, which made the treatment more affordable and increased access to the treatment in Argentina.¹⁰⁸¹ MSF stated that Bangladesh utilized its LDC IP exemption to make available a generic version of baricitinib. Melissa Barber, a health economist, testified that, because pharmaceutical compounds cannot be patented in Bangladesh, domestic production of a generic version of Paxlovid was announced soon after Pfizer received an emergency use authorization from the FDA.¹⁰⁸²

¹⁰⁷⁶ Watal, written submission to the USITC, May 3, 2023, 3.

¹⁰⁷⁷ AdvaMed, posthearing brief submission to the USITC, April 12, 2023, 7–8.

¹⁰⁷⁸ FIND, written submission to the USITC, May 16, 2023, 2, 8.

¹⁰⁷⁹ See chapter 2 for a discussion of the export limits of TRIPS Agreement flexibilities.

¹⁰⁸⁰ DAWN and ABIA, posthearing brief submission to the USITC, April 12, 2023, 2–3.

¹⁰⁸¹ The Ministry of Commerce of Bangladesh, written submission to the USITC, May 10, 2023, 1–2.

¹⁰⁸² MSF, written submission to the USITC, May 17, 2023, 5; USITC, hearing transcript, March 29, 2023, 186, 216 (testimony of Melissa Barber).

Some participants stated that CLs are useful as bargaining tools to encourage pharmaceutical companies to engage in programs for donations, price negotiations, and VLs.¹⁰⁸³ Two examples were provided by Public Citizen of countries, including in the United States, using the threat of CLs to obtain discounts when negotiating prices with originator companies.¹⁰⁸⁴ First, it stated that during an anthrax scare, the U.S. Secretary of Health and Human Services under President George W. Bush invoked the government's right to authorize a CL to produce a generic version of Bayer's Cipro. This action resulted in the United States obtaining a nearly 50 percent price reduction on purchases of Cipro. Second, Public Citizen stated that after initiating a CL protocol, Ecuador was able to use patent licensing and price negotiation to obtain medicine price reductions equivalent to 0.4 percent of its GDP.¹⁰⁸⁵

Sangeeta Shashikant of Third World Network (TWN), a nonprofit international research and advocacy organization, testified that in 2017, Malaysia used a CL to import a generic version of a drug to treat hepatitis C. Shashikant asserted that the use of the CL reduced the price of the drug by more than 99 percent and substantially increased the number of patients treated.¹⁰⁸⁶ Melissa Barber, a health economist, testified that a VL from Gilead for the hepatitis C drug was issued only after Malaysia issued the CL and a credible threat of Gilead being cut out of the market was perceived.¹⁰⁸⁷ Anu Osinusi of Gilead testified that Malaysia had the opportunity to enter into a VL for this drug but chose to issue a CL. Osinusi claimed that neighboring countries that did not issue CLs were able to treat more patients than were treated in Malaysia, and that the price achieved by Gilead's VL partners was actually lower than the prices from the production under Malaysia's CL.¹⁰⁸⁸

Challenges in Using TRIPS Agreement Flexibilities

Some participants discussed the challenges of using existing TRIPS Agreement flexibilities. Some discussed challenges such as the difficulty in establishing local production (in part because CLs do not involve the transfer of knowledge necessary for production) and public safety and quality concerns with local production. Other participants focused on political pressures (including pressure from diagnostic- and pharmaceutical-producing companies); limits on exports of products manufactured using a CL; and the complexities of the TRIPS Agreement rules and local regulations.

The IMANI Centre for Policy and Education, a think tank based in Ghana, stated that CLs can be hindered by the challenges of establishing new sources of production. Setting up a new production facility and receiving regulatory approvals can delay new supplies of therapeutics when speed is necessary during a pandemic.¹⁰⁸⁹ Duncan Matthews, a professor of intellectual property law at Queen Mary University of London, noted that CLs are limited in scope to patents and do not offer access to other IP that is relevant to production, such as trade secrets, and know-how.¹⁰⁹⁰ Anu Osinusi of Gilead testified that CLs do not include the type of technology transfer that occurs with VLs.¹⁰⁹¹

¹⁰⁸³ Jayashree Watal, written submission to the USITC, May 3, 2023, 3.

¹⁰⁸⁴ Public Citizen, written submission to the USITC, May 5, 2023, 18–20.

¹⁰⁸⁵ Public Citizen, written submission to the USITC, May 5, 2023, 18–20.

¹⁰⁸⁶ USITC, hearing transcript, March 29, 2023, 98, 117–118 (testimony of Sangeeta Shashikant, TWN).

¹⁰⁸⁷ USITC, hearing transcript, March 29, 2023, 215 (testimony of Melissa Barber).

¹⁰⁸⁸ USITC, hearing transcript, March 29, 2023, 207–208 (testimony of Anu Osinusi, Gilead).

¹⁰⁸⁹ IMANI Centre for Policy and Education, written submission to the USITC, May 1, 2023, 3.

¹⁰⁹⁰ USITC, hearing transcript, March 30, 2023, 262 (testimony of Duncan Matthews).

¹⁰⁹¹ USITC, hearing transcript, March 29, 2023, 212–213 (testimony of Anu Osinusi, Gilead).

PhRMA cited a study that found it took two years from the time a CL was issued for an antiretroviral treatment by the Brazilian government in 2007 until first production of a generic version of that treatment in Brazil.¹⁰⁹² The Institute for Policy Innovation, a nonprofit public policy think tank, discussed how the Serum Institute in India received a technology transfer agreement to produce AstraZeneca's COVID-19 vaccine but eventually halted production and 200 million stockpiled doses went to waste. Although those vaccine doses were not produced under TRIPS Agreement flexibilities, Institute for Policy Innovation used this as an example of the difficulties in setting up production and timing supply to meet demand during a pandemic.¹⁰⁹³

George Scangos of Vir Biotechnology testified that CLs do not facilitate the type of cooperation between the innovator of a therapeutic and the licensee that assures quality, safety, and advocacy of drugs produced by licensees.¹⁰⁹⁴ Anu Osinusi of Gilead testified that collaboration allows Gilead to work with licensees to halt the production and distribution of counterfeit medicines, but this kind of collaboration is not provided under a CL. Osinusi stated that early in the pandemic, Gilead saw examples of remdesivir that contained no active pharmaceutical ingredients that were seized by border control.¹⁰⁹⁵ Cynthia Cardona of Lilly testified that within weeks after Lilly signed royalty-free voluntary license agreements with local companies in India in May 2021, Lilly “found Indian-manufactured Baricitinib offered for sale illegally, eventually reaching as many as 34 countries and being sold to treat both COVID-19 and other indications.” Cardona stated that product diversion such as that creates safety risks, and she theorized that CLs could result in similar or worse product diversion.¹⁰⁹⁶

Political and economic pressures were frequently cited as reasons for the limited use of CLs. Several participants mentioned that Special 301 Reports published by the Office of the U.S. Trade Representative criticize countries for using flexibilities permitted by the TRIPS Agreement.¹⁰⁹⁷ ML&P noted that limitations on the use of TRIPS Agreement flexibilities are often included as part of trade agreements.¹⁰⁹⁸ Public Citizen described the experiences of Colombia and Ecuador as examples of pressure put on countries that attempt to use TRIPS Agreement flexibilities. Public Citizen stated that when Colombia began the process of initiating a CL for Glivec, a treatment for chronic myeloid leukemia produced by Swiss company Novartis, and when Ecuador's government issued a decree to establish procedures for CLs that would apply to pharmaceutical products, they were pressured by foreign governments to end these actions.¹⁰⁹⁹

According to some participants, limits on exports of products manufactured under a CL restrict use of existing TRIPS Agreement flexibilities.¹¹⁰⁰ James Love of KEI testified that Article 31(f) of the TRIPS Agreement, which restricts exports of national production under a CL, limits economies of scale and

¹⁰⁹² PhRMA, written submission to the USITC, May 5, 2023, 16.

¹⁰⁹³ Institute for Policy Innovation, written submission to the USITC, May 3, 2023, 4–5.

¹⁰⁹⁴ USITC, hearing transcript, March 29, 2023, 211 (testimony of George Scangos, Vir Biotechnology).

¹⁰⁹⁵ USITC, hearing transcript, March 29, 2023, 212–213 (testimony of Anu Osinusi, Gilead).

¹⁰⁹⁶ USITC, hearing transcript, March 29, 2023, 171 (testimony of Cynthia Cardona, Lilly).

¹⁰⁹⁷ USITC, hearing transcript, March 29, 2023, 92–93 (testimony of James Love, KEI), 179–180 (testimony of Tahir Amin, I-MAK), 313 (testimony of Rachel D. Thrasher); USITC, hearing transcript, March 30, 2023, 13 (testimony of Prathibha Sivasubramanian, CAMD).

¹⁰⁹⁸ ML&P, written submission to the USITC, May 2, 2023, 7.

¹⁰⁹⁹ Public Citizen, written submission to the USITC, May 5, 2023, 19–20.

¹¹⁰⁰ See chapter 2 for a discussion of the export limits of TRIPS Agreement flexibilities.

comparative advantage for countries without large domestic markets.¹¹⁰¹ It was noted that countries exploring the use of a CL for importation of a product typically do not have a domestic industry to produce a generic version of a product. They added that limitations on exports in the TRIPS Agreement can make finding a source for a generic product more difficult.¹¹⁰² Allana Kembabazi of the Initiative for Social and Economic Rights, a nonprofit organization based in Uganda, noted that for countries without production capacity, export restrictions were a limitation on the use of CLs.¹¹⁰³

Implementation of existing TRIPS Agreement flexibilities were also said to be restricted by complexities of the TRIPS Agreement rules and local regulations. Prathibha Sivasubramanian of the Campaign for Access to Medicines, Diagnostics, and Devices, India, a network of organizations working on access to medicines, diagnostics and devices in India, noted that Article 31*bis*, which waives export restrictions under Article 31(f) for products manufactured under a CL, is subject to cumbersome procedures.¹¹⁰⁴ Sangeeta Shashikant of TWN stated that Article 31*bis* is unworkable and has been used only once.¹¹⁰⁵ In addition, Sanya Reid Smith of Social Watch testified that the labeling, marketing, and special packaging requirements in TRIPS Agreement flexibilities raise the cost of production.¹¹⁰⁶ Peter Maybarduk of Public Citizen testified that some governments have difficulty even determining which of their agencies should implement the existing flexibilities.¹¹⁰⁷ ML&P noted that if national or regional laws and regulations are overly complex or otherwise not suitable, they can create a barrier to implementing TRIPS Agreement flexibilities.¹¹⁰⁸

To What Extent Further Clarifications of Existing TRIPS Flexibilities Would be Useful in Improving Access to Medicines

Few public views were provided about the extent to which further clarifications of existing TRIPS Agreement flexibilities would be useful in improving access to medicines. Some participants noted where certain improvements could be made. Other participants stated that IP protections were not a barrier to access to medicines and therefore, clarifications were not needed.

Multiple participants mentioned that clarifications could be useful at the national or regional level for the use of TRIPS Agreement flexibilities. As stated above, ML&P noted that national and regional laws and regulations are often too complex to implement these flexibilities in a timely manner during a crisis and Peter Maybarduk of Public Citizen testified that some governments have difficulty even determining

¹¹⁰¹ USITC, hearing transcript, March 29, 2023, 84–85 (testimony of James Love, KEI); KEI, prehearing brief submission to the USITC, March 20, 2023, 4.

¹¹⁰² USITC, hearing transcript, March 29, 2023, 91–92 (testimony of James Love, KEI); USITC, hearing transcript, March 30, 2023, 12 (testimony of Prathibha Sivasubramanian, CAMD), 47 (testimony of Gopakumar Madhavan, TWN TRUST).

¹¹⁰³ USITC, hearing transcript, March 30, 2023, 89 (testimony of Allana Kembabazi, Initiative for Social and Economic Rights).

¹¹⁰⁴ USITC, hearing transcript, March 30, 2023, 13 (testimony of Prathibha Sivasubramanian, CAMD).

¹¹⁰⁵ USITC, hearing transcript, March 29, 2023, 99 (testimony of Sangeeta Shashikant, TWN).

¹¹⁰⁶ USITC, hearing transcript, March 30, 2023, 149 (testimony of Sanya Reid Smith, Social Watch).

¹¹⁰⁷ USITC, hearing transcript, March 29, 2023, 77 (testimony of Peter Maybarduk, Public Citizen).

¹¹⁰⁸ ML&P, written submission to the USITC, May 2, 2023, 7.

which of their agencies should implement the existing flexibilities.¹¹⁰⁹ Several participants suggested that the WTO or the World Intellectual Property Organization (WIPO) could provide model legislation for the implementation of TRIPS Agreement flexibilities at national or regional levels.¹¹¹⁰ Sarah Gabriele, a Master of Bioethics candidate at Harvard Medical School, stated that because countries are left to draft their own mechanisms for utilizing the flexibilities, an organization such as WIPO should help countries develop national legislation that would allow for the use of the flexibilities.¹¹¹¹ KEI stated that the WTO could affirm that Article 30 of the TRIPS Agreement allows for export of the non-predominant portion of products under a CL as long as the legitimate interests of the patent holder were not unduly prejudiced in the importing country. For example, this could be done by payment of a reasonable and affordable royalty.¹¹¹²

The PVA asserted that the action being considered by the WTO is limited to clarifying the TRIPS text on production for export. In addition, James Love of KEI, Lori Wallach of Rethink Trade, and Sangeeta Shashikant of TWN testified that the 2022 Ministerial Decision would mainly act to lift the limitations on exports of products produced under a CL. The PVA stated that such a clarification would provide larger available markets in lower-middle-income countries and, therefore, provide incentives for production in those countries, allowing secure access to COVID-19 diagnostics and therapeutics for populations that need them. Such production would provide competition and lower prices for a sustained supply of COVID-19 diagnostics and therapeutics.¹¹¹³

The Alliance for Trade Enforcement, a coalition of trade associations and business groups, stated that the entire premise of clarifications to the TRIPS Agreement to increase access to medicines was wrong because IP protections are not a barrier to access.¹¹¹⁴ Some participants asserted that the true barriers to access to COVID-19 diagnostics and therapeutics and other medicines include inadequate local health systems, regulatory inefficiencies, logistical issues such as distribution and supply chain challenges, and export restrictions in producing countries.¹¹¹⁵

¹¹⁰⁹ USITC, hearing transcript, March 29, 2023, 77 (testimony of Peter Maybarduk, Public Citizen).

¹¹¹⁰ KEI, prehearing brief submission to the USITC, March 20, 2023, 11; ML&P, written submission to the USITC, May 2, 2023, 7.

¹¹¹¹ Gabriele, written submission to the USITC, May 5, 2023, 8.

¹¹¹² KEI, prehearing brief submission to the USITC, March 20, 2023, 10.

¹¹¹³ PVA, written submission to the USITC, May 4, 2023, 3.

¹¹¹⁴ AFTE, written submission to the USITC, May 5, 2023, 2.

¹¹¹⁵ For example, see IFPMA, written submission to the USITC, May 5, 2023, 11–12; MTAA, written submission to the USITC, May 8, 2023, 3; IMANI Centre for Policy and Education, written submission to the USITC, May 1, 2023, 4.

The TRIPS Agreement and COVID-19 Diagnostics and Therapeutics

How the TRIPS Agreement Promotes Innovation in and/or Limits Access to COVID-19 Diagnostics and Therapeutics

How the TRIPS Agreement Promotes Innovation

The TRIPS Agreement provides a global standard for IP protections, and some participants stated that IP protections are fundamental to innovations in medicine in general and in COVID-19 diagnostics and therapeutics specifically.¹¹¹⁶ It was noted that the investments necessary for innovation in diagnostics and therapeutics may not happen without IP protections that allow investors to see a financial return on long-term investments.¹¹¹⁷ PhRMA asserted that in recent decades, IP protections have become more important for innovation in the biopharmaceutical industry because of more complex clinical trials and increased R&D costs.¹¹¹⁸

Some participants stated that the decades-long R&D that supported the pandemic response would not have existed without IP protections. They noted that it was the foundational research enabled by IP protections that resulted in the rapid development of innovative products to address COVID-19.¹¹¹⁹ Novartis described its efforts to repurpose two existing drugs for the treatment of COVID-19. Although neither of those drugs led to the successful development of COVID-19 therapeutics, Novartis noted that IP protections enable not only the initial development of drugs but also the potential discovery of new uses for existing drugs.¹¹²⁰ Market Access Solutions noted that even research into drugs that are not successful is important because it informs future drug research.¹¹²¹ Natalie Buford-Young of Springboard Enterprises, a nonprofit organization dedicated to the mission of providing women entrepreneurs access to capital, provided an example of a company that produced a home testing kit for food sensitivities. Buford-Young stated that the company was later able to become a producer of COVID-19 home testing kits because IP protections facilitated its access to funding.¹¹²² In addition, BASF Corporation, a chemical

¹¹¹⁶ For example, see USITC, hearing transcript, March 29, 2023, 14 (testimony of Ashley Miller, AdvaMed); USITC, hearing transcript, March 30, 2023, 318 (testimony of Lori Otto Punke, WCIT); IFPMA, written submission to the USITC, May 5, 2023, 8. See chapter 2 for a discussion on the TRIPS Agreement.

¹¹¹⁷ For example, see USITC, hearing transcript, March 29, 2023, 280 (testimony of Frank Cullen, C4IP); WCIT, written submission to the USITC, April 19, 2023, 2; Gilead, prehearing brief submission to the USITC, March 17, 2023, 4–5.

¹¹¹⁸ PhRMA, written submission to the USITC, May 5, 2023, 16.

¹¹¹⁹ IFPMA, written submission to the USITC, May 5, 2023, 8–9; Novartis, written submission to the USITC, May 5, 2023, 3, 7, 10.

¹¹²⁰ Novartis, written submission to the USITC, May 5, 2023, 9–11.

¹¹²¹ Market Access Solutions, written submission to the USITC, May 5, 2023, 5.

¹¹²² USITC, hearing transcript, March 30, 2023, 232 (testimony of Natalie Buford-Young, Springboard Enterprises).

company based in Germany, stated that patents put information into the public domain and such public disclosures accelerate innovation.¹¹²³

These participants also stated that IP protections facilitate the partnerships necessary for innovation and the development of diagnostics and therapeutics. Patents are public and, therefore, allow researchers and producers of diagnostics and therapeutics to find appropriate potential partners, using the proprietary knowledge to which that potential partner has access. In addition, IP protections allow collaboration because each partner knows that it can share its knowledge without losing control over proprietary business information.¹¹²⁴ The International Federation of Pharmaceutical Manufacturers and Associations, a Switzerland-based association of the pharmaceutical industry, stated that these types of IP protections are particularly important for early-stage companies that need to form partnerships to access the expertise and resources necessary to bring new products to market.¹¹²⁵

In contrast, Jennifer Reid of Oxfam America testified that overly restrictive IP rules can limit innovation.¹¹²⁶ Rachel D. Thrasher, a legal researcher at the Boston University Global Development Policy Center, testified that some studies have shown that strong IP protections can have a negative impact on innovation, particularly in developing countries.¹¹²⁷ Oxfam America quoted studies that found that overly broad or strong patent rights can discourage innovation and found evidence suggesting that CLs increase innovation in both licensing and originator countries.¹¹²⁸

Cámara Industrial de Laboratorios Farmacéuticos Argentinos (Industrial Chamber of Argentinian Pharmaceutical Laboratories) (CILFA) stated that the innovations for COVID-19 diagnostics, therapeutics, and vaccines were primarily driven by factors other than IP, including “collaboration between governments and private sector companies through advance purchase agreements, public funding for development/testing/production, supply chain corrections and by expediting the approval processes by regulatory authorities.” CILFA noted that development of remdesivir was supported by the National Institutes of Health and that the U.S. Food and Drug Administration granted remdesivir emergency use status. Another example provided was that monoclonal antibody treatments for COVID-19 were developed with funding from the U.S. government for clinical trials and purchase agreements. CILFA also noted that the U.S. government’s Biomedical Advanced Research and Development Authority provided funding to more than 60 companies for the development of COVID-19 diagnostics.¹¹²⁹

How the TRIPS Agreement Limits Access to COVID-19 Diagnostics and Therapeutics

Some participants stated that patents and other IP protections reduce access to diagnostics and therapeutics. Several participants pointed to the TRIPS Agreement’s limitations on exports of products produced under a CL, which therefore limits access to diagnostics and therapeutics produced under a

¹¹²³ BASF, written submission to the USITC, May 3, 2023, 1.

¹¹²⁴ Geneva Network, written submission to the USITC, April 25, 2023, 16.

¹¹²⁵ IFPMA, written submission to the USITC, May 5, 2023, 7.

¹¹²⁶ USITC, hearing transcript, March 29, 2023, 31–32 (testimony of Jennifer Reid, Oxfam America).

¹¹²⁷ USITC, hearing transcript, March 29, 2023, 311 (testimony of Rachel D. Thrasher).

¹¹²⁸ Oxfam America, written submission to the USITC, May 5, 2023, 11.

¹¹²⁹ CILFA, written submission to the USITC, May 5, 2023, 8, 12–13.

CL.¹¹³⁰ As noted above, James Love of KEI testified that Article 31(f) of the TRIPS Agreement limits economies of scale and comparative advantage for countries without large domestic markets.¹¹³¹ It was noted that countries exploring the use of a CL to import a product typically do not have a domestic industry to produce a generic version of a product and limitations on exports in the TRIPS Agreement flexibilities can make finding a source for a generic product more difficult.¹¹³²

These participants asserted that monopolies created by patents and other IP protections result in products that are not affordable for widespread purchase in developing countries.¹¹³³ In addition, Prathibha Sivasubramanian of the Campaign for Access to Medicines, Diagnostics, and Devices, India testified that companies attempt to extend patents on some COVID-19 therapeutics by applying for patents on new uses or new forms of repurposed drugs, preventing lower-priced generic drugs from entering the market.¹¹³⁴ Rethink Trade also stated that because so many COVID-19 therapeutics are repurposed and require minimal R&D, the secondary patents filed result in patent evergreening, limiting competition.¹¹³⁵

Some participants stated that patented COVID-19 therapeutics remain unaffordable in less developed countries despite tiered pricing and other initiatives offered by patent holders.¹¹³⁶ Health Justice Initiative, a nonprofit organization based in South Africa, stated that Paxlovid is not accessible in South Africa because the private sector price is unaffordable and a generic option is lacking.¹¹³⁷ The Initiative for Social and Economic Rights stated that Paxlovid has cost \$250 per course in some developing countries, despite the \$25 per course price of generic Paxlovid negotiated by the Clinton Foundation.¹¹³⁸

Some participants asserted that high prices resulting from patent monopolies distort the measurements of demand for diagnostics and therapeutics. These participants contended that when evaluating access to diagnostics and therapeutics, demand cannot be judged in terms of product orders alone because orders for COVID-19 treatments are limited when these treatments are unaffordable. It was stated that high prices that reduce demand for diagnostics and therapeutics result from a lack of generic products.¹¹³⁹ Public Citizen also asserted that a lack of price transparency in supply agreements for

¹¹³⁰ USITC, hearing transcript, March 29, 2023, 45 (testimony of Lori Wallach, Rethink Trade); USITC, hearing transcript, March 30, 2023, 89 (testimony of Allana Kembabazi, Initiative for Social and Economic Rights).

¹¹³¹ USITC, hearing transcript, March 29, 2023, 84–85 (testimony of James Love, KEI).

¹¹³² USITC, hearing transcript, March 29, 2023, 91–92 (testimony of James Love, KEI); USITC, hearing transcript, March 30, 2023, 12 (testimony of Prathibha Sivasubramanian, CAMD), 47 (testimony of Gopakumar Madhavan, TWN TRUST).

¹¹³³ For example, see USITC, hearing transcript, March 29, 2023, 44 (testimony of Lori Wallach, Rethink Trade); USITC, hearing transcript, March 30, 2023, 33 (testimony of Allana Kembabazi, Initiative for Social and Economic Rights); MSF, written submission to the USITC, May 17, 2023, 5, 7; Oxfam America, written submission to the USITC, May 5, 2023, 7–8.

¹¹³⁴ USITC, hearing transcript, March 30, 2023, 11–12 (testimony of Prathibha Sivasubramanian, CAMD).

¹¹³⁵ Rethink Trade, written submission to the USITC, May 5, 2023, 4.

¹¹³⁶ For example, see Public Citizen, written submission to the USITC, May 5, 2023, 8–9, 14, 16–17; Rethink Trade, written submission to the USITC, May 5, 2023, 5.

¹¹³⁷ Health Justice Initiative, written submission to the USITC, May 12, 2023, 2.

¹¹³⁸ Initiative for Social and Economic Rights, written submission to the USITC, May 5, 2023, 2.

¹¹³⁹ For example, see Oxfam America, written submission to the USITC, May 5, 2023, 8–9; Public Citizen, written submission to the USITC, May 5, 2023, 8–10; USITC, hearing transcript, March 30, 2023, 17 (testimony of Karina Yong, CAP).

diagnostics and therapeutics complicates the decision-making process for purchasers and can result in countries placing fewer orders or waiting for more affordable supply options.¹¹⁴⁰

MSF discussed specific IP protection issues that limit access to diagnostics and stated that patents are not prominent for infectious disease diagnostics. Patents and patent thickets on reagents, instruments, methods, and software, however, are associated with diagnostics. MSF asserted that these IP protections limit competition and create confusion about whether other manufacturers can legally produce a diagnostic product.¹¹⁴¹

The Extent to which Products Not Yet on the Market, or New Uses for Existing Products, Could be Affected by an Extension of the Ministerial Decision to COVID-19 Diagnostics and Therapeutics

Some participants asserted that extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would reduce the incentives for developing new COVID-19 diagnostics and treatments or researching COVID-19 applications for existing drugs. Other participants stated that an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics should apply to products that will be developed in the future to ensure access to the most effective treatments.

Some participants expressed concern that extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would limit the future development of those products. A common argument from these participants was that waiving IP rights or weakening IP rights on COVID-19 diagnostics and therapeutics would reduce incentives to invest in the R&D of tests and treatments for future pandemics.¹¹⁴²

To address future pandemics even more quickly, some participants noted that investments would need to be directed toward readiness efforts, including investments in a range of therapeutic platforms that need to be developed to identify new efficacious and safe treatments for future pandemic pathogens. For companies to invest in that type of research, however, they need IP protections that allow them to realize a reasonable return on their investment.¹¹⁴³

Tiffany Smith of the National Foreign Trade Council, an organization that advocates on international tax and trade issues on behalf of U.S.-based businesses, testified that in a crisis like the COVID-19 pandemic, it is important for companies to examine any potential drugs that might be helpful. Companies could be

¹¹⁴⁰ Public Citizen, written submission to the USITC, May 5, 2023, 9–10.

¹¹⁴¹ MSF described a patent thicket as “an overlapping set of patent rights. The individual patents can apply differently in different jurisdictions, can expire at different times, and cannot be covered by a single patent license.” MSF, written submission to the USITC, May 17, 2023, 9–11. See chapter 2 for a discussion of the export limits of TRIPS Agreement flexibilities.

¹¹⁴² For example, see USITC, hearing transcript, March 29, 2023, 172 (testimony of Cynthia Cardona, Lilly), 321 (testimony of Frank Cullen, C4IP), 198 (testimony of George Scangos, Vir Biotechnology); USITC, hearing transcript, March 30, 2023, 318 (testimony of Lori Otto Punke, WCIT), 320 (testimony of Debbie Hart, BioNJ).

¹¹⁴³ For example, see Merck, written submission to the USITC, May 5, 2023, 14–15; Pfizer, written submission to the USITC, May 5, 2023, 24.

reluctant to search for COVID-19 applications for existing and new drugs if they think that those drugs would then be subject to a global TRIPS Agreement waiver.¹¹⁴⁴ Cynthia Cardona of Lilly testified that the introduction or even the threat of IP waivers would disincentivize the testing of existing products for COVID-19 or other pandemic applications.¹¹⁴⁵

Other participants stated that an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics should apply to products that will be developed in the future, including in some cases combination drugs.¹¹⁴⁶ Oxfam America noted that future COVID-19 products may face IP barriers because the prior inequalities of access to existing COVID-19 treatments are likely to recur for access to future COVID-19 treatments.¹¹⁴⁷ Sangeeta Shashikant of TWN testified that new COVID-19 variants are emerging and new therapeutics are needed, so it would not make sense to limit any list of products covered by extended TRIPS Agreement flexibilities to existing therapeutics.¹¹⁴⁸ Health Justice Initiative stated that VLs have excluded a large number of developing countries and there is no reason to believe that voluntary programs covering future COVID-19 treatments will ensure access.¹¹⁴⁹ Two participants noted that in addition to the importance of individual COVID-19 treatments, combination treatments could become relevant in the future because they have often proven to be the most effective treatments for infectious diseases in the past.¹¹⁵⁰ Oxfam America stated that, in addition to treatments for future variants, additional treatments for issues such as long COVID are also needed.¹¹⁵¹

The Relevance, if Any, of the Fact that Diagnostic and Therapeutic Products Used with Respect to COVID-19 May Also Have Application to Other Diseases

Some participants expressed concern that an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would cover an overly broad set of products and reduce incentives for companies to look for COVID-19 applications for their products. Other participants stated that it would be possible to limit the scope of an extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics or that a broader interpretation of covered products would be best to increase access to medicine.

Some participants were concerned that if the 2022 Ministerial Decision is extended to COVID-19 diagnostics and therapeutics, it could cover too broad a set of products. Participants contended that the lack of any definitions for COVID-19 diagnostics and therapeutics in the 2022 Ministerial Decision means

¹¹⁴⁴ USITC, hearing transcript, March 29, 2023, 325 (testimony of Tiffany Smith, NFTC).

¹¹⁴⁵ USITC, hearing transcript, March 29, 2023, 172 (testimony of Cynthia Cardona, Lilly).

¹¹⁴⁶ USITC, hearing transcript, March 29, 2023, 44 (testimony of Lori Wallach, Rethink Trade); USITC, hearing transcript, March 30, 2023, 215 (testimony of Mohga Kamal-Yanni, PVA).

¹¹⁴⁷ Oxfam America, written submission to the USITC, May 5, 2023, 9.

¹¹⁴⁸ USITC, hearing transcript, March 29, 2023, 86 (testimony of Sangeeta Shashikant, TWN).

¹¹⁴⁹ Health Justice Initiative, written submission to the USITC, May 12, 2023, 2.

¹¹⁵⁰ USITC, hearing transcript, March 29, 2023, 27 (testimony of James Love, KEI); Rethink Trade, written submission to the USITC, May 5, 2023, 3.

¹¹⁵¹ Oxfam America, written submission to the USITC, May 5, 2023, 9.

that an extension to diagnostics and therapeutics would result in many products with applications for other diseases being subject to the 2022 Ministerial Decision.¹¹⁵² The International Federation of Pharmaceutical Manufacturers and Associations noted that it would be difficult to prevent waived IP protections from being misused for products with non-COVID-19 applications.¹¹⁵³ Cynthia Cardona of Lilly testified that if products subject to waivers of IP protections are diverted to non-COVID-19 uses, there is a lack of pharmacovigilance, and there would be risks to patients.¹¹⁵⁴

It was noted that companies could be less willing to test existing drugs for COVID-19 applications if they thought that the drugs would then potentially lose IP protections. The EFPIA cited data from 2022 that showed 21 of 38 (55 percent) of the approved COVID-19 therapeutics were repurposed drugs and that 464 therapeutics not originally developed for the treatment of COVID-19 were being researched and tested for COVID-19 applications.¹¹⁵⁵

Several companies provided specific examples of how existing therapeutics could be affected by a broad interpretation of the 2022 Ministerial Decision. Anu Osinusi of Gilead testified that, in the future, remdesivir could potentially be used to treat multiple viruses and it would be nearly impossible to limit the application of an IP waiver to COVID-19 uses.¹¹⁵⁶ Merck stated that acetaminophen, a drug to treat fevers caused by both common colds and COVID-19, could be subject to a TRIPS Agreement waiver under a broad interpretation of COVID-19 therapeutics.¹¹⁵⁷ Merck also noted that its drug molnupiravir is currently being evaluated for treatment of respiratory syncytial virus and influenza, but a waiver of IP protections would reduce the incentives to develop new uses for therapeutics.¹¹⁵⁸ Pfizer noted that the research that eventually led to the development of Paxlovid began in 2003—as an attempt to address the severe acute respiratory syndrome (SARS) outbreak—but weakening IP protections could disincentivize that kind of research to repurpose drugs.¹¹⁵⁹

Ashley Miller of AdvaMed testified that extending the 2022 Ministerial Decision to COVID-19 diagnostics could be complicated. She stated that many testing devices have underlying platform technologies that run tests for various viral and bacterial conditions in addition to tests for COVID-19 and therefore it is not possible to separate the diagnostics with COVID-19 applications from diagnostics without COVID-19 applications. Miller asserted that extending the TRIPS Agreement waiver to COVID-19 diagnostics could result in numerous U.S. companies losing IP protections for many diagnostics where COVID-19-related uses are a small share of applications.¹¹⁶⁰

In contrast, other participants stated that it will be possible to limit the scope of an extension of the 2022 Ministerial Decision to diagnostics and therapeutics for COVID-19 uses. Sanya Reid Smith of Social

¹¹⁵² For example, see USITC, hearing transcript, March 29, 2023, 330 (testimony of Randy G. DeFrehn, PILMA), 330–331 (testimony of Stephen Ezell, ITIF).

¹¹⁵³ IFPMA, written submission to the USITC, May 5, 2023, 12.

¹¹⁵⁴ USITC, hearing transcript, March 29, 2023, 274 (testimony of Cynthia Cardona, Lilly).

¹¹⁵⁵ For example, see Geneva Network, written submission to the USITC, April 25, 2023, 11; USITC, hearing transcript, March 29, 2023, 274 (testimony of Cynthia Cardona, Lilly); EFPIA, written submission to the USITC, May 4, 2023, 4.

¹¹⁵⁶ USITC, hearing transcript, March 29, 2023, 272 (testimony of Anu Osinusi, Gilead).

¹¹⁵⁷ Merck, written submission to the USITC, May 5, 2023, 15.

¹¹⁵⁸ Merck, written submission to the USITC, May 5, 2023, 15.

¹¹⁵⁹ Pfizer, written submission to the USITC, May 5, 2023, 13–14, 26.

¹¹⁶⁰ USITC, hearing transcript, March 29, 2023, 14–15, 85–86 (testimony of Ashley Miller, AdvaMed).

Watch testified that any definitions would be heavily negotiated and that there are examples of CLs for HIV/AIDS medicines where workable definitions were found.¹¹⁶¹ Yoke Ling Chee of Third World Network Berhad, a nonprofit international research and advocacy organization based in Malaysia, testified that any CL would have to be requested for a specific diagnostic or therapeutic, which will make the scope of these CLs very narrow.¹¹⁶² Sangeeta Shashikant of TWN testified that the issue of diagnostics and therapeutics having applications to other diseases was not a problem because enough conditions are attached to the use of the 2022 Ministerial Decision. Shashikant noted that diagnostics and therapeutics imported under a CL need to be for the treatment of COVID-19 specifically and exporting a product produced under a CL would require following specified conditions such as notifying the WTO TRIPS Council.¹¹⁶³ Brook K. Baker of Health GAP testified that field-of-use restrictions would limit CL usage to diagnostics and therapeutics for use with COVID-19. He also noted that there would be essentially no difference between the field-of-use restrictions in CLs and those in VLs in use by industry.¹¹⁶⁴

Some participants asserted that using a broader interpretation of COVID-19 diagnostics and therapeutics when extending the 2022 Ministerial Decision would be most beneficial in terms of providing access to medicine. Rachel D. Thrasher testified that the large number of COVID-19 treatments that are potentially patent protected demonstrates that a broad TRIPS Agreement waiver would achieve the best results in terms of access to medicine. Mohga Kamal-Yanni of the PVA testified that therapeutic guidelines change as new medical evidence becomes available and the extension of the 2022 Ministerial Decision should cover all relevant medicines.¹¹⁶⁵

¹¹⁶¹ USITC, hearing transcript, March 30, 2023, 115 (testimony of Sanya Reid Smith, Social Watch).

¹¹⁶² USITC, hearing transcript, March 30, 2023, 116 (testimony of Yoke Ling Chee, TWN Berhad).

¹¹⁶³ USITC, hearing transcript, March 29, 2023, 88–89 (testimony of Sangeeta Shashikant, TWN).

¹¹⁶⁴ USITC, hearing transcript, March 29, 2023, 322–323 (testimony of Brook K. Baker, Health GAP).

¹¹⁶⁵ USITC, hearing transcript, March 29, 2023, 314 (testimony of Rachel D. Thrasher); USITC, hearing transcript, March 30, 2023, 214 (testimony of Mohga Kamal-Yanni, PVA).

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Chapter 8

Literature Review

Introduction

Academic research has studied the effect of intellectual property (IP) rules on different outcomes related to pharmaceuticals.¹¹⁶⁶ Per the request letter, this chapter catalogs the academic research and provides a critical and detailed assessment of the literature for the following IP-related topics:

- The relationship between patent protection and innovation in the health sector, including available information for low-income countries (LICs), lower-middle-income countries (LMICs), upper-middle-income countries (UMICs), and high-income countries (HICs);
- The relationship between patent protection and access to medicine, including available information for LICs, LMICs, UMICs, and HICs;
- The outcomes of using compulsory licenses (CLs) by WTO members for pharmaceutical products, including available information on product access, innovation, and global health; and
- The effect, or lack thereof, of the Medicine Patent Pool (MPP) on access to COVID-19 diagnostics and therapeutics.¹¹⁶⁷

While the chapter reviews some theoretical predictions from the literature and includes a few descriptive studies, it is focused on model-based studies that cover one of the four topics listed above. The studies selected for inclusion in this chapter all meet several criteria: they describe procedural and analytical steps to understand how a conclusion was reached, provide necessary context and background information for their research question, and use reliable data and discuss data limitations. In addition to providing a discussion of the selected studies in this chapter, appendix G catalogs all of the included sources. A large body of academic research has studied IP rules; however, this chapter focuses only on studies that are related to the topics listed above. In this way, while this literature review is detailed in its coverage of the relevant topics, it is not a complete listing of all research articles related to IP rules.

Academic research on the reasons for market segmentation and barriers to a more diverse geographical distribution of the global manufacturing industries for COVID-19 diagnostics and therapeutics, another

¹¹⁶⁶ IP protections not only include patents, but also include topics such as copyright, trademarks, industrial designs, geographical indications, and trade secrets. As will be discussed, this chapter does not cover all available IP protections and focuses on the topics from the request letter. WIPO, “What Is Intellectual Property?,” accessed May 23, 2023.

¹¹⁶⁷ Academic literature on the relationship between the MPP and access to COVID-19 diagnostics and therapeutics is currently not available. This chapter covers the relationship between the MPP and access to other pharmaceutical products that have been studied in the literature. This chapter does not cover, and the Commission’s literature review did not target literature on, the effect of voluntary licenses outside of those associated with the MPP on access to pharmaceutical products, such as BLAs discussed in chapter 5.

topic from the request letter, is limited.¹¹⁶⁸ For this reason, market segmentation and barriers to a more diverse geographical distribution are covered within chapter 4 on the COVID-19 diagnostics and therapeutics manufacturing supply chain and not in this chapter.¹¹⁶⁹ This chapter addresses the academic research on CLs and some alternatives to CLs such as the MPP. Additional information on CLs, including the actions taken by WTO members to use or attempt to use CLs for the production, importation, or exportation of pharmaceutical products, and alternatives to compulsory licensing available to WTO Members, are covered in chapter 5.

This chapter begins by reviewing methodologies commonly used in the literature, including a summary of each approach and its strengths and limitations. The chapter then turns to an assessment of the literature related to the topics outlined above. Studies included in the literature review are organized by each of these topics. Within each topic, studies are further organized by the economic outcomes covered in each study or, when more practical, by the primary research methodology. When appropriate, findings for different country income groupings are discussed. However, research that separates effects by country income groupings often uses broader groupings, such as developed and developing countries, and not the LICs, LMICs, UMICs, and HICs groupings from the World Bank.¹¹⁷⁰

For country-specific analyses, literature commonly focuses on the United States, and less is known about other countries. For country-specific analyses that are available for developing countries, India is usually the country of focus. The reviews of the studies in this chapter include discussions on the research questions of interest, data and methodologies used, primary findings, and strengths and potential limitations of each analysis.¹¹⁷¹ The chapter concludes with a discussion of gaps in the literature.

The literature meeting the criteria noted above is limited and the literature would benefit from more research. There are many challenges, such as limited data availability and the difficulty of identifying the causal effect, that researchers face when studying the effects of patent protection, CLs, and the MPP. For the effect of patent protection on innovation in the health sector, there is survey evidence that provides support for the importance of patents to pharmaceutical firms and their investments in research and development (R&D). However, more detailed analyses find mixed results on the relationship between patent protection and innovation in the health sector, suggesting that patent protection does not support innovation in all countries. One important result is that patent protection is generally found to be more beneficial to innovation in the health sector for more developed countries and less for developing countries.

When studying patent protection and access to medicine, researchers have used a range of different measures related to access. Studies have generally found that patent protection results in higher prices for medicine, with different magnitudes of price increases across different studies. There is little available evidence on the effect of patent protection on the sale of pharmaceuticals. Trade flows of

¹¹⁶⁸ Researchers have focused more on COVID-19 vaccine supply chains; however, this literature is out of scope for this chapter. Bown and Bollyky, “How COVID-19 Vaccine Supply Chains Emerged,” February 2022, 468–522.

¹¹⁶⁹ In general, supply chains for pharmaceutical products are complex, and pharmaceuticals are subject to a range of different regulations across different countries. WIPO, *The Economics of Intellectual Property*, January 1, 2009, 159.

¹¹⁷⁰ Some studies that use the groupings of LICs, LMICs, UMICs, and HICs follow different definitions than provided by the World Bank. More information on developed and developing countries can be found in chapter 5.

¹¹⁷¹ Some of the selected papers cover more than one research question. This chapter only discusses the research questions and findings that are relevant to the literature review as specified in the request letter.

pharmaceuticals are often found to have increased due to patents, with differences depending on the direction of trade flows and if the countries are developed or developing economies. While there is evidence that patents reduce the time lag of drug launches, the diffusion of medicine across the world continues to be limited.¹¹⁷² Two studies on India estimated negative welfare effects due to patent protection, with most of the negative effects being faced by local consumers.

The literature on CLs and the MPP is more limited than the literature on patent protection. For the impact of CLs on pharmaceutical products, researchers have generally found that CLs are associated with decreased pharmaceutical prices and increased numbers of people with access to patented products in countries using CLs. One study on the United States and another study on Germany provided evidence that CLs may encourage innovation.¹¹⁷³ A study on India estimated that CLs can increase consumer welfare.¹¹⁷⁴ For the impact of the MPP on pharmaceutical products, there is evidence that the MPP increased the share of generic drugs and encouraged technology diffusion. There is some evidence that the MPP is associated with lower prices for pharmaceutical products.

Methodologies

Existing research on the topics covered in this literature review can generally be categorized into the following methodologies: descriptive analyses, structural models, and reduced-form econometric models. Descriptive methods summarize data and identify relationships between explanatory and outcome variables.¹¹⁷⁵ For example, researchers have tabulated survey results on the importance for patent protection from the perspective of firms.¹¹⁷⁶ While advantageous for their simplicity and ease of communicating findings, descriptive methods can also lead to misleading interpretations of relationships if other factors, not considered in the analysis, also influence the economic outcomes being studied.

Alternatively, model-based methodologies use statistical or mathematical methods to isolate and quantify relationships between explanatory variables and economic outcomes while controlling for other variables that may also be influencing outcomes. Within model-based methodologies, structural economic models consist of a system of mathematical equations based on economic theory that represents a simplified representation of an economy and can be used to isolate how different variables influence economic outcomes.

Researchers also use reduced-form econometric models, which combine historical data and statistical methods to identify how changes in IP rules affect economic outcomes. For example, researchers have

¹¹⁷² The diffusion of medicine is referring to the availability of medicine across geographic areas.

¹¹⁷³ Baten, Bianchi, and Moser, “Compulsory Licensing and Innovation,” May 2017, 231–42; Moser and Voena, “Compulsory Licensing,” February 1, 2012, 396–427; Moser, “Patents and Innovation in Economic History,” February 2016, 16–17, 26.

¹¹⁷⁴ Chatterjee, Kubo, and Pingali, “The Consumer Welfare Implications of Governmental Policies,” December 2015, 255–73.

¹¹⁷⁵ The term “explanatory” refers to variables that are used to explain the differences in or predict the impact on “outcome” variables.

¹¹⁷⁶ Mansfield, Schwartz, and Wagner, “Imitation Costs and Patents,” 1981, 907–18; Mansfield, “Patents and Innovation,” 1986, 173–81; Levin et al., “Appropriating the Returns from Industrial Research and Development,” 1987, 783–831; Cohen, Nelson, and Walsh, “Protecting Their Intellectual Assets,” February 2000, 1–50; Graham et al., “High Technology Entrepreneurs and the Patent System,” June 30, 2009, 255–327.

studied the effect of changes in IP regimes across countries due to the TRIPS Agreement.¹¹⁷⁷ These models allow researchers to separate the effects of IP rules from effects of other confounding variables.¹¹⁷⁸ The advantages and limitations of each of these methodologies, as outlined in this section, apply to a varying extent to the papers described throughout the literature review. However, to avoid repetition, these general advantages and limitations are only mentioned in this section.

Descriptive Analysis

Descriptive methodologies are used to summarize data and to study historical relationships between different variables of interest. For example, researchers have commonly used descriptive methodologies and survey data to attempt to understand the importance of patent protection for firms.¹¹⁷⁹ Descriptive methods have several advantages for studying the outcomes of IP rights. Because descriptive statistics use less technical methods, they are often easier to communicate to broader audiences than economic modeling. Descriptive methods generally have fewer data requirements and can generally be easily used in conjunction with survey data when data availability from other sources is limited, as is often the case when studying IP rights.

In terms of disadvantages, the inability of descriptive methods to identify cleanly or quantify causal relationships between variables significantly limits descriptive methods. Relationships or the extent of relationships highlighted by descriptive methods can be spurious, meaning other factors are influencing or driving the observed relationships. For example, with a simple comparison of pharmaceutical prices across countries, it is unclear if price differences reflect differences in patent protection or other country-specific characteristics. When a spurious relationship exists, descriptive analyses can lead researchers to draw incorrect conclusions about relationships being studied. For this reason, descriptive methodologies are most often used to identify and communicate observable economic trends and to provide motivation for developing more complex model-based analyses that address potentially confounding variables and spurious relationships.

Structural Economic Models

Economic researchers can use structural economic models to study the effects of IP rights. To do so, researchers use economic theory to describe the features of a simplified version of an economy. By constructing this simplified representation of an economy, researchers impose assumptions about how the economy operates within their model and construct a system of mathematical equations to represent these economic features. Researchers can then use the structural model to simulate the effect of a change in the IP regime.

¹¹⁷⁷ See chapter 2 for details of the TRIPS Agreement. Agreement on Trade-Related Aspects of Intellectual Property Rights, April 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 319.

¹¹⁷⁸ A confounding variable is a variable that is not explicitly accounted for in the analysis but one that influences both the explanatory variable and the outcome variable, potentially creating spurious links.

¹¹⁷⁹ Mansfield, Schwartz, and Wagner, "Imitation Costs and Patents," 1981, 907–18; Mansfield, "Patents and Innovation," 1986, 173–81; Levin et al., "Appropriating the Returns from Industrial Research and Development," 1987, 783–831; Cohen, Nelson, and Walsh, "Protecting Their Intellectual Assets," February 2000, 1–50; Graham et al., "High Technology Entrepreneurs and the Patent System," June 30, 2009, 255–327.

Although they are not widely adopted in the literature due to their complexity and data requirements, structural models have several advantages. First, structural models incorporate economic theory, meaning that models are constructed to reflect features of an economy that are well documented and debated within broader economic research. Another key advantage of structural models is they allow researchers to modify parameters of the structural model to simulate the response of an economy to different hypothetical scenarios and see how economic outcomes vary across these simulations. Structural models are also well suited for estimating the welfare effects of changes in IP regimes.

However, structural economic models still face several limitations. Most notably, these models rely on simplifying assumptions about how economies operate. As such, structural models can fail to account for all the complex interactions and features of a real economy. Additionally, by relying on simplifying assumptions to represent specific structures within an economy, structural models are often limited in the number of economic outcomes that a single structural model can properly identify. Structural models will typically abstract from, or not consider, other structures and mechanisms that influence outcomes.

Reduced-Form Econometric Models

The most common approach taken by researchers when studying the effects of IP rules is the use of reduced-form econometric models. Reduced-form models require significantly fewer assumptions about the underlying structure of an economy compared to structural models. In contrast with structural models that begin with a theory-driven assumption of how an economy operates, reduced-form models begin with a hypothesized relationship between economic variables that is based more loosely on economic theory and an outcome of interest.¹¹⁸⁰ This hypothesized relationship is then expressed as a model where the economic outcome being studied is represented as a mathematical function of explanatory variables. Researchers use historical data and econometric methods to quantify the relationship between the outcome of interest and the individual variables specified in the model. By using econometrics and historical data, these relationships can be tested for statistical significance, where researchers determine whether a relationship exists between a variable of interest and the studied economic outcome.

Reduced-form econometric models are powerful tools for demonstrating empirical relationships between economic variables and outcomes, but they face several limitations. In particular, reduced-form models are tailored to specific research questions they are designed to examine; and findings from these models are often limited in their ability to be generalized beyond the specific research application, leading to a narrow interpretation of findings from models.¹¹⁸¹ Unlike structural models, reduced-form models are generally not well suited to answer questions about general equilibrium economic effects not explicitly featured in the reduced-form framework.

¹¹⁸⁰ Economic theory, other economic research, or even intuition can inform this hypothesized relationship.

¹¹⁸¹ Generalizing findings to other products and countries is a challenge for all methodologies.

The Effect of Patent Protection on Pharmaceuticals

At the center of the debate regarding the use of patent protection and pharmaceuticals is balancing the incentives to induce innovation in the health sector with a period of market exclusivity when firms can charge monopoly prices versus access to medicine that may be affected by this monopoly pricing.¹¹⁸² This tradeoff was highlighted in the theoretical work of Nordhaus and echoed by numerous researchers.¹¹⁸³ In addition, if innovation is cumulative with new innovations building on previous ones, then patents for earlier inventions may also lower the incentives for future investments in R&D for later innovations during the period of market exclusivity.¹¹⁸⁴ Therefore, potential differing effects of patents make it difficult to predict the overall effects of patent protection on innovation and access.¹¹⁸⁵

This section reviews the available evidence on the relationship between patent protection and innovation in the health sector, and the relationship between patent protection and access to medicine. While the topics are related, the organization of the chapter separates the discussion of innovation and access. The literature on patent protection and innovation in the health sector is organized by the primary research methodology used, starting with descriptive analyses and then model-based analyses. Within the model-based analyses, literature is further organized by cross-country and country-specific analyses and research related to follow-on innovation. The literature on patent protection and access to medicine is organized by the different outcomes related to access.

The TRIPS Agreement requires countries to introduce both process and product patents.¹¹⁸⁶ To estimate the effect of patent protection on innovation or access, researchers have used changes in patent protection offered by countries for both process and product patents. Changes in countries' patent regimes to become compliant with the minimum patent protections outlined in the TRIPS Agreement are commonly used by researchers to study the effect of patent protection on innovation or access.¹¹⁸⁷

There are many reasons why researchers have focused on changes due to the TRIPS Agreement. First, the agreement is a relatively large policy change prior to which many developing countries did not offer patent protection. For countries that did provide some patent protection, these protections were often expanded. For example, prior to the TRIPS Agreement, India allowed only process patents on pharmaceuticals, meaning that a producer could produce the same pharmaceutical product if it

¹¹⁸² Monopoly pricing refers to the higher prices that a firm may charge if they are the only supplier, compared to a competitive market with many firms offering the pharmaceutical product.

¹¹⁸³ Nordhaus did not focus specifically on the health sector. Nordhaus, "An Economic Theory of Technological Change," May 1969, 18–28.

¹¹⁸⁴ Scotchmer, "Standing on the Shoulders of Giants," March 1991, 29–41.

¹¹⁸⁵ Moser, "Patents and Innovation: Evidence from Economic History," February 2013, 23.

¹¹⁸⁶ For pharmaceutical products, process patents protect the methods used to produce the pharmaceutical. Product patents protect the actual pharmaceutical product no matter the production method.

¹¹⁸⁷ The TRIPS Agreement entered into force on January 1, 1995. Chapter 2 provides more details on the TRIPS Agreement. In addition to the studies on the agreement, some research looks at TRIPS-Plus provisions, which go beyond the TRIPS Agreement or limit some flexibilities of the agreement. Tenni et al. review literature looking at TRIPS-Plus provisions and access to medicine. Tenni et al., "What Is the Impact of Intellectual Property Rules on Access to Medicines?," April 15, 2022, 1–40.

developed a new method of production.¹¹⁸⁸ Following the TRIPS Agreement, India introduced three amendments to the country's patent law, which included product patents on pharmaceuticals in early 2005.¹¹⁸⁹

Second, there are variations in the time periods for country compliance with the TRIPS Agreement, with lower-income countries having longer periods to become compliant with the minimum standards.¹¹⁹⁰ Third, many researchers have argued that these changes in patent regimes due to the TRIPS Agreement are exogenous from the perspective of developing economies, and these changes provide a natural experiment.¹¹⁹¹ Researchers commonly note that many developing economies did not want the increases of patent protection and that developed countries pushed for these increases in patent protection.¹¹⁹² Some studies are more critical of this exogeneity assumption and have attempted to use different econometric techniques to focus on exogenous variation in patent protection changes.

There are some disadvantages of using changes in response to the TRIPS Agreement for studying the effects of patent protection. First, the agreement encompasses a broad range of IP rules that go beyond patent protection. For example, in addition to requiring patents for pharmaceuticals, the agreement also included flexibilities available to countries, such as CLs. This implies that reduced-form econometric estimates are capturing an average effect and not only the effect of patent protection. Moreover, related to the previous discussion on the exogeneity of the TRIPS Agreement, interpretation of empirical results is dependent on the plausibility of the exogeneity of patent protection regimes in response to the agreement. For example, the time at which countries become compliant with the TRIPS Agreement may be non-random, with some countries becoming compliant prior to the deadline and other countries such as India taking the full allowed time.¹¹⁹³

Second, using an indicator variable for changes in the patent regime does not consider the nuances of enforcement of patent protection. Researchers have used the Ginarte-Park Patent Index, along with other indexes, to capture more details of patent protections.¹¹⁹⁴ However, these indexes do not necessarily capture expectations about the status of future patent protection, which can be important for firms' behavior.¹¹⁹⁵ Third, for some countries the patent policy change is more minor, with changes

¹¹⁸⁸ Duggan, Garthwaite, and Goyal, "Market Impacts of Pharmaceutical Product Patents," January 2016, 113.

¹¹⁸⁹ Dutta, "From Free Entry to Patent Protection," February 1, 2011, 162.

¹¹⁹⁰ See boxes 2.1 and 5.3 for more information on the rules for least-developed countries (LDCs).

¹¹⁹¹ An exogenous variable is determined outside of the economic model and is taken as given. From a researcher's perspective, and as noted by Qian, the ideal experiment would be for the availability of patent protection to be randomly assigned to countries. Then the effect of patent protection would simply be a comparison of the mean outcome, such as a measure of innovation, for countries with patents to the mean outcome for countries without patents. However, as these types of experiments are often not possible in the literature for a variety of reasons, researchers often use policy changes to study the outcomes of interest. Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 438.

¹¹⁹² Kyle and McGahan, "Investments in Pharmaceuticals Before and After TRIPS," November 1, 2012, 1157, 1162.

¹¹⁹³ Sampat, "A Survey of Empirical Evidence on Patents and Innovation," December 2018, 12.

¹¹⁹⁴ Liu and La Croix, "The Impact of Stronger Property Rights in Pharmaceuticals," March 12, 2014, 2; Gamba, "The Effect of Intellectual Property Rights on Domestic Innovation," November 2017, 16; Ginarte and Park, "Determinants of Patent Rights," October 1997, 283–301; Park, "International Patent Protection," May 2008, 761–66.

¹¹⁹⁵ Kyle and McGahan, "Investments in Pharmaceuticals Before and After TRIPS," November 1, 2012, 1165.

from 17 years from the patent grant date to 20 years from the patent application date.¹¹⁹⁶ Patent protection increased only for patents with a processing time of less than three years. In addition, most countries separately represent only a small share of the total pharmaceutical market, implying that changes to patent protection may not have a large effect on pharmaceutical firms in other countries.¹¹⁹⁷

Patent Protection and Innovation in the Health Sector

One argument made in favor of patent protection is that new and innovative pharmaceuticals would not be developed without patent protection. For example, Cockburn and Long reviewed the importance of IP rights to biopharmaceutical innovation in the United States.¹¹⁹⁸ The authors noted that patents are often considered essential to the development of new drugs since such drug development is costly, lengthy, and risky and that patents can also serve as a signal to future investors. In contrast, the investment requirements are often substantially lower for generic drugs. In this way, patent protection allows for firms to have market exclusivity for a period of time and collect profits that help to offset these high costs and risks.

However, there are some counterpoints to the importance of patent protection. Boldrin and Levine made the case against patent protection increasing innovation in general.¹¹⁹⁹ For the pharmaceutical industry, the authors noted four features to take into account when considering the roles of patents.¹²⁰⁰ First, patents are one element among the wide range of regulations, such as clinical testing requirements. Second, the first-mover advantage may be larger than what is ordinarily imagined, suggesting that generics may not immediately enter the market even if there were no patent protections. Third, many parts of the development for pharmaceuticals takes place outside of the private sector, implying that firms do not bear the full costs of new drug development. Fourth, the authors argued that there has been a “drought” in the development of new pharmaceutical products even with the availability of patent protection.¹²⁰¹

This section reviews literature that examines the relationship between patent protection and innovation in the health sector, including available information for LICs, LMICs, UMICs, and HICs. Included literature in this section either primarily focuses on the health sector or has some detailed discussion of the health sector. It is difficult to know how more general research on the effects of patents, such as analysis that groups together different industries, would extend to the health sector.¹²⁰² Thus, studies that do not

¹¹⁹⁶ Abrams, “Did TRIPS Spur Innovation?,” June 2009, 1614, 1621.

¹¹⁹⁷ Kyle and McGahan, “Investments in Pharmaceuticals Before and After TRIPS,” November 1, 2012, 1160.

¹¹⁹⁸ In the declaration of interest, the authors noted that the research was supported in part by the Pharmaceutical Research and Manufacturers of America (PhRMA). Cockburn and Long, “The Importance of Patents to Innovation,” July 3, 2015, 739–42.

¹¹⁹⁹ Boldrin and Levine, “The Case against Patents,” February 2013, 3–22.

¹²⁰⁰ Boldrin and Levine, “The Case against Patents,” February 2013, 13–14.

¹²⁰¹ Kyle noted that there was an increase in development of new pharmaceutical products since the article by Boldrin and Levine, where “the number of new molecular entities or biologics approved by the FDA has increased from an average of 25 per year from 2000 to 2013, to more than 38 per year from 2014 to 2020.” Kyle, “Incentives for Pharmaceutical Innovation,” September 1, 2022, 6; Boldrin and Levine, “The Case against Patents,” February 2013, 3–22.

¹²⁰² Gamba, “The Effect of Intellectual Property Rights,” November 1, 2017, 15.

provide health sector-specific analysis are out of scope of the request letter and not included in this section.

Descriptive studies that use firm-level survey data on the role of IP rules generally provide strong support for the importance of patent protection for innovation in the health sector, especially for pharmaceuticals. However, while survey data attempt to provide context on whether patent protection leads to further innovation, this data alone does not establish the causal effect of patent protection. In addition, survey evidence has generally focused on HICs, such as the United States, with less known about LICs, LMICs, and UMICs.

Model-based analysis that uses reduced-form econometrics often finds mixed results on the relationship between patent protection and innovation in the health sector. Some cross-country studies have provided evidence that patent protection supports innovation in the health sector in more developed countries and has little to no effect for innovation in developing countries. Country-specific studies do not always follow these general trends. For example, one study found positive effects of patent protection for India, while another study found no effects for Japan.¹²⁰³ Detailed analyses within countries yield additional important insights. Some studies find that within the United States there is evidence that patents distort innovation away from research with longer time lags, and that patents can have varying effects on follow-on innovation depending on the sector.¹²⁰⁴

Measuring Innovation in the Health Sector

How to measure innovation is a challenge. Innovation could take many forms, such as innovations in the production process or with new products.¹²⁰⁵ Innovations could be physically observable or even unobservable, such as the knowledge of employees. Researchers often proxy for innovation using different measures to provide a sense of the robustness of the relationship with patent protection that they identify. Measures of innovation can generally be classified as inputs into the innovation process, such as R&D spending, or outputs of the innovative process, such as patent counts.¹²⁰⁶ R&D spending and patents are the most common measures of innovation in the literature.¹²⁰⁷ Some other measures of innovation, such as clinical trials, are used and these are discussed when reviewing relevant papers.¹²⁰⁸

R&D Spending as a Measure of Innovation

Various measures of innovation have their advantages and disadvantages. The advantage of using R&D spending as a measure is that the unit of measurement is a currency, which places a potential value on the innovation. However, it could be the case that a firm that spends less on R&D is more innovative than a firm with higher R&D spending if the former firm more efficiently uses its resources. Aggregated

¹²⁰³ Chadha, “TRIPs and Patenting Activity,” March 2009, 499–505; Sakakibara and Branstetter, “Do Stronger Patents Induce More Innovation?,” 2001, 77–100.

¹²⁰⁴ Budish, Roin, and Williams, “Do Firms Underinvest in Long-Term Research?,” July 2015, 2044–85; Galasso and Schankerman, “Patents and Cumulative Innovation,” February 2015, 317–69.

¹²⁰⁵ Bryan and Williams defined innovation as the “invention, development, and diffusion of new goods, services, or production processes.” Bryan and Williams, “Innovation: Market Failures and Public Policies,” 2021, 283.

¹²⁰⁶ Qian, “Do National Patent Laws Stimulate Domestic Innovation,” August 1, 2007, 447.

¹²⁰⁷ Chen and Puttitanun, “Intellectual Property Rights and Innovation in Developing Countries,” December 1, 2005, 483.

¹²⁰⁸ Bryan and Williams, “Innovation: Market Failures and Public Policies,” 2021, 292.

R&D spending for a firm also does not provide insights into the types of inventions that firms are pursuing.¹²⁰⁹ Additionally, obtaining detailed R&D data for a range of products and countries is difficult.¹²¹⁰ R&D data are commonly more available for HICs, although many firms do not publicly disclose their R&D spending.¹²¹¹

For example, Qian used country-level R&D spending data for 23 Organisation for Economic Co-operation and Development (OECD) countries as one measure of innovation.¹²¹² The author also imputed R&D spending for non-OECD countries. As another example, Chadha used firm-level R&D data in India, where disclosure norms required R&D data to be reported by firms only if R&D was more than 1 percent of sales.¹²¹³ However, it is common for firms in developing countries to have R&D spending below the 1 percent threshold, implying many firms are not required to report the R&D data in India.

Using Patent Counts to Measure Innovation

Using patent counts helps alleviate the concern regarding R&D spending and the efficiency of the spending as patents are approved through external government agencies, such as the U.S. Patent and Trademark Office (USPTO). However, it is difficult to measure the value of each patent.¹²¹⁴ Patent policy does not generally separate major and minor innovations.¹²¹⁵ Some studies have used a measure of patents that also incorporates patent citations to better understand each patent's value.¹²¹⁶ Another potential drawback to using patents to measure innovation is that the propensity to patent inventions may vary.¹²¹⁷ In addition, patent data do not capture innovations that may occur outside the patenting system, which historical evidence suggests is important.¹²¹⁸ As with R&D spending data, patent data availability can vary by country.

Some studies have used patents in the United States or Europe to proxy for the innovation in foreign countries by using applicants' country of residence listed on the patent applications. The idea is that the United States and Europe are large markets and innovators would want their innovations to have patent protection in such markets, so patents in these countries should provide an indication of the innovations in other countries.¹²¹⁹

Descriptive Analysis

Firm-level survey results for the United States on firms' views and use of patents have generally implied that patent protection is more important for the pharmaceutical industry than for other industries. In

¹²⁰⁹ Bryan and Williams, "Innovation: Market Failures and Public Policies," 2021, 292.

¹²¹⁰ Lakdawalla, "Economics of the Pharmaceutical Industry," June 2018, 426; Kyle and McGahan, "Investments in Pharmaceuticals Before and After TRIPS," November 1, 2012, 1163.

¹²¹¹ Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 439.

¹²¹² Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 439.

¹²¹³ Chadha, "TRIPs and Patenting Activity," March 2009, 501.

¹²¹⁴ Kyle and McGahan, "Investments in Pharmaceuticals Before and After TRIPS," November 1, 2012, 1163; Liu and La Croix, "The Impact of Stronger Property Rights in Pharmaceuticals," March 12, 2014, 4.

¹²¹⁵ Kyle, "Incentives for Pharmaceutical Innovation," September 1, 2022, 5.

¹²¹⁶ Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 436–53.

¹²¹⁷ Bryan and Williams, "Innovation: Market Failures and Public Policies," 2021, 291.

¹²¹⁸ Moser, "Patents and Innovation: Evidence from Economic History," February 2013, 24, 40.

¹²¹⁹ Gamba, "The Effect of Intellectual Property Rights," November 1, 2017, 20.

their 1981 study, Mansfield, Schwartz, and Wagner used survey data for major firms in the chemical, drug, electronics, and machinery industries in the northeastern United States related to 48 product innovations.¹²²⁰ The authors found that patents in the drug industry impact imitation costs by a larger amount than in other industries. They defined imitation costs as “all costs of developing and introducing the imitative product, including applied research, product specification, pilot plant or prototype construction, investment in plant and equipment, and manufacturing and marketing startup.”¹²²¹ This also includes the costs of inventing an alternative that does not infringe the claims if the innovation is already patented. Each innovating firm was asked if the firm would still introduce the patented innovation if patents were not available, and about half of the patented innovations across all four industries would have not been introduced.¹²²² When excluding drugs from the sample, less than one-fourth of the patented innovations would have not been introduced if patents were unavailable.¹²²³

In a later study, Mansfield used survey data for 100 randomly selected U.S. manufacturing firms.¹²²⁴ The sample covered 12 industries and excluded firms with sales below \$25 million. The survey asked R&D executives for the period between 1981 to 1983 to provide estimates of the proportion of the firm’s inventions that were developed that would have not been developed if patent protection were unavailable and estimates of the proportion of commercially introduced inventions by the firm that would have not been introduced if patent protection were unavailable. The sampled pharmaceutical industry viewed patent protection as more important for the development or introduction of products relative to other industries. For pharmaceuticals, an estimated 65 percent of inventions would have not been introduced and 60 percent would have not been developed if there was no patent protection.¹²²⁵

Levin et al. reported results from the Yale survey regarding R&D appropriability conditions across U.S. industries.¹²²⁶ R&D executives were asked to report the industry’s experiences, and not just the experiences of their firm. This included 650 respondents from 130 lines of business, with at least 10 responses in 18 of the industries. Firms without publicly traded securities were excluded, implying that smaller companies were also likely underrepresented. Relative to other industries with at least 10 survey responses, the pharmaceutical industry had the highest mean score for the effectiveness of process and product patents.¹²²⁷

Cohen, Nelson, and Walsh used the Carnegie Mellon Survey on Industrial R&D in U.S. manufacturing sectors.¹²²⁸ Compared to the Yale survey, the Carnegie Mellon survey included a wider range of firm sizes. The survey covered 1991 to 1993 and received 1,478 responses from R&D labs or units in U.S. manufacturing industries. For the descriptive statistics, the authors focused on firms with at least \$5 million in sales or at least 20 employees in the business unit, which yielded a final sample of 1,165 responses. Compared to other industries, the medical equipment and drugs industries reported patents

¹²²⁰ Mansfield, Schwartz, and Wagner, “Imitation Costs and Patents,” 1981, 907–18.

¹²²¹ Mansfield, Schwartz, and Wagner, “Imitation Costs and Patents,” 1981, 907.

¹²²² The responses cover 31 innovations.

¹²²³ Mansfield, Schwartz, and Wagner, “Imitation Costs and Patents,” 1981, 915.

¹²²⁴ Mansfield, “Patents and Innovation,” 1986, 173–81.

¹²²⁵ Mansfield, “Patents and Innovation,” 1986, 175.

¹²²⁶ Levin et al., “Appropriating the Returns from Industrial Research and Development,” 1987, 783–831.

¹²²⁷ The petroleum refining industry had the same mean score as drugs for process patents. Levin et al., “Appropriating the Returns from Industrial Research and Development,” 1987, 797.

¹²²⁸ Cohen, Nelson, and Walsh, “Protecting Their Intellectual Assets,” February 2000, 1–50.

as being more effective for product innovations.¹²²⁹ However, no industry in the sample reported patents as the most effective method for protecting its competitive advantage. The medical instruments and drugs industries also reported patents as being more effective for process innovations than most other industries.¹²³⁰

Graham et al. summarized the results of the 2008 Berkeley Patent Survey of 1,332 early-stage technology companies founded since 1998 in the United States.¹²³¹ As with the above surveys that excluded smaller companies, the authors also found differences on the importance of patent protection across industries. Health-related sectors commonly used patents and considered them important relative to other sectors. Patents were ranked as more important for biotechnology and medical device industries than for the software industry in terms of a company's ability to capture a competitive advantage from its technology inventions.¹²³²

In addition to surveys in the United States, there have been some other descriptive studies that have generally focused on HICs and also have found evidence for the importance of patent protection for the pharmaceutical industry. For example, Harabi used Switzerland survey data in 1988, building on the Yale survey, that covers 358 Swiss experts and 127 lines of business.¹²³³ The author found that patents were effective in only a few industries, such as the chemical industry that included pharmaceuticals, to protect against imitation of process and product innovations. Taylor and Silberston covered survey results for the United Kingdom.¹²³⁴ For a sample of 25 responding firms on 1968 R&D expenditures, the pharmaceutical industry was reported to be more dependent on patent protection than other industries.¹²³⁵

Related literature for non-HICs has generally focused on India and used qualitative analyses. For example, Horner used interview evidence and showed that the Indian pharmaceutical industry continued to grow after India's introduction of additional patent protection in 2005, additional patent protection required by the TRIPS Agreement.¹²³⁶ Kale and Little used interviews and case studies to show that the Indian pharmaceutical industry has moved from duplicative imitation to creative imitation of products, and that the strengthening of patent laws due to the TRIPS Agreement helped pushed the industry to learn to create its own innovative R&D when patent protection prohibited imitation of new pharmaceuticals.¹²³⁷

¹²²⁹ Cohen, Nelson, and Walsh, "Protecting Their Intellectual Assets," February 2000, 32.

¹²³⁰ Cohen, Nelson, and Walsh, "Protecting Their Intellectual Assets," February 2000, 33.

¹²³¹ Graham et al., "High Technology Entrepreneurs and the Patent System," June 30, 2009, 1255–1327.

¹²³² In software, patents were ranked as the least important for capturing a competitive advantage from technology inventions, and first-mover advantage was ranked as the most important. Graham et al., "High Technology Entrepreneurs and the Patent System," June 30, 2009, 1290.

¹²³³ Harabi, "Appropriability of Technical Innovations an Empirical Analysis," November 1, 1995, 981–92.

¹²³⁴ Taylor and Silberston, *The Economic Impact of the Patent System*, December 6, 1973.

¹²³⁵ Taylor and Silberston, *The Economic Impact of the Patent System*, December 6, 1973, 198–99.

¹²³⁶ Horner, "The Impact of Patents on Innovation, Technology Transfer and Health," May 4, 2014, 384–406.

¹²³⁷ Kale and Little, "From Imitation to Innovation," September 6, 2007, 589–609.

Model-Based Analysis

Cross-Country Analysis

While descriptive analyses are helpful for understanding the relationship between patent protection and innovation, the descriptive analyses do not necessarily identify how patent protection affects innovation in the health sector. To provide more detailed analyses that attempt to isolate the effect of patent protection on innovation in the health sector, model-based procedures control for other related factors that could drive the relationship between patent protection and innovation.

Qian studied the effect of patent protection on pharmaceutical innovations for a sample of 26 countries that established pharmaceutical patent laws between 1978 and 2002.¹²³⁸ The author used reduced-form econometrics that proceeded in two steps. First, the author matched countries with newly established patent laws with countries that did not have patent protection, or with countries that already had patent protection. The 26 countries that enacted pharmaceutical patent protections and the control countries that are used for the matching method yielded a sample of 92 countries. The goal of the country matching was to compare innovation outcomes across countries that were similar in observable characteristics but differed in their patent protection. Country characteristics are much more balanced after matching; however, some characteristics were still statistically different across the country groupings, implying estimates in the second step could potentially capture at least some differences not due to patent protection.

In the second step, Qian performed econometric analysis on the matched countries to identify the effect of patent protection on pharmaceutical innovations.¹²³⁹ The primary measure of innovation by a country, referred to as domestic innovation, is the citation-weighted U.S. pharmaceutical patents which are linked with each country using the country of residence of the listed innovator. As alternative measures of innovation, the author used raw counts of U.S. pharmaceutical patents, pharmaceutical R&D expenditures for a subsample of 23 OECD countries, the number of R&D personnel, imputed R&D values for non-OECD countries, and pharmaceutical exports to the United States.

Using the empirical approach described above, Qian found that national patent laws alone do not stimulate domestic pharmaceutical innovation, on average.¹²⁴⁰ However, the results suggest that patent laws did stimulate domestic pharmaceutical innovation for countries with higher levels of development, education, and economic freedom. While the author does not separate analysis by the income groupings, results suggest that patent protection is more likely to help innovation in HICs compared to LICs, LMICs, and UMICs. In addition, the author provided evidence that after a certain level of IP protection, strengthening IP protections discouraged innovation.¹²⁴¹

Liu and La Croix also studied pharmaceutical patent protection and patenting behavior in the United States for 66 countries from 1985 to 2005.¹²⁴² As a proxy for a country's innovation, they used a variable that indicates whether any U.S. pharmaceutical patents were awarded to the country's citizens and the

¹²³⁸ Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 436–53.

¹²³⁹ Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 436–53.

¹²⁴⁰ Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 436–53.

¹²⁴¹ Qian, "Do National Patent Laws Stimulate Domestic Innovation," August 1, 2007, 450.

¹²⁴² Liu and La Croix, "The Impact of Stronger Property Rights in Pharmaceuticals," March 12, 2014, 1–46.

number of U.S. pharmaceutical patents. The Pharmaceutical Intellectual Property Protection Index is used to measure pharmaceutical patent protection for each country.¹²⁴³ Using reduced-form econometrics, the authors did not find a relationship between patent protection and patenting for developing countries.¹²⁴⁴ For developed countries, they found some evidence of a positive relationship between patent protection and patenting when there are higher levels of education within countries and the economies are more open.

Gamba studied the effect of IP rights on domestic pharmaceutical innovation for 74 countries.¹²⁴⁵ The author used information on the introduction of IP protection or modifying of protections during the 1977–98 period. Unlike Qian, who used patents awarded by the USPTO, Gamba used data on yearly patent applications filed at the European Patent Office.¹²⁴⁶ The author’s primary measure of innovation also used information on patent citations to better measure the innovative value of patents. The reduced-form econometric results suggest that TRIPS Agreement–compliant protection supports innovation, on average.¹²⁴⁷ However, Gamba found that lower levels of patent protection also had a positive effect on innovation like TRIPS Agreement–compliant protection.¹²⁴⁸ In other words, the existence of IP protection may be more important than the degree of protection. Gamba showed that patent applications from developing countries benefited less than developed countries from IP protection, which is also consistent with Qian’s finding that the effect of patent protection on innovation increases with the country’s level of economic development.¹²⁴⁹ Finally, the author showed that the positive effect of patent protection on innovation disappeared after six years, suggesting short-run effects of IP protection on innovation.¹²⁵⁰

Kyle and McGahan build on the work by Lanjouw and Cockburn to study the effect of patent protection from the TRIPS Agreement on new drug development between 1990 and 2006 for 192 countries.¹²⁵¹ The authors hypothesized that if TRIPS Agreement patent protection helped to promote innovation, then there should be more R&D for pharmaceuticals that treat diseases that affect the local population. New clinical trials serve as a measure of R&D effort for pharmaceuticals. Using reduced-form econometrics, TRIPS Agreement patent protection in HICs was associated, on average, with increases in the number of new clinical trials for diseases most prevalent in these countries. For developing countries, the authors did not find greater clinical trials for pharmaceuticals that treat diseases most prevalent in these countries.¹²⁵²

¹²⁴³ Liu and La Croix, “A Cross-Country Index of Intellectual Property Rights in Pharmaceutical Inventions,” February 1, 2015, 206–16.

¹²⁴⁴ Liu and La Croix, “The Impact of Stronger Property Rights in Pharmaceuticals,” March 12, 2014, 1–46.

¹²⁴⁵ Gamba, “The Effect of Intellectual Property Rights on Domestic Innovation,” November 1, 2017, 15–27.

¹²⁴⁶ Qian, “Do National Patent Laws Stimulate Domestic Innovation,” August 1, 2007, 436–53.

¹²⁴⁷ Gamba, “The Effect of Intellectual Property Rights on Domestic Innovation,” November 1, 2017, 15–27.

¹²⁴⁸ Gamba, “The Effect of Intellectual Property Rights on Domestic Innovation,” November 1, 2017, 16.

¹²⁴⁹ Qian, “Do National Patent Laws Stimulate Domestic Innovation,” August 1, 2007, 436–53.

¹²⁵⁰ Gamba, “The Effect of Intellectual Property Rights,” November 2017, 16, 22, 24.

¹²⁵¹ In 2001, Lanjouw and Cockburn concluded that it was too early to determine how the TRIPS Agreement affected new medicines in developing countries. Kyle and McGahan, “Investments in Pharmaceuticals Before and After TRIPS,” November 1, 2012, 1157–72; Lanjouw and Cockburn, “New Pills for Poor People?,” February 1, 2001, 265–89.

¹²⁵² Kyle and McGahan, “Investments in Pharmaceuticals Before and After TRIPS,” November 1, 2012, 1157.

Country-Specific Analysis

While the previous cross-country studies have generally found that patent protection did not promote innovation for developing economies or that the effect was smaller compared to developed countries, there is some evidence that patent activity has responded to patent protection in India. Chadha studied the process patenting activity of 65 Indian pharmaceutical firms between 1991 and 2004.¹²⁵³ Using reduced-form econometrics, the author found that patent activity of Indian pharmaceutical firms increased after the introduction of the new patent regime in India, that was in response to the TRIPS Agreement. One limitation of the analysis is it used the change in India's patent protection in 1999 due to the Patent Amendment Act of 1999 and not the implementation of product patents that were introduced in January 2005.¹²⁵⁴ In addition, India is generally considered a special case since the pharmaceutical industry is larger in India than in other developing countries.

For the United States, Arora, Ceccagnoli, and Cohen used data from the previously discussed Carnegie Mellon survey and estimated the returns to patent protection and how the returns impact firm R&D investment with a structural model.¹²⁵⁵ The estimates suggest that the expected premium of patents' net of patent application costs does not support patenting in most industries. Medical instruments are an exception: They had slightly larger patent premiums than costs. Biotech and pharmaceuticals had a net premium that implied indifference between patenting and not patenting. However, the expected patent premium for the case of innovations that were patented is larger. In health-related industries, such as medical instruments, biotech, and pharmaceuticals, firms with a patented case earned a premium of about 60 percent more than a case with no patenting. When studying how patents impact R&D investments, the estimates imply that increasing the mean of the patent premium distribution would stimulate R&D investments, especially in health-related industries that already have higher patent premiums. The authors noted that the analysis has some limitations. For example, they did not model the impact of patents on entry and the strategic interactions among rivals.¹²⁵⁶

Other country-specific analyses have found that patent protection has not supported innovation in the health sector. Sakakibara and Branstetter examined innovative efforts by Japanese firms following the Japanese reforms in 1988 that expanded the scope of patenting.¹²⁵⁷ They used Japanese and U.S. patent data for 307 Japanese firms. Using reduced-form econometrics, the authors found no evidence of increases in either R&D spending or innovative output directly related to the patent reform. The authors also considered analysis specifically for the pharmaceutical industry, as the Japanese patent reform also included partial-term restoration for drug patents that increased the length of the effective patents. For pharmaceuticals, they also found no significant increase in R&D spending due to the patent reform. One limitation of the pharmaceutical analysis is that it decreases the sample size from 307 to 26 Japanese pharmaceutical firms.

¹²⁵³ Chadha, "TRIPs and Patenting Activity," March 2009, 499–505.

¹²⁵⁴ Government of India, The Patents (Amendment) Act, March 26, 1999.

¹²⁵⁵ The authors excluded firms with less than 10 employees, yielding a sample of 790 R&D units. Arora, Ceccagnoli, and Cohen, "R&D and the Patent Premium," September 2008, 1153–79.

¹²⁵⁶ Arora, Ceccagnoli, and Cohen, "R&D and the Patent Premium," September 2008, 1154, 1173.

¹²⁵⁷ Sakakibara and Branstetter, "Do Stronger Patents Induce More Innovation?," 2001, 77–100.

Scherer and Weisburst studied the effect of Italy's 1978 IP regime change that allowed pharmaceutical product patents.¹²⁵⁸ Using descriptive analysis and simple reduced-form econometrics, the authors concluded that pharmaceutical product patents did not lead to significant changes in the behavior of Italian pharmaceutical manufacturers. However, the analysis did not control for other important determinants of innovation, and the trends are likely correlations and not the causal effect. For example, the authors noted that the Italian government had stringent price controls that could have limited firms' interest in investing in innovative products.¹²⁵⁹

Budish, Roin, and Williams studied whether firms underinvest in long-term research with long time lags from the time of an idea to a commercial product.¹²⁶⁰ The authors developed a theoretical model that shows that short-termism and fixed patent terms are potential sources of distortion that discourage long-term projects.¹²⁶¹ Since many patents are filed at the time of discovery and not the first sale, longer time lags between patent application and commercialization implies the innovator receives shorter effective patent terms. The authors test the hypothesis that firms invest more in late-stage cancer drugs and not enough in early-stage cancer and cancer prevention pharmaceuticals. This builds on the observation that late-stage cancer drugs can reach the market quicker than early-stage and cancer prevention drugs. The empirical analysis used descriptive statistics and reduced-form econometrics to study clinical trials for cancer treatments in the United States between 1973 and 2011. The results suggest that the patent protection provides little incentive for firms to pursue long-term research. Relatedly, Gaessler and Wagner provided reduced-form econometric evidence that firms' willingness to undertake new drug development is sensitive to the time of expected market exclusivity.¹²⁶²

Patent Protection and Follow-On Innovation

Studies have found that patent protection can have important implications for follow-on innovation in the health sector; however, available evidence focuses only on the United States. For example, Gallini reviewed how patents could possibly affect follow-on innovation.¹²⁶³ One view is that strong IP rights may reduce innovation if technology transfer is impeded by earlier patents. Another view is that patents may help with the coordination of new ideas. Overall, Gallini noted that previous studies have provided support that patents do not deter follow-on research for pharmaceuticals.¹²⁶⁴ In addition, Grootendorst et al. discussed that patent protection may increase the costs for the development of new drugs, since innovators need to be cognizant of the patents that already exists on essential research inputs.¹²⁶⁵

¹²⁵⁸ Scherer and Weisburst, "Economic Effects of Strengthening Pharmaceutical Patent Protection in Italy," 1995, 1009–24.

¹²⁵⁹ Scherer and Weisburst, "Economic Effects of Strengthening Pharmaceutical Patent Protection in Italy," 1995, 1023.

¹²⁶⁰ Budish, Roin, and Williams, "Do Firms Underinvest in Long-Term Research?," July 2015, 2044–85.

¹²⁶¹ This highlights a potential disadvantage of having patents as a one-size-fits-all policy.

¹²⁶² Gaessler and Wagner, "Patents, Data Exclusivity, and the Development of New Drugs," May 9, 2022, 571–86.

¹²⁶³ Gallini, "Do Patents Work?," November 2017, 893–926.

¹²⁶⁴ However, the author argued that patents are inadequate for generating new antibiotic drugs. Gallini, "Do Patents Work?," November 2017, 896.

¹²⁶⁵ Grootendorst et al., "New Approaches to Rewarding Pharmaceutical Innovation," April 5, 2011, 681–85.

Murray and Stern conducted one of the first empirical studies on the effect of patent protection on follow-on innovation.¹²⁶⁶ The authors used the concept of dual knowledge to guide their analysis, where a discovery may contribute to scientific research with an academic journal article and be helpful for commercial applications with a separate patent. They used a sample of 340 peer-reviewed life sciences articles between 1997 and 1999 and linked these articles with patents granted by the USPTO. The authors used reduced-form econometrics and estimated changes in citations of scientific articles that are patented to similar articles that are not patented. Overall, the results yield a statistically significant but modest decline in the future article citation rate of about 10 to 20 percent after a patent, which suggest a slight negative effect of patents on follow-on innovation, but the authors do not separate pharmaceuticals for the analysis.¹²⁶⁷

Galasso and Schankerman also studied the effect of patents on follow-on innovation.¹²⁶⁸ Using reduced-form econometrics, the authors estimated the effect of the removal of patent rights on later research efforts through court invalidation in the United States, as measured by later citations related to the focal patent. The authors used the random assignment of judges at the U.S. Court of Appeals for the Federal Circuit to estimate the causal effect. Overall, the results imply that for all industries, patents block follow-on innovation as patent invalidation led to 50 percent more patent citations, on average. The results vary depending on the broad technology field: for health-related industries, patents block later innovation in medical instruments—including biotechnology—but do not block later innovation in drugs.¹²⁶⁹

In a related article, Galasso and Schankerman used a similar empirical strategy and focused on later innovation by the firms that experienced patent invalidation.¹²⁷⁰ The analysis used a five-year window of the patent owner's subsequent patenting activity after invalidation and found that, for all industries, patent invalidation reduced that firm's follow-on innovation, as the firm's future patent applications decreased by 50 percent on average. The authors also considered patenting effects on small firms by different technology fields, showing patent invalidation reduced small firms' follow-on innovation by the largest amount (in absolute value) in the pharmaceuticals category. The effect on follow-on innovation was stronger in the drugs subcategory than genetics and biotechnology. One limitation for both studies is that because of the high costs of litigation, patents that are litigated in the Federal Circuit are commonly high-value patents, implying the sample of patents is likely not representative of the average patent.¹²⁷¹

Sampat and Williams studied whether patents on human genes affect gene-level follow-on innovation in the United States.¹²⁷² They used data on USPTO patent applications covering those applications filed after November 28, 2000, and published by the end of 2013. The measures of follow-on innovation for each gene sequence include the number of scientific publications, number of clinical trials, and

¹²⁶⁶ Murray and Stern, "Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge?," August 1, 2007, 648–87.

¹²⁶⁷ Murray and Stern, "Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge?," August 2007, 648.

¹²⁶⁸ Galasso and Schankerman, "Patents and Cumulative Innovation," February 2015, 317–69.

¹²⁶⁹ Galasso and Schankerman, "Patents and Cumulative Innovation," February 2015, 321–22.

¹²⁷⁰ Galasso and Schankerman, "Patent Rights, Innovation, and Firm Exit," February 9, 2018, 64–86.

¹²⁷¹ Galasso and Schankerman, "Patents and Cumulative Innovation," February 2015, 321.

¹²⁷² Sampat and Williams, "How Do Patents Affect Follow-On Innovation?," January 2019, 203–36.

information on diagnostic tests. Using descriptive statistics and reduced-form econometrics, the authors used two approaches to estimate the effect of patents on follow-on innovation. First, they compared follow-on innovation for genes claimed in accepted applications to those applications abandoned by applicants. The estimates on follow-on innovation were economically small and precisely estimated. Second, the authors used an alternative econometric strategy, and the estimates of follow-on innovation were similar but less precisely estimated. Overall, the two approaches taken together suggest that gene patents did not have important effects on follow-on scientific research or commercial investments. One limitation of the analyses is that the focus is on human genes; the USPTO has more stringent requirements for disclosure of sequenced genetic data that could be important for follow-on innovation.

Gilchrist studied how patent protection for a firm affected subsequent entry of substitute drugs.¹²⁷³ For the analysis, the author used information on pharmacologic classes of new molecular entities. The groupings included drugs that are differentiated at the molecular level but are related in their chemical composition and have similar physiological effects. These groupings of drugs allow for comparison of drugs that are likely viewed as substitutes for prescribers and patients but are differentiated in that each new molecular entity requires clinical trials; patents on one new molecular entity did not prevent entry of other new molecular entities. The final sample included 111 classes, representing 252 drugs, covering new molecular entities approvals in the United States between 1987 and 2011. Using reduced-form econometrics, the author showed that the length of the first entrant's patent protection positively affected subsequent entry within the same drug class. A one-year increase in first-in-class exclusivity was estimated to increase subsequent entry by about 0.2 drugs, on average.¹²⁷⁴

Patent Protection and Access to Medicine

Another potential effect of IP rules is the relationship between patent protection and access to medicine. Compared to other healthcare products, medicines are generally considered to be easier to transport and to distribute.¹²⁷⁵ However, researchers have documented the limited diffusion of medicines across the world. The topic of access to medicine is particularly relevant for lower-income countries that have expressed concerns that patents would increase prices and affect how governments could protect public health.¹²⁷⁶

When studying access to medicine, there are different ways that access could be defined and hence different ways to measure access. Broadly, access to medicine encompasses the accessibility and affordability of medicines.¹²⁷⁷ Accessibility refers to medicine being marketed and sold in the market of interest, while affordability refers to the medicine being sold at prices that consumers in the market can pay given their income.¹²⁷⁸ This section reviews findings in the literature on access to medicine by including studies that cover a range of different outcomes related to accessibility and affordability.

¹²⁷³ Gilchrist, "Patents as a Spur to Subsequent Innovation?," October 2016, 189–221.

¹²⁷⁴ Gilchrist, "Patents as a Spur to Subsequent Innovation?," October 2016, 189, 193, 218.

¹²⁷⁵ Kyle, "Incentives for Pharmaceutical Innovation," September 1, 2022, 1.

¹²⁷⁶ Tenni et al., "What Is the Impact of Intellectual Property Rules?," April 15, 2022, 2.

¹²⁷⁷ Watal and Dai, "Product Patents and Access," July 17, 2019, 3.

¹²⁷⁸ The lack of health insurance available to individuals in many developing countries affects the ability of consumers to pay for medicine. Kyle, "Incentives for Pharmaceutical Innovation," September 1, 2022, 4.

In summary, researchers generally find that patent protection results in higher prices for medicine, where the magnitude of price changes differs by country income groupings and by researchers' methodology. There is little available evidence on the effect of patent protection on pharmaceutical sales. Trade flows of pharmaceuticals are often found to increase because of patent protection, with differences in outcomes depending on the development status of countries and the direction of trade flows. Patent protection has been found to be an important factor for the launch of drugs; patents generally help speed the launch and reduce time lags. The diffusion of medicine tends to be limited in lower-income countries; however, researchers have noted that other factors beyond patent protection are important determinants for this limited diffusion. Finally, there is some evidence for India that patents have negative welfare effects and that implies consumers face the majority of these costs.

Patent Protection and Medicine Prices

The literature generally finds that patent protection was associated with higher drug prices. This is expected because patent protection grants the firm market exclusivity for a period before generics can enter the market. The magnitudes of the price impacts in the literature differ by country income groupings and by researchers' methodology.¹²⁷⁹

Kyle and Qian studied the effect of patent protection for pharmaceuticals on different outcomes related to access of medicine.¹²⁸⁰ The analysis covered 60 countries between 2000 and 2013. The authors used reduced-form econometrics to estimate the effect of patents by grouping pharmaceutical products by whether they had patents before or after the TRIPS Agreement went into effect, compared to pharmaceuticals that were never patented in the country. The authors suggested that the grouping of products was exogenously determined by TRIPS Agreement compliance deadlines. For an alternative approach, they used another econometric approach to attempt to address that patent protection was determined by who applies for the patent and the government that grants the patent. The authors found that, on average, patents were associated with higher drug prices. However, estimates of the price premium for patented drugs was smaller in magnitude for lower-income countries.

Borrell tested the hypothesis that drug prices are higher when patents are available.¹²⁸¹ The author used reduced-form econometrics to study the effect of the availability of patents on human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) drug prices in 34 developing countries between 1995 and mid-2000. By comparing country-drug pairs that had product patent rights to pairs that did not have product patents, the results provide evidence that patents increased the pricing for HIV/AIDS drugs, on average. Data on patents granted were not directly available, so the author used information on the availability of patents or other market exclusivity status. Finally, the results suggest that in countries with patent regimes, pharmaceutical firms start with higher prices and decrease them as time progresses.

¹²⁷⁹ Islam et al. is another literature review on IP protections and access to medicine. Islam et al., "Impacts of Intellectual Property Provisions in Trade Treaties on Access to Medicine in Low and Middle Income Countries: A Systematic Review," December 2019, 1–14.

¹²⁸⁰ Kyle and Qian, "Intellectual Property Rights and Access to Innovation," December 2014, 1–52.

¹²⁸¹ Borrell, "Pricing and Patents of HIV/AIDS Drugs," March 1, 2007, 505–18.

Hellerstein estimated the effect of drug monopolies on pharmaceutical prices for a sample of developing countries.¹²⁸² The data included import prices between 2000 and 2003 for antiretroviral drugs used to treat HIV. The author used African countries that did not have widespread generic antiretroviral availability to proxy for monopolistic markets while countries with widespread availability of antiretroviral generics proxy for competitive markets. Using reduced-form econometrics, the author estimated that markups are \$0.50 higher per capsule for antiretroviral drugs in monopolistic markets compared to those in competitive markets. The estimate controls for cross-country differences in consumers' purchasing power. An advantage of the method is that price-cost markups can be estimated without observable cost data that are difficult to obtain.

Chaudhuri et al. used a structural model to study pharmaceutical price effects of product patents for pharmaceuticals in India.¹²⁸³ The authors used monthly product-level data between January 1999 and December 2000 on the fluoroquinolones subsegment of the systemic antibacterials (i.e., antibiotics), where products were grouped by the presence of the same quinolone molecule and by production by domestic or foreign firms.¹²⁸⁴ To estimate the effect of patent protection, the authors simulated the withdrawal of domestic quinolone product groups from India's market.¹²⁸⁵ The simulations suggest that prices of foreign patented products in India would rise between 100 and 400 percent in the case of no price regulation.

Dutta also developed a structural model to study the effect of patents and price deregulation on pharmaceutical prices in India.¹²⁸⁶ The author used retail sales data for 155 pharmaceutical products covering five broad therapeutic categories between 2001 and 2003 and simulated the effect of patent enforcement and price deregulation for 43 drugs. Simulations estimate that patent enforcement and price deregulation would lead to an average price increase of about 42 percent. One limitation of this analysis is that the patent simulations cannot be compared directly to observed changes in prices after implementation of patent protection in India that is consistent with the TRIPS Agreement, because the agreement did not allow for patent enforcement for generic pharmaceuticals already in the market.

Duggan et al. studied the effects of the enactment of India's product patent system in 2005, as required by the TRIPS Agreement, on different outcomes related to access of medicine.¹²⁸⁷ The authors used aggregate data and longitudinal data that cover more than 6,000 products that contained about 1,000 molecules. The empirical approach used reduced-form econometrics that uses variation in the timing of patent decisions. Overall, the authors estimated positive price effects for molecules that received a patent in India that are statistically significant but economically modest, with an average price increase of 3 to 6 percent, which is smaller than the two previous studies that used structural models. These

¹²⁸² Hellerstein, "What Do Drug Monopolies Cost Consumers in Developing Countries?," July 2012, 108–11.

¹²⁸³ Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1477–1514.

¹²⁸⁴ The quinolone molecules include ciprofloxacin, norfloxacin, ofloxacin, and sparfloxacin. Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1482.

¹²⁸⁵ According to the authors, the "idea here is that had U.S. patents for, say, ciprofloxacin, been recognized in India, all domestic products containing ciprofloxacin would not be present in the market. That would leave only the foreign ciprofloxacin product group in the market." Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1479.

¹²⁸⁶ Dutta, "From Free Entry to Patent Protection," February 1, 2011, 160–78.

¹²⁸⁷ Duggan, Garthwaite, and Goyal, "Market Impacts of Pharmaceutical Product Patents," January 2016, 99–135.

smaller effects for India are likely related to other provisions in the TRIPS Agreement beyond patent protection that were included to try to limit the impact on access to medicine and with challenges of implementing a new patent system and enforcing it.

Patent Protection and Sales of Medicine

The available literature on the effect of patent protection on pharmaceutical sales is limited, and the findings are mixed. Two of the previously discussed studies that estimated price effects also estimated changes in the quantity or sales of pharmaceuticals. Kyle and Qian used reduced-form econometrics and found that patents are associated with higher sales on average for a cross-country sample.¹²⁸⁸ Duggan et al. also used reduced-form econometrics but focused on pharmaceuticals in India.¹²⁸⁹ The authors estimated that following India's patent reform after the TRIPS Agreement entered into force, quantity effects generally experienced a modest decline, but were statistically insignificant. This is consistent with the small price effects that the authors also estimated for India.¹²⁹⁰ Ivus, discussed in the next section, examined how increases in patent rights in developing countries affected exports from developed countries.¹²⁹¹ Using data for 1994–2000, the author estimated that the increase in exports was driven by quantity and not price increases.

Patent Protection and Trade in Medicine

The literature generally finds that patent protection affects trade flows, with increases in the trade of pharmaceutical products in different circumstances. Literature on the effects of patent protection often has found that trade from developed countries to developing countries increased with patent protection. Maskus and Penubarti wrote one of the first papers to study how different international levels of patent protection affected trade flows.¹²⁹² Using data for 77 countries in 1984 and reduced-form econometrics, the authors estimated that greater patent protection increases bilateral imports on average for the sample with all industries.¹²⁹³ For pharmaceuticals, they estimated that patent protection increases trade flows into small and large developing countries.

Ivus examined how increasing patent rights in developing countries affected exports from developed countries during the 1962–2000 period.¹²⁹⁴ The author separately studied developed countries' exports during the pre- (1962–94) and post- (1994–2000) TRIPS Agreement periods using data for 24 OECD countries and 55 developing countries. The author grouped industries into those which are patent-sensitive and patent-insensitive and used colonial origin to attempt to isolate exogenous variation in patents. Using reduced-form econometrics, the author found that, for both periods, increased patent rights in developing countries led to greater exports by patent-sensitive industries in developed

¹²⁸⁸ Kyle and Qian, "Intellectual Property Rights and Access to Innovation," December 2014, 1–52.

¹²⁸⁹ Duggan, Garthwaite, and Goyal, "The Market Impacts of Pharmaceutical Product Patents," January 2016, 99–135.

¹²⁹⁰ The authors also provide evidence that there is a small impact on how many pharmaceutical firms operate in India. Duggan, Garthwaite, and Goyal, "The Market Impacts of Pharmaceutical Product Patents," January 2016, 99, 129.

¹²⁹¹ Ivus, "Do Stronger Patent Rights Raise High-Tech Exports," May 1, 2010, 38–47.

¹²⁹² Maskus and Penubarti, "How Trade-Related Are Intellectual Property Rights?," November 1, 1995, 227–48.

¹²⁹³ The export data covered 22 OECD countries.

¹²⁹⁴ Ivus, "Do Stronger Patent Rights Raise High-Tech Exports," May 1, 2010, 38–47.

countries relative to patent-insensitive industries, on average. The author also conducted similar analyses for each industry separately and found that industries such as medical and pharmaceutical products, which are generally considered to be the most reliant on patent protection, had the strongest effect on exports.

Delgado et al. studied how IP rights in developing countries following the implementation of the TRIPS Agreement affected goods trade for 158 countries between 1993 and 2009.¹²⁹⁵ The authors used reduced-form econometrics to compare knowledge-intensive goods with trade in products that are not IP-intensive. They considered trade between a country and the world and other aggregate trade flows. For all the industries in the sample, the authors found that implementation of TRIPS Agreement rules was associated with an increase in trade of high-IP products, on average. Exports of biopharmaceuticals are estimated to increase for developing countries and HICs, but exports of medical devices are estimated to increase for HICs only. Imports of biopharmaceuticals and medical devices are estimated to increase for HICs, and there is some evidence that imports of medical devices increase in developing countries.

Boring studied U.S. exports of pharmaceutical products to 108 developing countries.¹²⁹⁶ Using reduced-form econometrics with panel data covering 1995–2010, the author provided evidence that TRIPS Agreement-level patent protection had a positive effect on U.S. exports to these developing countries on average. The primary approach used information on whether the destination country had minimum standards of IP protection like those under the TRIPS Agreement.¹²⁹⁷ The empirical analysis also included a free trade agreement indicator variable to attempt to capture the effect of patent protection associated with free trade agreements on U.S. exports. Overall, the author found that free trade agreements do not have a statistically significant impact on U.S. exports of pharmaceutical products after controlling for country characteristics. Just as with the changes in patent protection due to the TRIPS Agreement, free trade agreements also encompass other policy changes, such as tariff changes, beyond changes in only patent protection.

Brunel and Zylkin used highly disaggregated trade and patent data to study the effect of cross-border patents on trade flows.¹²⁹⁸ The data covered 149 countries and 249 industries between 1974 and 2006. The measure of cross-border patents used patents filed in the destination country by an inventor in the origin country, where the authors considered the flow of new patents and stock of patents each year. Overall, using reduced-form econometrics, the authors estimated that cross-border patents increased the patent-filing country's exports to the patent-granting country, on average. The authors estimated a statistically insignificant effect for imports flowing in the opposite direction. For the pharmaceutical industry, the authors estimated that the effect of exports is more than four times larger in magnitude than the baseline estimate that includes all industries, which implies a larger importance of patent protection for pharmaceutical exports.

¹²⁹⁵ Delgado, Kyle, and McGahan, "Intellectual Property Protection and the Geography of Trade," September 2013, 733–62.

¹²⁹⁶ The author refers to the 108 countries as nonadvanced countries. Boring, "The Impact of Patent Protection on US Pharmaceutical Exports," January 6, 2015, 1314–30.

¹²⁹⁷ The author found similar results when using the Ginarte-Park Patent Index on the strength of patent protection. Ginarte and Park, "Determinants of Patent Rights," October 1, 1997, 283–301.

¹²⁹⁸ Brunel and Zylkin, "Do Cross-Border Patents Promote Trade?," February 2022, 379–418.

Co studied the effect of importers' patent protection along with the importers' imitative abilities using reduced-form econometrics.¹²⁹⁹ Data included U.S. exports to 71 countries between 1970 and 1992. The author used the Ginarte-Park Patent Index for the level of patent protection and the share of R&D spending by the importer to proxy for imitative ability.¹³⁰⁰ For R&D-intensive exports, the author found that patent protection helps to offset the negative effects of the importers' imitative ability, but that patent protection alone does not affect U.S. exports. For the drug industry, patent protection also helps to offset negative imitative ability effects, where patent protection on its own decreased U.S. exports. This implies that patent protection alone may not be enough to increase exports, but that the importer's imitation ability also needs to be above a certain level.¹³⁰¹

Patent Protection and Launch of New Medicine

The launch of new medicine around the world is important to the accessibility of medicines. Multinational firms may delay or even avoid launching drugs in countries with lower pricing if they have concerns about implications for pricing in other countries.¹³⁰² The literature has commonly found that patent protection is associated with faster launches of medicine, with some variation in results depending on the type of patent protection and development level of countries. Kyle and Qian, previously discussed, use reduced-form econometrics and found that, on average, patents are associated with an earlier launch of new drug products.¹³⁰³

Lanjouw studied drug launch patterns, such as the likelihood and speed of launch, for 68 countries at different income levels between 1982 and 2002.¹³⁰⁴ Descriptive analyses highlighted that few drugs are launched worldwide, with firms mostly launching drugs first in higher-income countries, especially in Japan. The speed of drug launches varied from a few months to more than 10 years. For the reduced-form econometrics, the author separated the sample by country income groupings. For LICs and MICs, moving from short process patents to a regime with long process patents encouraged entry of drugs within two years.¹³⁰⁵ There is little evidence that product patents increased the likelihood of entry within two years.¹³⁰⁶

For a sample of new chemical entities, Lanjouw estimated that moving from a short process patents regime to one with long process patents, adding short product patents to a regime with short process patents, or the inclusion of long product patents and long process patents are each estimated to have a

¹²⁹⁹ Co, "Do Patent Rights Regimes Matter?," July 30, 2004, 359–73.

¹³⁰⁰ Ginarte and Park, "Determinants of Patent Rights," October 1, 1997, 283–301.

¹³⁰¹ The author noted that "sufficiently high imitation ability sends a signal that domestic firms have the potential to satisfy any unmet domestic demand. This signal acts as an incentive for US exports to increase with importing country's patent regime stringency." Co, "Do Patent Rights Regimes Matter?," July 30, 2004, 368.

¹³⁰² Lanjouw, "Patents, Price Controls, and Access to New Drugs," May 2005, 2.

¹³⁰³ Kyle and Qian, "Intellectual Property Rights and Access to Innovation," December 2014, 1–52.

¹³⁰⁴ Lanjouw, "Patents, Price Controls, and Access to New Drugs," May 2005, 1–72.

¹³⁰⁵ For process and product patents, the author experimented with different thresholds for the "short" and "long" periods, but for the main analysis used less than 15 years for "short" patent terms for lower-income countries and at least 15 years for "long" patent terms. For higher-income countries, the main analysis used less than 20 years for "short" patent terms for higher-income countries and at least 20 years for "long" patent terms. Lanjouw, "Patents, Price Controls, and Access to New Drugs," May 2005, 2–3, 27, 35.

¹³⁰⁶ Lanjouw, "Patents, Price Controls, and Access to New Drugs," May 2005, 30.

positive effect on launch within two years for LICs and MICs.¹³⁰⁷ For launches within 10 years in LICs and MICs, moving from a short process patents regime to a regime with long process patents or adding short product patents to a regime with short process patents increased the likely of launch. Similarly, when estimating the speed of drug launch, adding long process patents or short product patents are each estimated to increase the speed of drug launch for LICs and MICs. For HICs, there is less variation in patent regimes, but the author provided evidence that patent protection increases the likelihood of launch in those countries.

Watal and Dai studied the relationship between the availability of product patent protection and the launch of drugs in 70 markets between 1980 and 2017.¹³⁰⁸ Using reduced-form econometrics, the authors found a positive effect of patents on the launch likelihood of drugs, on average, where this effect is stronger for innovative pharmaceuticals.¹³⁰⁹ They showed that the relationship between patents and the speed of drug launch also varies by disease categories. Separating effects by income levels, they found that HICs had a positive association between patents and drug launches, MICs only had a positive association of patents for innovative medicines, and for LICs there was no statistically significant relationship.

Relatedly, Borrell studied the introduction on new HIV/AIDS drugs in 34 developing countries between 1995 and 1999.¹³¹⁰ Using reduced-form econometrics, the author found that patent regimes are associated with HIV/AIDS drug availability only when countries have more equally distributed incomes. This is consistent with the view that pharmaceutical firms may not want to enter markets that cannot support higher price premiums.

Cockburn, Lanjouw, and Schankerman studied the effect of patent policies on the speed and scope of diffusion, which is discussed in the next section, of new pharmaceutical products across countries.¹³¹¹ The analysis covered 642 new drugs in 76 countries, including all levels of economic development, between 1983 and 2002. The authors first used descriptive statistics and reduced-form econometrics to highlight the limited and slow pace of global diffusion of new drugs. This included both long launch delays of often 10 years or more, and many drugs never being launched outside of a few richer countries.

To further study the timing of drug launches, Cockburn and co-authors used an alternative reduced-form econometric approach and found that both process patents and product patents strongly affect launch lags.¹³¹² On average, relative to no patent protection, a short process patent regime is estimated to reduce launch delays 19 percent, and medium process patent regimes reduces launch delays by

¹³⁰⁷ Lanjouw, "Patents, Price Controls, and Access to New Drugs," May 2005, 1–72.

¹³⁰⁸ Watal and Dai, "Product Patents and Access," July 17, 2019, 1–52.

¹³⁰⁹ The authors used the drug innovation categories developed by Lanthier and co-authors. Lanthier et al., "An Improved Approach to Measuring Drug Innovation," August 2013, 1433–39.

¹³¹⁰ Borrell, "Patents and the Faster Introduction of New Drugs in Developing Countries," May 15, 2005, 379–82.

¹³¹¹ Cockburn, Lanjouw, and Schankerman, "Patents and the Global Diffusion of New Drugs," January 2016, 136–64.

¹³¹² Cockburn, Lanjouw, and Schankerman, "Patents and the Global Diffusion of New Drugs," January 2016, 136–64.

32 percent.¹³¹³ Also, long-duration product patents strongly affected drug diffusion and are estimated to reduce launch delays by 55 percent.¹³¹⁴ The effects of patent regimes were similar when they dropped HICs from the sample. The authors also used an alternative econometric strategy, which generally confirmed the previous results, but found different magnitudes for the estimates.

Patent Protection and Diffusion of Medicine

As covered in the previous section, Cockburn, Lanjouw, and Schankerman highlighted the limited and slow diffusion of new drugs around the world.¹³¹⁵ In addition, some descriptive analysis focused on lower-income countries suggests that patent protection may have not been the primary factor to limit the diffusion of medicine in lower-income countries.

Attaran and Gillespie-White provided descriptive analysis of the relationship between patents and the access for antiretroviral drugs in Africa by testing whether patents were the primary barrier to the diffusion of AIDS treatment in Africa.¹³¹⁶ The authors focused on 15 antiretroviral drugs in 53 African countries and used surveys between October 2000 to March 2001 of major pharmaceutical companies. In the sample, antiretroviral drugs were patented in few African countries (median of 3 countries).¹³¹⁷ The authors noted that many African countries offered patent protection, suggesting that limited patenting activity was likely not driven by the availability of patent protection. In addition, the authors showed that there did not appear to be a correlation between geographic patent coverage in Africa and antiretroviral treatment. The authors suggested that other barriers may be more responsible for limited access to this HIV/AIDS treatment, such as the treatment's high costs, national regulatory requirements, taxes, and limited international financial aid.

In a later study, Attaran focused on the relationship between patents and access to 319 products on the World Health Organization's (WHO) Model List of Essential Medicines.¹³¹⁸ To supplement available data, the author surveyed pharmaceutical companies and their patent agents in 65 countries, which covered all countries in Africa and other countries including Brazil, China, India, Indonesia, Mexico, and Russia. For the sample of 65 low- and middle-income countries, patenting was rare for essential medicines. Only 17 of the products were patentable, and the patent incidence was 1.4 percent and concentrated in larger markets. The author suggested that poverty in developing countries was likely a greater barrier to access of medicines.

¹³¹³ The authors defined "short" patents as those with a patent term duration (from the patent application date) of 12 years or less, "medium" patents as those with a patent term duration of 13 years to 17 years, and "long" patents as those with a patent term duration of 18 years or longer. The authors noted that they experimented with alternative years for these three categories. Cockburn, Lanjouw, and Schankerman, "Patents and the Global Diffusion of New Drugs," January 2016, 144, 152.

¹³¹⁴ Cockburn, Lanjouw, and Schankerman, "Patents and the Global Diffusion of New Drugs," January 2016, 152.

¹³¹⁵ Cockburn, Lanjouw, and Schankerman, "Patents and the Global Diffusion of New Drugs," January 2016, 136–64.

¹³¹⁶ Attaran and Gillespie-White, "Do Patents for Antiretroviral Drugs Constrain Access" October 17, 2001, 1886–92.

¹³¹⁷ A more recent study by Motari et al. also showed the low levels of patenting activity in Africa. Motari et al., "The Role of Intellectual Property Rights on Access," March 11, 2021, 11.

¹³¹⁸ Attaran, "How Do Patents and Economic Policies Affect Access To Essential Medicines In Developing Countries?," May 2004, 155–66.

Jung and Kwon used the WHO's World Health Surveys from 2002 and 2003 to study the effect of IP rights, measured using the Ginarte-Park Patent Index, on individuals' access to medicines in 35 low- and middle-income countries and households' catastrophic expenditure for medicines.¹³¹⁹ To measure access, the authors used responses to questions from the World Health Surveys about access to prescribed medicines. Using reduced-form econometrics, the authors showed that higher levels of IP rights increased the likelihood of not having access to prescribed medicines, on average.

Jung and Kwon also considered results by separating the sample by income levels, but the results were no longer statistically significant for low-income countries (less than \$1,000 GDP per capita).¹³²⁰ The authors noted that low access to healthcare in low-income countries could lead to a sample selection problem because their analysis included only individuals who visited healthcare providers and were prescribed medicine. When studying household catastrophic expenditure for medicines, they do not find a statistically significant effect for the levels of IP rights.¹³²¹ However, the authors noted that many people cannot afford to purchase any medicines due to the high prices and their low purchasing capacity. These households would be excluded from the analysis because the authors focused on households with positive spending for medicines during the last month.

Patent Protection and Welfare Effects

The previously discussed structural models by Chaudhuri et al. and Dutta, which simulated pharmaceutical price effects in India resulting from changes in patent protection, also include estimates of the impact on economic welfare.¹³²² In the case of price regulation that would hold prices fixed at pre-TRIPS Agreement levels, Chaudhuri et al. estimated that total annual welfare losses to the Indian economy would be \$305 million caused by the removal of all domestic products, or about half of the systemic antibacterial sales in 2000.¹³²³ Profit losses for domestic producers in India constituted about \$50 million, implying most of the estimated total welfare loss was from loss of consumer welfare. This suggests that the consumer welfare loss resulting from the reduction of varieties available for consumers under patent protection is important. The authors suggested this as capturing the ease of access because domestic products may be easier for local consumers to access.

An important contribution of the structural model developed by Chaudhuri et al. was that it allowed for a range of different cross-product group substitution effects and cross-molecule substitution effects, which suggested that adding up estimated effects separately for each patentable market may lead to understated effects of consumer welfare losses.¹³²⁴ However, as noted by the authors, one limitation of

¹³¹⁹ Jung and Kwon, "The Effects of Intellectual Property Rights on Access," July 2015, 507–29; Ginarte and Park, "Determinants of Patent Rights," October 1, 1997, 283–301.

¹³²⁰ Jung and Kwon, "The Effects of Intellectual Property Rights on Access," July 2015, 507–29.

¹³²¹ Catastrophic expenditure is defined as out-of-pocket payments for medicine exceeding 40 percent of the household's capacity to afford. Jung and Kwon, "The Effects of Intellectual Property Rights on Access," July 2015, 510–11.

¹³²² Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1477–1514; Dutta, "From Free Entry to Patent Protection," February 1, 2011, 160–78.

¹³²³ In the case of no price regulation, the total annual welfare losses increase to about \$450 million. Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1477–1514.

¹³²⁴ Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1477–1514.

the study is extrapolating the results to other pharmaceuticals that may have different demand structures. Another limitation of the analysis is that the welfare losses focused only on static costs of patent protection and did not address potential dynamic benefits from product innovations.¹³²⁵

Dutta estimated total consumer welfare losses of \$378.5 million, a loss of about 8.5 million patients, and average annual gains of about \$1.4 million per drug to the foreign patent holder.¹³²⁶ As in Chaudhuri et al., consumers bear a relatively high cost of the policies, while the benefit to firms was relatively low. This relatively low benefit to firms was likely related to the global context, where even for a larger pharmaceutical market like India, a single country is fairly small.

The Effects of Compulsory Licenses

The TRIPS Agreement establishes minimum IP protections for WTO members and also includes flexibilities to help promote access to medicine and address concerns that IP protections could limit countries' right to protect public health.¹³²⁷ Among these flexibilities, CLs allow a government to license patented inventions to local firms or itself without the consent of patent owners. This section reviews literature on the impact of CLs on outcomes related to pharmaceutical products, including product access, innovation, and global health. The previous discussion on challenges with measuring innovation in the health sector and access to medicine also apply when studying the effects of CLs. Chapter 5 includes additional information on CLs.

Empirical evidence on the effects of compulsory licensing is limited because it is difficult to separate the effect of CLs from other country and industry characteristics.¹³²⁸ For the available literature on the impact of CLs on pharmaceutical products, researchers have generally found that CLs are associated with decreased pharmaceutical prices and CLs increased the number of people with access to patented products in countries in which they were used.¹³²⁹ In the literature, one study on the United States provided evidence that CLs may encourage innovation with firms that gain necessary knowledge through increased access to patented inventions. Another study on Germany showed that CLs may encourage innovation with the original owners of licensed patents investing more when facing increased competition.¹³³⁰ A study on India estimated that the issuance of CLs can increase consumer welfare.¹³³¹ Still, consumer welfare could decrease if CL policies discourage foreign innovators from entering the

¹³²⁵ The authors noted that profit benefits to foreign producers in the simulation were small, at about \$53 million per year without price regulation and \$19.6 million per year with price regulation in India. Chaudhuri, Goldberg, and Jia, "Estimating the Effects of Global Patent Protection in Pharmaceuticals," December 2006, 1506.

¹³²⁶ Dutta, "From Free Entry to Patent Protection," February 1, 2011, 160–78.

¹³²⁷ See chapter 2 for details of the TRIPS Agreement. World Trade Organization, "Declaration on the TRIPS Agreement and Public Health," November 20, 2001.

¹³²⁸ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 236.

¹³²⁹ Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020, 367–84; Bond and Saggi, "Compulsory Licensing, Price Controls, and Access," July 1, 2014, 217–28; Stavropoulou and Valletti, "Compulsory Licensing and Access to Drugs," January 2015, 83–94.

¹³³⁰ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 231–42; Moser and Voena, "Compulsory Licensing," February 1, 2012, 396–427; Moser, "Patents and Innovation in Economic History," February 2016, 16–17, 26.

¹³³¹ Chatterjee, Kubo, and Pingali, "The Consumer Welfare Implications of Governmental Policies," December 2015, 255–73.

market and domestic firms fail to produce their version of the patented drugs.¹³³² However, the limited empirical evidence regarding the effects of using CLs, even more so than the effects of patent protection, makes it challenging to know how these findings are generalizable to other cases of CLs not studied in the literature or for CLs that may occur in the future.

Compulsory Licenses and Access

As previously mentioned in the section on the effect of patent protection on pharmaceuticals, access to pharmaceutical products broadly encompasses affordability and accessibility. One would expect access to medicine to increase following the use of CLs, but little is known about the actual effect of CLs on improving access to medicine.¹³³³ Urias and Ramani reviewed research on price changes affected by CLs. The authors collected 51 cases of pre- and post-compulsory licensing prices from 15 existing studies.¹³³⁴ These cover the use of 24 CLs in eight countries and 16 different drug formulations, most of which were for treating HIV/AIDS.¹³³⁵ The authors noted that price reductions following CLs range from 6.7 to 98 percent of the original price, with a mean price decrease between 66.2 and 73.9 percent.¹³³⁶ One limitation noted by the authors is the challenge in obtaining price data; for example, 11 of the 24 compulsory licensing events used data that were not from official sources.¹³³⁷ In addition, simple comparisons of prices before and after the use of CLs do not identify the causal effect of CLs on prices.

To help overcome data limitations and empirical challenges, researchers have also used theoretical models to study how CLs may affect access to pharmaceutical products. Bond and Saggi showed that CLs help more local people from a developing country (requestor) access a lower quality version of a patented good when the patent holder from a developed country does not enter the market.¹³³⁸ The authors developed a theoretical model to examine the interaction between a country seeking access to a patented good and the patent holder. In the model, the country seeking access first sets a price control on the patent holder's product. Next, the patent holder has two options: either sell its product in the other country's market or voluntarily license the product to a local firm. Finally, if the patent holder

¹³³² Chatterjee, Kubo, and Pingali, "The Consumer Welfare Implications of Governmental Policies," December 2015, 270.

¹³³³ Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020, 369.

¹³³⁴ Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020, 367–84.

¹³³⁵ The eight countries are Brazil, Ecuador, India, Indonesia, Thailand, Malaysia, Rwanda, and Zimbabwe.

¹³³⁶ The minimum reduction of the original price increases to 15.6 percent if two compulsory licensing events are removed; the authors noted that these reductions were attributed to manufacturer's discounts and not actual CLs. The range for the mean value is due to price variations reported by researchers. Urias and Ramani, "Access to Medicines after TRIPS," December 1, 2020, 373, 381.

¹³³⁷ Tenni et al. also completed a literature review on the impact of IP rules on access to medicine, which included literature focused on CLs. For example, three of the included studies covered the impact of Thailand's implementation of CLs from 2006 to 2008. According to these studies, implementing CLs facilitated greater patient access to the pharmaceutical products, leading to gains in quality-adjusted life years and decreased national healthcare spending. Quality-adjusted life years is a measure that combines information on the length of life and quality of life into a single index. Tenni et al., "What Is the Impact of Intellectual Property Rules?," April 15, 2022, 11–13, 36; Prieto and Sacristán, "Problems and Solutions in Calculating Quality-Adjusted Life Years," December 19, 2003, 1.

¹³³⁸ The authors introduce the assumption of two fictitious countries: the North and the South. The South refers to a developing country seeking access to a patented good. The North refers to a developed country holding the patent. Bond and Saggi, "Compulsory Licensing, Price Controls, and Access," July 1, 2014, 217–28.

did not sell the product and did not license the patent to the local firm, the country seeking access decides whether to issue a CL.

The analysis concluded that there were three main benefits of issuing CLs in the above scenario: CLs helped increase access to a lower-quality version of the patented good; CLs generated pressure on the patent holder to improve the terms of voluntary licensing; and if the patent holder switches from licensing to entering the market, CLs can lead to improvement in the product quality available to consumers.¹³³⁹ Some of the benefits of CLs could be offset if there are delays in accessing the product under the CL compared to shorter times to implement voluntary licensing or market entry by the patent holder.¹³⁴⁰

Stavropoulou and Valletti also constructed a theoretical model to analyze the decision-making process between the patent holder and the country seeking access to a patented good.¹³⁴¹ The authors showed that access depends in large part on the requestor's ability to produce a generic version of the pharmaceutical product. If the costs for the requestor to produce the pharmaceutical product decreases, then CLs become a more credible threat that would result in lower prices in that country. However, if the patent-holding country continues to supply the good at lower prices to the developing country, then the manufacturer has an incentive to cover less of the population to maximize profits at the lower prices. The pharmaceutical product reaches its highest level of access when the CL occurs because the requestor has incentives to cover the widest population as possible.

A limitation for the latter two theoretical studies—Bond and Saggi, and Stavropoulou and Valletti—is they require a series of simplifying assumptions.¹³⁴² For example, they require assumptions related to the existence of two countries, and the sequence and structure of events within the models.

Compulsory Licenses and Innovation

The impacts of CLs on innovation continue to be a debated topic because research on this has been rare.¹³⁴³ Most literature does not focus specifically on the pharmaceutical industry, but on the broader chemical industry. The literature offers two primary hypotheses: either CLs encourage innovation by raising the threat of competition that motivates market leaders to further invest to increase their lead over competitors, or CLs discourage innovation by lowering the expected R&D returns.¹³⁴⁴ For example, Stavropoulou and Valletti used a theoretical model and showed that CLs can undermine innovation incentives.¹³⁴⁵ In the model, however, global welfare increases in many circumstances because the positive access effects may offset the reductions in global R&D.

¹³³⁹ Bond and Saggi, "Compulsory Licensing, Price Controls, and Access," July 1, 2014, 217–28.

¹³⁴⁰ The authors also considered the effects of price controls to be mutually reinforcing with CLs.

¹³⁴¹ Stavropoulou and Valletti, "Compulsory Licensing and Access to Drugs," January 2015, 83–94.

¹³⁴² Bond and Saggi, "Compulsory Licensing, Price Controls, and Access," July 1, 2014, 217–28; Stavropoulou and Valletti, "Compulsory Licensing and Access to Drugs," January 2015, 83–94.

¹³⁴³ Moser noted that it is impossible to predict the effects of CLs on innovation and that historical uses of CLs allow for empirical analysis. Moser, "Patents and Innovation in Economic History," February 2016, 16.

¹³⁴⁴ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 232.

¹³⁴⁵ Stavropoulou and Valletti, "Compulsory Licensing and Access to Drugs," January 2015, 83–94.

Two model-based studies from the literature, covered below, provide evidence that CLs may encourage innovation.¹³⁴⁶ Baten et al. used the example of the Trading with the Enemy Act, which the United States enacted on October 6, 1917, and was followed by Executive Order 2729-A, signed by President Woodrow Wilson October 22, 1917, creating the Office of Alien Property Custodian under the act.¹³⁴⁷ That Custodian had power to confiscate property, including German-owned patents, from anyone whose actions might be considered a possible threat to the war effort. At that time, the United States licensed all of the German-owned patents.¹³⁴⁸

Baten et al. used reduced-form econometrics and historical firm-level data covering 79,591 chemical patents in Germany between 1890 and 1930.¹³⁴⁹ Their findings showed an increase of 30 percent in licensed patents after 1918 by German firms in research fields, which indicated the positive impact of CLs on inventions.¹³⁵⁰ Firm-level patent data analysis showed that the number of research-active firms in research fields with licensing increased significantly. Almost 40 percent of all patents issued after 1918 in fields involving licensing were issued by firms that did not have pre-1918 patents in these fields.¹³⁵¹ The authors argued that by encouraging new competitors to join the market, CLs raised the competitive pressure on the current licensing owner and pushed the current licensing owner to invest more in inventions. In addition, the authors specified that the impact of CLs are more significant in a concentrated industry than in a competitive industry.

Moser and Voena also used the Trading with the Enemy Act to study the impact of CLs on U.S. domestic inventions.¹³⁵² The authors used data from the USPTO, which included 128,953 patents of organic chemicals from 1875 to 1945, and covered 7,248 subclasses, of which 336 had at least one license under the Trading with the Enemy Act. The authors used reduced-form econometrics to examine if CLs impacted the number of annual patents by U.S. domestic chemical firms affected by the Trading with the Enemy Act during the 1875–1939 period. The results showed a 24 to 40 percent increase in domestic inventions by firms in subclasses benefiting from CLs after 1919. When testing the timing effect of CLs, the authors found that the impact took several years to start. The impact became strongest about 1929 and was persistent during the 1930s. The authors argued that those U.S. firms took several years from the acquisition of the German firms' patents under the Trading with the Enemy Act to gain the necessary knowledge in order to create their own domestic patents.

Compulsory Licenses and Global Health

While the relationship between CLs and global health is related to the previous discussion of the effects of CLs on access to pharmaceutical products and innovation, this section covers an additional study that

¹³⁴⁶ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 231–42; Moser and Voena, "Compulsory Licensing," February 1, 2012, 396–427; Moser, "Patents and Innovation in Economic History," February 2016, 16–17, 26.

¹³⁴⁷ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 231–42; Trading with the Enemy Act of 1917 Pub. L. No. 65–91, 40 Stat. 411 (codified as amended at 50 U.S.C. §§ 4301–4341); Exec. Order No. 2729-A, (October 12, 1917).

¹³⁴⁸ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 232.

¹³⁴⁹ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 231–42.

¹³⁵⁰ 1918 is noted as the end of the World War I.

¹³⁵¹ Baten, Bianchi, and Moser, "Compulsory Licensing and Innovation," May 2017, 241.

¹³⁵² Moser and Voena, "Compulsory Licensing," February 1, 2012, 396–427.

estimated the effect of CLs on consumer welfare. Chatterjee et al. focused on studying the welfare effect of differential pricing and voluntary licensing strategies on the dipeptidyl peptidase-4 inhibitor, a new class of oral antidiabetic drugs, in India.¹³⁵³ The authors used the Secondary Stockist Audit as the primary source to construct their dataset on quarterly market shares and prices of 17 molecules of six classes of oral antidiabetic drugs from 2004 to 2011. To estimate the market share of oral antidiabetic drugs, the author used the number of diabetic patients in India. The authors estimated consumer welfare under different compulsory licensing simulations. Results showed that consumer welfare reached the highest level in the scenario when a local firm provided dipeptidyl peptidase-4 inhibitors under a CL. However, consumer welfare could decrease if CL policies discourage foreign innovators from entering the market and domestic firms fail to produce their versions of the patent drugs.¹³⁵⁴ The study confirmed the positive impact of CLs on consumer surplus and raised questions for future research, such as the impact CLs might have on producer surplus and whether price controls are an efficient method of accessing a market under the threat of CLs.

The Effects of the Medicines Patent Pool

The MPP, an institution founded by the United Nations (UN), pools patents across geographical markets and enters into voluntary licenses with producers in eligible countries to increase access to lifesaving medicines for LICs and LMICs, and to facilitate the development of those medicines. The licenses typically include provisions for the licensor to transfer technology to the licensee. Academic literature has not studied the relationship between the MPP and access to COVID-19 diagnostics and therapeutics. Some literature discusses the relationship between the MPP and access to other pharmaceutical products; these studies are reviewed in this section. Overall, studies on the impact of the MPP on pharmaceutical products showed that the MPP increased the share of generic drugs and encouraged technology diffusion.¹³⁵⁵ There is some evidence that the MPP is associated with lower prices for pharmaceuticals. This literature has generally analyzed the case of drugs for HIV/AIDS treatment and emphasizes the positive impacts of the MPP on increasing the diffusion of those drugs.

Martinelli et al. used reduced-form econometrics to show that the MPP was an efficient mechanism for allowing manufacturers to access licenses from originators, providing low-cost versions of patented drugs in more significant amounts.¹³⁵⁶ Their study showed that the MPP raises the share of generics in the global HIV/AIDS drug market. Moreover, the authors emphasized the role of MPP as a channel providing the most updated information on IP rights across countries between originators and generics manufacturers. They argued that asymmetric information on IP rights limits the capability to utilize all available resources.

¹³⁵³ Chatterjee, Kubo, and Pingali, “The Consumer Welfare Implications of Governmental Policies,” December 2015, 255–73.

¹³⁵⁴ Chatterjee, Kubo, and Pingali, “The Consumer Welfare Implications of Governmental Policies,” December 2015, 270.

¹³⁵⁵ Martinelli et al. defined the share of generic drugs as the total number of units sold by generic companies over the total for active pharmaceutical ingredients bought by procurement agencies for a country. The authors estimated it by using reduced-form econometrics. Martinelli, Mina, and Romito, “Collective Licensing and Asymmetric Information,” 2021, 15.

¹³⁵⁶ Martinelli, Mina, and Romito, “Collective Licensing and Asymmetric Information,” 2021, 1–46.

Another study by Morin et al. used a model-based methodology to estimate the impact of the MPP on patient access to two medications for HIV/AIDS treatment, dolutegravir and daclatasvir.¹³⁵⁷ The authors compared the differences in three outcomes using the actual scenario with the MPP and the counterfactual scenario without the MPP across low- and middle-income countries.¹³⁵⁸ The MPP was estimated to increase the number of patient-years with access to dolutegravir by 15.494 million patient-years, decrease the number of deaths by 151,839, and save \$3.074 billion from 2017 to 2032. Similarly, the MPP was estimated to increase the number of patients with access to daclatasvir by 428,244, decrease the number of deaths by 4,070, and save \$107.593 million from 2015 to 2026.

Galasso and Schankerman used data on licensing and sales of HIV/AIDS, hepatitis C, and tuberculosis drugs to investigate the impact of the MPP on generic firms' licensing, entry, and sales of drugs.¹³⁵⁹ The data covered 173 pharmaceutical products from 129 countries between 2005 to 2018. Using reduced-form econometrics, they showed that the MPP increased the sales quantities of pharmaceutical products and was associated with reduced pharmaceutical prices, on average. The MPP raised the probability of licensing by five times, and the impact of the MPP on licensing differed across countries. In smaller, non-sub-Saharan countries, the impact of the MPP on licensing was greater, but in countries with substantial HIV exposure, the effect was smaller.¹³⁶⁰

Research by Wang examined the impact of the MPP on drug diffusion and innovation in HIV drug treatment.¹³⁶¹ The share of generic drugs purchased for each drug, country, and year was used to represent the diffusion of generic HIV drugs.¹³⁶² Using reduced-form econometrics, the author found that adding a drug in the MPP for a country resulted in an increase of about 7 percentage points in the market share of generic drugs within the country. As a robustness check, the author also considered the effects of the MPP on prices and quantity supplied. The estimates suggest that the MPP led to price reductions, that were primarily due to price reductions of generic drugs. Similarly, the positive effects of the MPP on the quantity supplied were mostly driven by increases in generic drugs. The study also identified the impact of the MPP in promoting more clinical trials in firms inside and outside the patent pool and more drug approvals from generic drug firms. As a result, the MPP played a crucial role in cutting licensing costs and providing a new way of marketing in LICs and LMICs.

Research Gaps

Current gaps in knowledge would benefit from further research. This section briefly covers three important research gaps. First, additional research is needed to estimate the causal effect of patent protection, CLs, and the MPP. Some challenges that have limited the ability for researchers to provide

¹³⁵⁷ Morin et al., "The Economic and Public Health Impact of Intellectual Property Licensing," February 1, 2022, 169–76.

¹³⁵⁸ According to the authors, the estimates "relied on assumption at several points, such as the effect of licensing on generic competition, generic competition on price, price on uptake, and uptake on outcomes." Morin et al., "The Economic and Public Health Impact of Intellectual Property Licensing," February 1, 2022, 175.

¹³⁵⁹ Galasso and Schankerman, "Licensing Life-Saving Drugs for Developing Countries," March 2021, 1–47.

¹³⁶⁰ Galasso and Schankerman, "Licensing Life-Saving Drugs for Developing Countries," March 2021, 30.

¹³⁶¹ Wang, "Global Drug Diffusion and Innovation with the Medicines Patent Pool," September 2022, 1–19.

¹³⁶² For the share of generic drugs, the author "divided the number of purchases from generic firms by the total number of purchases for a drug within a country-year." Wang, "Global Drug Diffusion and Innovation with the Medicines Patent Pool," September 2022, 7.

additional analysis include data availability and the difficulty in isolating plausibly exogenous changes in patent regimes or changes in the use of CLs and the MPP. While this literature review includes detailed economic analyses that use methods to estimate the causal effect, for many papers—especially those that use descriptive methods—the estimates are correlative, not causal. Additional causal evidence for lower-income countries would be helpful to better understand the potential effects of different IP policies. For example, it is currently unclear how patent protection affects follow-on innovation specifically in developing countries because the follow-on innovation literature has focused on the United States. Future research on the topics covered in this literature review will require researchers to continue to explore innovative and creative ways to study these topics.

Second, the literature reviewed in this chapter does not pinpoint or cover COVID-19 diagnostics and therapeutics specifically. This lack of coverage may change as more data become available. At present, it may be too early for researchers to use information on COVID-19–related patents.¹³⁶³ However, even with increased data availability, separation of the effect of patent protection, CLs, or the MPP from other contemporaneous effects will be challenging.

Finally, there is little research focusing on LDCs. Much of the literature, especially on the effect of patent protection on pharmaceuticals, used changes in patent protection that were implemented as a result of the TRIPS Agreement. For lower-income countries, the agreement established longer periods for the transition of their IP regimes to become compliant with its requirements. That will require additional time so that researchers can further study the effects of the agreement in these countries.¹³⁶⁴ However, the limited availability of detailed data for LDCs will likely continue to be a challenge for researchers.

¹³⁶³ Agarwal and Gaule, “What Drives Innovation?,” March 2022, 4.

¹³⁶⁴ The transition period for LDCs was extended until July 1, 2034. WTO, “WTO Members Agree to Extend TRIPS Transition Period,” June 29, 2021.

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Appendix A Request Letter



THE UNITED STATES TRADE REPRESENTATIVE
EXECUTIVE OFFICE OF THE PRESIDENT
WASHINGTON

December 16, 2022

The Honorable David S. Johanson
Chairman
U.S. International Trade Commission
500 E Street, S.W.
Washington, DC 20436

Dear Chairman Johanson:

COVID-19 is a global health crisis that has killed more than 6 million people, left millions more with long-term physical challenges, and is not yet over. It has also taken a severe economic toll worldwide and, according to the World Bank, aggravated inequality among countries. The pandemic has reinforced the longstanding concern about the sufficiency of access to medicines and, in particular, global inequity in access to medicines. This is not a new concern, but rather one that has persisted since the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) entered into force in 1995.

The HIV/AIDS crisis was perhaps the first global health crisis after the TRIPS Agreement to illustrate the tension between intellectual property rights protection and access to medicines. The TRIPS Agreement struck a balance in which innovators could enjoy, for example, a 20-year patent term, but all governments would enjoy flexibilities with respect to these rules. In the context of patents, these flexibilities include Article 30 (“Exceptions to Rights Conferred”), Article 31 (commonly understood as the article authorizing compulsory licensing), and Article 31*bis*.

In June 2022, Members of the World Trade Organization (WTO) agreed to provide further flexibilities with respect to COVID-19 vaccines, as well as to consider extending those flexibilities to diagnostics and therapeutics. USTR has consulted with Congress and a wide range of stakeholders on the question of extending those flexibilities. The positions are divergent, even on basic questions around whether there is adequate global supply of diagnostics and therapeutics. These interested parties also diverge on whether extending these flexibilities to diagnostics and therapeutics would in fact improve access, particularly in non-high-income countries, or undermine innovation.

To help inform this discussion, given the Commission’s expertise in studying markets and its robust, transparent processes for soliciting input from a wide range of stakeholders, I am asking today that the Commission conduct an investigation and prepare a report under section 332(g) of the Tariff Act of 1930 that, to the extent practicable with available data and information while also identifying where there are significant information gaps:

- Identifies the range of definitions for “diagnostics” and “therapeutics” in the medical field.
- Identifies and defines the universe of existing COVID-19 diagnostics and therapeutics covered by patents as well as COVID-19 diagnostics and therapeutics in development.
- Provides a broad overview of relevant COVID-19 diagnostics and therapeutics, including a description of the products and any intellectual property protections, and containing, to the extent practicable and where data are available:
 - An overview of production and distribution, including key components, the production processes, key producing countries, major firms, operational costs, a description of the supply chain, and the level of geographic diversification within the supply chain;
 - An overview of demand, including key demand factors, an assessment of where unmet demand exists, supply accumulation and distribution, and the impact of the relationship between testing and demand for treatment, if any exists;
 - Information on market segmentation of global demand and consumption, which may be delineated by low-income countries (LICs), lower middle-income countries (LMICs), upper middle-income countries (UMICs), and high-income countries (HICs);
 - Information on availability and pricing (or manufacturing costs in the cases where goods are donated) for COVID-19 diagnostics and therapeutics, if available; and
 - Global trade data for COVID-19 diagnostics and therapeutics or diagnostics and therapeutics in general if specific data are not available.
- Catalogs, to the extent practicable based on available information and a critical review of the literature:
 - The reasons for market segmentation and barriers to a more diverse geographical distribution of the global manufacturing industries for COVID-19 diagnostics and therapeutics;
 - The relationship between patent protection and innovation in the health sector and between patent protection and access to medicine in LICs, LMICs, UMICs, and HICs;
 - Actions taken by WTO Members to use or attempt to use compulsory licenses for the production, importation, or exportation of pharmaceutical products and the outcomes of those actions, including the effect on product access, innovation, and global health;
 - A description of any alternatives to compulsory licensing available to WTO Members, such as voluntary licenses, including through the Medicines Patent Pool (MPP); multilateral programs, including the GlobalFund and United Nations Children's Fund (UNICEF); government-to-government programs; and private-sector donations; and
 - The effect, or lack thereof, of the MPP on access to COVID-19 diagnostics and therapeutics.

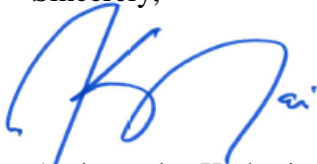
I further request that the Commission, following its usual practice, solicit comments from the public and hold a hearing. In particular, participation from foreign governments, non-

governmental health advocates, organizations such as MPP and Foundation for Innovative New Diagnostics (FIND), and diagnostic and therapeutic manufacturers on these issues is encouraged. I would find public input on the following to be particularly salient:

- How the TRIPS Agreement promotes innovation in and/or limits access to COVID-19 diagnostics and therapeutics;
- Successes and challenges in using existing TRIPS flexibilities;
- The extent to which products not yet on the market, or new uses for existing products, could be affected by an extension of the Ministerial Decision to diagnostics and therapeutics;
- Whether and how existing TRIPS rules and flexibilities can be deployed to improve access to medicines;
- To what extent further clarifications of existing TRIPS flexibilities would be useful in improving access to medicines;
- The relationship between intellectual property protection and corporate research and development expenditures, taking into account other expenditures, such as share buybacks, dividends, and marketing;
- The relevance, if any, of the fact that diagnostic and therapeutic products used with respect to COVID-19 may also have application to other diseases; and
- The location of jobs associated with the manufacturing of diagnostics and therapeutics, including in the United States.

I am not asking the Commission to draw any policy conclusions, but rather I am seeking a robust record with respect to these issues. I ask that you provide this report no later than October 17, 2023.

Sincerely,



Ambassador Katherine Tai

Appendix B

***Federal Register* Notice**

Suitability Assessment was included as an appendix to the park's 2004 General Management Plan, the Assessment remained unfinished until 2022.

NPS will take no action that would diminish the wilderness eligibility of the area found to be possessing wilderness characteristics until the legislative process of wilderness designation has been completed, as required by Chapter 6 of MP 2006. All of the assessed lands remain subject to management in accordance with the NPS Organic Act and all other laws, Executive orders, regulations, and policies applicable to units of the National Park System; the 3,636 acres of ineligible lands will not be subject to the additional requirements of MP 2006 Chapter 6.

If/when a formal wilderness study is conducted to determine which of the eligible lands, if any, should be proposed for inclusion in the National Wilderness Preservation System, tribal consultation will be initiated, as will public review and comment under NEPA and the National Historic Preservation Act.

Charles F. Sams, III,
Director, National Park Service.

[FR Doc. 2023-02469 Filed 2-3-23; 8:45 am]

BILLING CODE 4312-52-P

INTERNATIONAL TRADE COMMISSION

[Investigation No. 332-596]

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

AGENCY: United States International Trade Commission.

ACTION: Notice of investigation and scheduling of a public hearing.

SUMMARY: Following receipt on December 16, 2022, of a request from the U.S. Trade Representative (USTR), under the Tariff Act of 1930, the U.S. International Trade Commission (Commission) instituted Investigation No. 332-596, *COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities*. The USTR requested that the Commission conduct an investigation and prepare a report that analyzes the universe of existing COVID-19 diagnostics and therapeutics in relation to the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement)—including the range of definitions for diagnostics and therapeutics; diagnostics and therapeutics covered by

patents and those in development; an overview of production, distribution, and demand; information on market segmentation of global demand and consumption; and other information relevant to the discussion of TRIPS Agreement flexibilities.

DATES:

March 15, 2023: Deadline for filing requests to appear at the public hearing.

March 17, 2023: Deadline for filing prehearing briefs and statements.

March 22, 2023: Deadline for filing electronic copies of oral hearing statements.

March 29-30, 2023: Public hearing.

April 12, 2023: Deadline for filing posthearing briefs and statements.

May 5, 2023: Deadline for filing all other written submissions.

October 17, 2023: Transmittal of Commission report to the USTR.

ADDRESSES: All Commission offices, including the Commission's hearing rooms, are located in the U.S. International Trade Commission Building, 500 E Street SW, Washington, DC. All written submissions should be addressed to the Secretary, U.S. International Trade Commission, 500 E Street SW, Washington, DC 20436. The public record for this investigation may be viewed on the Commission's electronic docket (EDIS) at <https://edis.usitc.gov>.

FOR FURTHER INFORMATION CONTACT:

Project Leader Philip Stone (202-205-3424 or philip.stone@usitc.gov) or Deputy Project Leader Dixie Downing (202-205-3164 or dixie.downing@usitc.gov) for information specific to this investigation. For information on the legal aspects of this investigation, contact Brian Allen (202-205-3034 or brian.allen@usitc.gov) or William Gearhart (202-205-3091 or william.gearhart@usitc.gov) of the Commission's Office of the General Counsel. The media should contact Jennifer Andberg, Office of External Relations (202-205-3404 or jennifer.andberg@usitc.gov). Hearing-impaired individuals are advised that information on this matter can be obtained by contacting the Commission's TDD terminal on 202-205-1810. General information concerning the Commission may be obtained by accessing its internet address (<https://www.usitc.gov>). Persons with mobility impairments who will need special assistance in gaining access to the Commission should contact the Office of the Secretary at 202-205-2000.

SUPPLEMENTARY INFORMATION:

Background: As requested in the letter received from the USTR on December 16, 2022, the Commission has instituted

an investigation under section 332(g) of the Tariff Act of 1930 (19 U.S.C. 1332(g)) that analyzes the universe of existing COVID-19 diagnostics and therapeutics in relation to the TRIPS Agreement. Specifically, the USTR has requested that the Commission prepare a report that:

- Identifies the range of definitions for "diagnostics" and "therapeutics" in the medical field.

- Identifies and defines the universe of existing COVID-19 diagnostics and therapeutics covered by patents as well as COVID-19 diagnostics and therapeutics in development.

- Provides a broad overview of relevant COVID-19 diagnostics and therapeutics, including a description of the products and any intellectual property protections, and containing, to the extent practicable and where data are available:
 - An overview of production and distribution, including key components, the production processes, key producing countries, major firms, operational costs, a description of the supply chain, and the level of geographic diversification within the supply chain;
 - An overview of demand, including key demand factors, an assessment of where unmet demand exists, supply accumulation and distribution, and the impact of the relationship between testing and demand for treatment, if any exists;
 - Information on market segmentation of global demand and consumption, which may be delineated by low-income countries (LICs), lower middle-income countries (LMICs), upper middle-income countries (UMICs), and high-income countries (HICs);
 - Information on availability and pricing (or manufacturing costs in the cases where goods are donated) for COVID-19 diagnostics and therapeutics, if available; and
 - Global trade data for COVID-19 diagnostics and therapeutics or diagnostics and therapeutics in general if specific data are not available.

- Catalogs, to the extent practicable based on available information and a critical review of the literature:
 - The reasons for market segmentation and barriers to a more diverse geographical distribution of the global manufacturing industries for COVID-19 diagnostics and therapeutics;
 - The relationship between patent protection and innovation in the health sector and between patent protection and access to medicine in LICs, LMICs, UMICs, and HICs;
 - Actions taken by WTO Members to use or attempt to use compulsory

licenses for the production, importation, or exportation of pharmaceutical products and the outcomes of those actions, including the effect on product access, innovation, and global health;

- A description of any alternatives to compulsory licensing available to WTO Members, such as voluntary licenses, including through the Medicines Patent Pool (MPP); multilateral programs, including the GlobalFund and United Nations Children's Fund (UNICEF); government-to-government programs; and private-sector donations; and
- The effect, or lack thereof, of the MPP on access to COVID-19 diagnostics and therapeutics.

The USTR explicitly asked that the Commission solicit input on the above issues from a wide variety of participants, including foreign governments, non-governmental health advocates, organizations such as the MPP and Foundation for Innovative New Diagnostics (FINN), and manufacturers of diagnostics and therapeutics. The USTR stated that input on the following would be particularly salient:

- How the TRIPS Agreement promotes innovation in and/or limits access to COVID-19 diagnostics and therapeutics;
- Successes and challenges in using existing TRIPS flexibilities;
- The extent to which products not yet on the market, or new uses for existing products, could be affected by an extension of the Ministerial Decision to diagnostics and therapeutics;
- Whether and how existing TRIPS rules and flexibilities can be deployed to improve access to medicines;
- To what extent further clarifications of existing TRIPS flexibilities would be useful in improving access to medicines;
- The relationship between intellectual property protection and incorporate research and development expenditures, taking into account other expenditures, such as share buybacks, dividends, and marketing;
- The relevance, if any, of the fact that diagnostic and therapeutic products used with respect to COVID-19 may also have application to other diseases; and
- The location of jobs associated with the manufacturing of diagnostics and therapeutics, including in the United States.

As requested by the USTR, the Commission will deliver the report on October 17, 2023. Since the USTR has indicated that USTR intends to make this report available to the public in its entirety, the Commission will not include confidential business or

national security classified information in its report. However, as detailed below, participants may submit confidential information to the Commission to inform its understanding of these issues, and such information will be protected in accordance with the Commission's *Rules of Practice and Procedure*. Participants are strongly encouraged to provide any supporting data and information along with their views.

Public Hearing: A public hearing in connection with this investigation will be held beginning at 9:30 a.m., March 29, 2023, and continuing, if necessary, on March 30, 2023, in the Main Hearing Room of the U.S. International Trade Commission, 500 E Street SW, Washington DC 20436. The hearing can also be accessed remotely using the WebEx videoconference platform. A link to the hearing will be posted on the Commission's website at <https://www.usitc.gov/calendarpad/calendar.html>.

Requests to appear at the hearing should be filed with the Secretary to the Commission no later than 5:15 p.m., March 15, 2023, in accordance with the requirements in the "Written Submissions" section below. Any requests to appear as a witness via videoconference must be included with your request to appear. Requests to appear as a witness via videoconference must include a statement explaining why the witness cannot appear in person; the Chairman, or other person designated to conduct the investigation, may at their discretion for good cause shown, grant such requests. Requests to appear as a witness via videoconference due to illness or a positive COVID-19 test result may be submitted by 3 p.m. the business day prior to the hearing. All prehearing briefs and statements should be filed no later than 5:15 p.m., March 17, 2023. To facilitate the hearing, including the preparation of an accurate written public transcript of the hearing, oral testimony to be presented at the hearing must be submitted to the Commission electronically no later than noon, March 22, 2023. All posthearing briefs and statements should be filed no later than 5:15 p.m., April 12, 2023. Posthearing briefs and statements should address matters raised at the hearing. For a description of the different types of written briefs and statements, see the "Definitions" section below.

In the event that, as of the close of business on March 15, 2023, no witnesses are scheduled to appear at the hearing, the hearing will be canceled. Any person interested in attending the hearing as an observer or nonparticipant

should check the Commission website as indicated above for information concerning whether the hearing will be held.

Written submissions: In lieu of or in addition to participating in the hearing, interested parties are invited to file written submissions concerning this investigation. All written submissions should be addressed to the Secretary, and should be received no later than 5:15 p.m., May 5, 2023. All written submissions must conform to the provisions of section 201.8 of the Commission's *Rules of Practice and Procedure* (19 CFR 201.8), as temporarily amended by 85 FR 15798 (March 19, 2020). Under that rule waiver, the Office of the Secretary will accept only electronic filings at this time. Filings must be made through the Commission's Electronic Document Information System (EDIS, <https://edis.usitc.gov>). No in-person paper-based filings or paper copies of any electronic filings will be accepted until further notice. Persons with questions regarding electronic filing should contact the Office of the Secretary, Docket Services Division (202-205-1802), or consult the Commission's Handbook on Filing Procedures.

Definitions of types of documents that may be filed; Requirements: In addition to requests to appear at the hearing, this notice provides for the possible filing of four types of documents: prehearing briefs, oral hearing statements, posthearing briefs, and other written submissions.

(1) *Prehearing briefs* refers to written materials relevant to the investigation and submitted in advance of the hearing, and includes written views on matters that are the subject of the investigation, supporting materials, and any other written materials that you consider will help the Commission in understanding your views. You should file a prehearing brief particularly if you plan to testify at the hearing on behalf of an industry group, company, or other organization, and wish to provide detailed views or information that will support or supplement your testimony.

(2) *Oral hearing statements (testimony)* refers to the actual oral statement that you intend to present at the hearing. Do not include any confidential business information (CBI) in that statement. If you plan to testify, you must file a copy of your oral statement by the date specified in this notice. This statement will allow Commissioners to understand your position in advance of the hearing and will also assist the court reporter in preparing an accurate transcript of the hearing (*e.g.*, names spelled correctly).

(3) *Posthearing briefs* refers to submissions filed after the hearing by persons who appeared at the hearing. Such briefs: (a) should be limited to matters that arose during the hearing; (b) should respond to any Commissioner and staff questions addressed to you at the hearing; (c) should clarify, amplify, or correct any statements you made at the hearing; and (d) may, at your option, address or rebut statements made by other participants in the hearing.

(4) *Other written submissions* refers to any other written submissions that interested persons wish to make, regardless of whether they appeared at the hearing, and may include new information or updates of information previously provided.

In accordance with the provisions of section 201.8 of the Commission's Rules of Practice and Procedure (19 CFR 201.8) the document must identify on its cover (1) the investigation number and title and the type of document filed (*i.e.*, prehearing brief, oral statement of (name), posthearing brief, or written submission), (2) the name and signature of the person filing it, (3) the name of the organization that the submission is filed on behalf of, and (4) whether it contains CBI. If it contains CBI, it must comply with the marking and other requirements set out below in this notice relating to CBI. Submitters of written documents (other than oral hearing statements) are encouraged to include a short summary of their position or interest at the beginning of the document, and a table of contents when the document addresses multiple issues.

Confidential business information: Any submissions that contain CBI must also conform to the requirements of section 201.6 of the Commission's Rules of Practice and Procedure (19 CFR 201.6). Section 201.6 of the rules requires that the cover of the document and the individual pages be clearly marked as to whether they are the "confidential" or "nonconfidential" version, and that the CBI is clearly identified by means of brackets. All written submissions, except for CBI, will be made available for inspection by interested parties.

As requested by the USTR, the Commission will not include any CBI in its report. However, all information, including CBI, submitted in this investigation may be disclosed to and used: (i) by the Commission, its employees and Offices, and contract personnel (a) for developing or maintaining the records of this or a related proceeding, or (b) in internal investigations, audits, reviews, and

evaluations relating to the programs, personnel, and operations of the Commission, including under 5 U.S.C. Appendix 3; or (ii) by U.S. government employees and contract personnel for cybersecurity purposes. The Commission will not otherwise disclose any CBI in a way that would reveal the operations of the firm supplying the information.

Summaries of written submissions: Persons wishing to have a summary of their position included in the report should include a summary with their written submission on or before May 5, 2023, and should mark the summary as having been provided for that purpose. The summary should be clearly marked as "summary for inclusion in the report" at the top of the page. The summary may not exceed 500 words and should not include any CBI. The summary will be published as provided if it meets these requirements and is germane to the subject matter of the investigation. The Commission will list the name of the organization furnishing the summary and will include a link where the written submission can be found.

By order of the Commission.

Issued: February 1, 2023.

Katherine Hiner,

Acting Secretary to the Commission.

[FR Doc. 2023-02466 Filed 2-3-23; 8:45 am]

BILLING CODE 7020-02-P

INTERNATIONAL TRADE COMMISSION

[Investigation No. 337-TA-1292]

Certain Replacement Automotive Lamps II; Notice of Request for Submissions on the Public Interest

AGENCY: U.S. International Trade Commission.

ACTION: Notice.

SUMMARY: Notice is hereby given that on January 24, 2023, the presiding administrative law judge ("ALJ") issued an Initial Determination on Violation of Section 337. The ALJ also issued a Recommended Determination on remedy and bonding should a violation be found in the above-captioned investigation. The Commission is soliciting submissions on public interest issues raised by the recommended relief should the Commission find a violation. This notice is soliciting comments from the public only.

FOR FURTHER INFORMATION CONTACT: Lynde Herzbach, Esq., Office of the General Counsel, U.S. International

Trade Commission, 500 E Street SW, Washington, DC 20436, telephone (202) 205-3228. Copies of non-confidential documents filed in connection with this investigation may be viewed on the Commission's electronic docket (EDIS) at <https://edis.usitc.gov>. For help accessing EDIS, please email EDIS3Help@usitc.gov. General information concerning the Commission may also be obtained by accessing its internet server at <https://www.usitc.gov>. Hearing-impaired persons are advised that information on this matter can be obtained by contacting the Commission's TDD terminal on (202) 205-1810.

SUPPLEMENTARY INFORMATION: Section 337 of the Tariff Act of 1930 provides that, if the Commission finds a violation, it shall exclude the articles concerned from the United States unless, after considering the effect of such exclusion upon the public health and welfare, competitive conditions in the United States economy, the production of like or directly competitive articles in the United States, and United States consumers, it finds that such articles should not be excluded from entry. (19 U.S.C. 1337(d)(1)).

The Commission is soliciting submissions on public interest issues raised by the recommended relief should the Commission find a violation, specifically: a limited exclusion order directed to certain replacement automotive lamps imported, sold for importation, and/or sold after importation by respondents TYC Brother Industrial Co., Ltd. of Tainan, Taiwan, Genera Corporation (dba. TYC Genera) of Brea, California, LKQ Corporation of Chicago, Illinois, and Keystone Automotive Industries, Inc. of Exeter, Pennsylvania. Parties are to file public interest submissions pursuant to 19 CFR 210.50(a)(4).

The Commission is interested in further development of the record on the public interest in this investigation. Accordingly, members of the public are invited to file submissions of no more than five (5) pages, inclusive of attachments, concerning the public interest in light of the ALJ's Recommended Determination on Remedy and Bonding issued in this investigation on January 24, 2023. Comments should address whether issuance of the recommended remedial orders in this investigation, should the Commission find a violation, would affect the public health and welfare in

Appendix C

Calendar of Hearing Witnesses

Office of the Secretary



UNITED STATES INTERNATIONAL TRADE COMMISSION

WASHINGTON, DC 20436

PUBLIC HEARING MATERIALS

March 29 and 30, 2023

MEMORANDUM

TO: Docket Services
Office of Administrative Services
Office of the Secretary

FROM: Tyrell T. Burch
Management Analyst

SUBJECT: **PUBLIC** Hearing Materials of March 29 and 30, 2023

RE: Inv. No. 332-596 (COVID-19 Diagnostics and Therapeutics:
Supply, Demand, and TRIPS Agreement Flexibilities)

Attached please find the following **PUBLIC** hearing materials for the above referenced hearing:

- 1.) Memorandum of Record
- 2.) Final Calendar of Witnesses

Office of the Secretary



UNITED STATES INTERNATIONAL TRADE COMMISSION

WASHINGTON, DC 20436

MEMORANDUM OF RECORD

RE: Inv. No. 332-596

CONCERNING: COVID-19 Diagnostics and Therapeutics: Supply, Demand,
and TRIPS Agreement Flexibilities

A public hearing in this investigation was held on:

March 29 and 30, 2023

A copy of the calendar of this hearing is attached. For further information, consult the transcript of the hearing, the exhibits, and the minutes of the Commission.

FILED BY: *Tyrell Burch*
Tyrell Burch
Management Analyst

CALENDAR OF PUBLIC HEARING

Those listed below appeared in the United States International Trade Commission's hearing:

Subject: COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Inv. No.: 332-596

Dates and Times: Wednesday, March 29, 2023 - 9:30 a.m. EDT and Thursday, March 30, 2023 - 9:30 a.m. EDT

Sessions were held in connection with this investigation in the Main Hearing Room (Room 101), 500 E Street, SW., Washington, DC and virtual attendance via Webex.

Wednesday, March 29, 2023

EMBASSY APPEARANCE:

**Embassy of Madagascar
Washington, DC**

Niriniavisoa Marceda Amielle Pelenne, Chargée d'Affaires

PANEL 1:

ORGANIZATION AND WITNESSES:

Advance Medical Technology Association ("AdvaMed")
Washington, DC

Ashley Miller, Executive Vice President

Zachary Rothstein, Executive Director

Alliance for Trade Enforcement ("AFTE")
Washington, DC

Joshua Teitelbaum, Senior Counsel

Biotechnology Innovation Organization ("BIO")
Washington, DC

John Murphy, Chief Policy Officer

Knowledge Ecology International ("KEI")
Washington, DC

James Love, Director

PANEL 1 (continued):

ORGANIZATION AND WITNESSES:

Oxfam America
Washington, DC

Jennifer Reid (remote witness), Senior Advisor, Health and Vaccine Equity

Pharmaceutical Research and Manufacturers of America (“PhRMA”)
Washington, DC

Kevin Haninger, Vice President, International Policy

Public Citizen Access to Medicine
Washington, DC

Peter Maybarduk, Director

Rethink Trade
Washington, DC

Lori Wallach, Director

Third World Network (“TWN”)
Geneva, Switzerland

Sangeeta Shashikant (remote witness), Legal Advisor, Coordinator Development
and Intellectual Property Programme

U.S. Chamber of Commerce (“Chamber”)
Washington, DC

Patrick Kilbride, Senior Vice President, Global Innovation Policy Center

PANEL 2:

ORGANIZATION AND WITNESSES:

Access to Medicine Foundation
Amsterdam, The Netherlands

Jayasree K. Iyer (remote witness), Chief Executive Officer

Eli Lilly and Company (“Lilly”)
Washington, DC

Cynthia Cardona, Associate Vice President for Social Impact

Gilead Sciences (“Gilead”)
Foster City, CA

Anu Osinusi, Vice President, Clinical Development

PANEL 2 (continued):

ORGANIZATION AND WITNESSES:

Initiative for Medicines, Access & Knowledge (“I-MAK”), Inc
New York, New York

Tahir Amin, Co-Executive Director

Melissa Barber
Boston, MA

Melissa Barber (remote witness), PhD candidate, Harvard University

Merck & Co., Inc. (“Merck”)
Rahway, NJ

Gregg Szabo, Vice President and
Global Commercial Leader of Hospital and Infectious Disease

SAB Biotherapeutics, Inc.
Sioux Falls, SD

Eddie J. Sullivan, President and Chief Executive Officer

Vir Biotechnology
San Francisco, CA

Dr. George Scangos (remote witness), Chief Executive Officer

PANEL 3:

ORGANIZATION AND WITNESSES:

Council for Innovation Promotion (“C4IP”)
Washington, DC

Frank Cullen, Executive Director

Health Global Access Project, Inc. (“Health GAP”)
New York, New York

Brook K. Baker (remote witness), Senior Policy Analyst, Health GAP and
Law professor at Northeastern University School of Law

Information Technology and Innovation Foundation (“ITIF”)
Washington, DC

Stephen Ezell, Vice President, Global Innovation Policy

PANEL 3 (continued):

ORGANIZATION AND WITNESSES:

Intellectual Property Owners Association (IPO)
Washington, DC

Daniel Enebo (remote witness), Treasurer

Marc L. Busch
Washington, DC

Marc L. Busch, Professor of International Business, Georgetown University
Edmund A. Walsh School of Foreign service

National Foreign Trade Council (“NFTC”)
Washington, DC

Tiffany Smith, Vice President of Global Trade Policy

Pharmaceutical Industry Labor Management Association (“PILMA”)

Randy G. DeFrehn, Vice President, Policy & Advocacy

Rachel D. Thrasher
Boston, MA

Rachel D. Thrasher (remote witness), Researcher, Boston University
Global Development Policy Center

Richard Wilder
Baltimore, MD

Richard Wilder, Global Health Consultant

Thursday, March 30, 2023

PANEL 4:

ORGANIZATION AND WITNESSES:

Campaign for Access to Medicine, Diagnostics and Devices, India (“CAMD”)
Delhi, India

Prathibha Sivasubramanian (remote witness), Legal Consultant

Conseil sur la santé et l’Académie de Médecine (“COSAMED”)
Goma, The Democratic Republic of Congo

Dr. Elia Badjo (remote witness), Coordinator

PANEL 4 (continued):

ORGANIZATION AND WITNESSES:

Consumers' Association of Penang (“CAP”)
Pulau Pinang, Malaysia

Karina Yong (remote witness), Legal Advisor

Development Alternatives with Women for a New Era (“DAWN”)
Suva, Fiji

Rajnia Rodrigues (remote witness), Campaign Associate

Health Justice Initiative (“HJI”)
Cape Town, South Africa

Fatima Hassan (remote witness), Founder and Director

Initiative for Social and Economic Rights (“ISER”)
Kampala, Uganda

Allana Kembabazi (remote witness), Program Manager

Public Services International (“PSI”)
Accra, Ghana

George Poe Williams (remote witness), Secretary General Emeritus of the National
Health Workers Union of Liberia

Social Watch
Uruguay

Sanya Reid Smith (remote witness), Legal Advisor and Senior Researcher

Third World Network Berhad (TWNB)
Penang, Malaysia

Yoke Ling Chee (remote witness), Executive Director

TWN TRUST India
Delhi, India

Gopakumar Madhavan (remote witness)

PANEL 5:

ORGANIZATION AND WITNESSES:

Adam Mossoff
Arlington, VA

Adam Mossoff, Professor of Law, George Mason University, Antonin Scalia Law School

Center for Medicine in the Public Interest
New York, NY

Peter J. Pitts, President and Co-Founder

David S. Levine and Joshua D. Sarnoff
Chicago, IL

David S. Levine (remote witness), Professor of Law, Elon University School of Law

Duncan Matthews
London, United Kingdom

Duncan Matthews (remote witness), Professor, Queen Mary University of London

Health Action International (“HAI”)
Amsterdam, The Netherlands

Jaume Vidal (remote witness), Senior Policy Advisor, European Projects

Just Treatment
United Kingdom

Aasiya Versi (remote witness), Pharma Organizer

Missing Medicines Coalition
London, United Kingdom

Molly Pugh-Jones (remote witness), Covid-19 Advocacy Officer

Partnership to Fight Infectious Disease (“PFID”)
Washington, DC

Candace DeMatteis, Vice President, Policy & Advocacy

The People’s Vaccine Alliance (“PVA”)
Oxford, United Kingdom

Mohga Yanni-Kamal (remote witness), Policy Co-Lead

Springboard Enterprises
McLean, VA

Natalie Buford-Young, Chief Executive Officer

PANEL 5 (continued):

ORGANIZATION AND WITNESSES:

Incubate Coalition
Washington, DC

John Stanford, Executive Director

PANEL 6:

ORGANIZATION AND WITNESSES:

Aisling Capital LLC
New York, NY

Dennis Purcell, Founder

BioNJ
Trenton, NJ

Debbie Hart, President and Chief Executive Officer

Brazilian AIDS Interdisciplinary Association (“GTPI/ABIA”)
Rio de Janeiro, Brazil

Susana van der Ploeg (remote witness)

Global Colon Cancer Association
Washington, DC

Andrew Spiegel (remote witness), Co-Founder and Chief Executive Officer

Medical IMPACT
Mexico City, Mexico

Giorgio Franyuti (remote witness), Executive Director

Vacunas para la Gente (“PVA LAC”)
Latin American Chapter of the People's Vaccine Alliance
Guatemala City, Guatemala

Sofia Montenegro (remote witness)

The Washington Council on International Trade (“WCIT”)
Seattle, WA

Lori Otto Punke (remote witness), President

- END -

Appendix D

Summary of Views of Interested Persons

Interested persons had the opportunity to file written submissions to the U.S. International Trade Commission (Commission) in the course of this investigation and to provide summaries of the positions expressed in the submissions for inclusion in this report. This appendix contains these written summaries, provided that they meet certain requirements set out in the notice of investigation (see appendix B). The Commission has not edited these summaries. This appendix also contains the names of other interested parties who filed written submissions during this investigation but did not provide written summaries. A copy of each written submission is available in the Commission's Electronic Document Information System (EDIS, <https://www.edis.usitc.gov>), by searching for submissions related to Investigation No. 332-596. In addition, the Commission held a public hearing in connection with this investigation on March 29–30, 2023. The full text of the transcript of the Commission's hearing is also available on EDIS.

Summaries Included in Written Submissions

Access to Medicine Foundation

The COVID-19 pandemic has underscored the challenges facing global health, highlighting longstanding issues regarding access to essential medicines and healthcare treatment – particularly for 80% of the world's population who live in low- and middle-income countries (LMICs). COVID-19 has become a case in point; even though effective vaccines and treatments for the virus have been developed and launched over the last three years, reliable and affordable access to those products is lacking in LMICs. This is despite the fact that the need for these products remains critical worldwide.

For almost two decades, the Access to Medicine Foundation has been assessing how pharmaceutical companies perform on expanding access to medicine in LMICs, with findings published in the Access to Medicine Index and other reports. Through its activities, the Foundation has sought – among other key priorities – to stimulate companies to explore facilitated registration pathways; to engage in voluntary licensing; and to use technology transfers to expand the availability and affordability of their products, including COVID-19 treatments and diagnostics.

Voluntary licensing, often facilitated by intermediaries such as the Medicines Patent Pool (MPP), enables generic versions of patented drugs to be produced under specific terms and conditions. This is one key way that treatments for HIV and Hepatitis have reached millions around the world. More recently, the first voluntary license for a product targeting a non-communicable disease was agreed, and companies have also issued voluntary licenses for several COVID-19 products. However, companies must continue to proactively explore partnerships and collaborations, with entities such as the MPP and Coalition for Epidemic Preparedness Innovations (CEPI), that facilitate the licensing of COVID-19 products, with the ultimate goal of increasing accessibility and fostering global health equity.

Technology transfers are another effective way to empower local manufacturers to efficiently produce high-quality medicines and vaccines, thereby expanding supply and potentially lowering costs for patients. However, the 2022 Index found that the transfers are currently concentrated in a few countries – particularly India, South Africa and Brazil. Transferring technology to manufacturers in a wider range of LMICs would enhance global access.

Regarding the Doha Declaration on the TRIPS Agreement and Public Health, the Foundation calls on companies to commit to TRIPS flexibilities, not only in public statements but also in their actions. For example, it is crucial for companies to eliminate lobbying activities against these issues, including via trade associations – especially during global health emergencies.

The Foundation urges companies to incorporate voluntary licensing and technology transfers in their pandemic preparedness strategies. In addition to expanding access to products that are already on the market, companies should already be planning out how they will expand access to products before they even reach the market – ideally as early as phase II of clinical development. Pharmaceutical companies, governments, and other stakeholders must collaborate to overcome barriers and ensure equitable access to essential healthcare products for all patients, regardless of where they live or their socioeconomic status. The Foundation asks the USITC to take these considerations forward when looking for solutions to trade and IP issues.

Adam Mossoff – George Mason University

If the United States is committed to evidence-based policymaking and the rule of law, it should oppose additional TRIPS waivers for patents on COVID-19 therapeutics and diagnostics. Evidence-based policymaking and the rule of law are essential principles of good governance. These principles make it possible for individuals to know that their rights are protected according to settled rules and institutions, and that these rules are based on evidence. Economists, historians, and legal scholars have consistently demonstrated that innovators and creators drive economic growth and create flourishing societies based on predictable laws and stable institutions that clearly define their rights and duties. Thus, evidence-based policymaking and the rule of law are the key metrics by which to evaluate a proposed one-time waiver of the legal rules and institutions that have driven the global innovation economy, created veritable miracles in modern healthcare, and ultimately led to the historically unprecedented response by the global biomedical industry to the COVID-19 pandemic.

As a matter of evidence-based policymaking, a spokesperson for the European Union stated in 2021 that “there is no evidence that IP rights in any way hamper access to COVID-19-related medicines and technologies.” In fact, reliable and effective patent rights served as the legal platform for massive investments over decades in biotech research and development, in startups like BioNTech and Moderna, and in the creation of licensing agreements and knowledge-sharing agreements that made possible the unprecedented biomedical response to the COVID-19 pandemic. Compared to this clear evidence, there is no evidence that patents obstructed the creation or worldwide distribution of the vaccines that saved millions of lives in the COVID-19 pandemic. In fact, there is now a worldwide glut of vaccines. Distributional inefficiencies and lack of access have been created by national regulatory impediments like trade barriers, lack of distribution infrastructure, or simply the lack of know-how in extremely complex biotech supply chains and manufacturing that are distinct from the technological knowledge secured by patents.

A one-time suspension TRIPS in securing international protections for patent rights also undermines the rule of law, especially when this treaty already sets forth a clear mechanism with balanced substantive protections and requirements in Article 31. Thus, these waivers destabilize the key legal foundation of national patent laws and international treaties that make possible the modern global commercial innovation economy that benefits everyone around the world. This was the legal and institutional

platform that was the launching pad for the unprecedented response by healthcare innovators to COVID-19, and continued waivers threaten to degrade this vital foundation for continued innovation and economic growth. This will ultimately harm the very people for whom the waiver is supposed to help by reducing or eliminating the continued development and distribution of new life-saving vaccines, diagnostics, and therapeutics.

Alliance for U.S. Startups and Inventors for Jobs

USIJ appreciates the opportunity to submit comments pursuant to the U.S. Trade Representative’s request that the U.S. International Trade Commission (“USITC”) conduct a factfinding investigation (“Inv. No. 332-596”) to inform policymakers’ consideration of a possible waiver of intellectual protections for Covid-19 diagnostics and therapeutics under the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). USIJ is a group of inventors, startup companies, venture capitalists, incubators, and research institutions who have come together in the interest of safeguarding our nation’s innovation ecosystem.

Undermining intellectual property protections for Covid-19 diagnostics and therapeutics would have a devastating impact on America’s innovative industries, particularly life sciences, which accounts for an outsized share of U.S. job growth.¹³⁶⁵ Strong, predictable patent protections fueled the development of revolutionary mRNA technology, which allowed firms in the United States and western Europe to produce viable Covid-19 vaccine candidates just days after researchers first sequenced the virus.¹³⁶⁶ Similarly, reliable patent productions enabled firms to make massive investments in the development and production of additional Covid-19 countermeasures, including diagnostics and therapeutics.

Continuing to weaken intellectual property guarantees will undoubtedly leave society far less equipped to respond to future pandemics. Life sciences companies will hesitate to initiate risky vaccine and treatment development projects without assurances that successful products will qualify for a reasonable period of market exclusivity.

More broadly, a waiver extension would signal to all patent-intensive industries -- not just life sciences -- that the United States’ iron-clad commitment to intellectual property is slipping. As the U.S. Patent and Trade Office (“USPTO”) noted in 2022, industries that rely on America’s world-class intellectual property system account for nearly \$8 trillion in gross GDP and contribute as much as 44% of total U.S. employment.¹³⁶⁷ A TRIPS waiver extension could inadvertently trigger a massive outflow of investment from patent-intensive sectors such as clean energy, artificial intelligence, and advanced manufacturing.

A TRIPS waiver extension is clearly a solution in search of a problem. Evidence shows that patents were not to blame for vaccine access issues that arose throughout the pandemic. Rather, access delays were largely due to distribution and administration challenges. The same is true of Covid-19 treatments. There is a global oversupply of Covid-19 treatments, and weakening patent protections would not solve

¹³⁶⁵ <https://ipo.org/wp-content/uploads/2023/01/2023-Patent-300-and-IPO-Top-Patent-Owners-List-FINAL-1.pdf>.

¹³⁶⁶ <https://www.cnn.com/2021/07/03/how-moderna-made-its-mrna-covid-vaccine-so-quickly-noubar-afeyan.htm>.

¹³⁶⁷ <https://www.uspto.gov/about-us/news-updates/latest-uspto-report-finds-industries-intensively-use-intellectual-property-0>.

the logistical and distribution challenges that some countries have faced.¹³⁶⁸¹³⁶⁹ And rather than limiting access to treatments, robust intellectual property protections have enabled the many voluntary licensing agreements that Covid-19 treatment developers have signed with generic manufacturing facilities around the world.¹³⁷⁰ ¹³⁷¹ These agreements have bolstered access to Covid antivirals in over 100 low- and middle-income countries.¹³⁷²

USIJ strongly opposes any attempt to weaken America's fundamental commitment to intellectual property protection both at home and abroad.

Association of the British Pharmaceutical Industry (ABPI)

The ability of innovative biopharmaceutical companies to effectively respond to COVID-19 resulted from years of scientific research and innovation, underpinned by the international intellectual property (IP) system. The World Trade Organisation (WTO) IP waiver for COVID-19 vaccines has failed to provide WTO members with the solutions required to address inequitable access to COVID-19 vaccines and has set a concerning precedent that undermines the international IP framework and innovation in the future. As such, we are of the strong view that agreeing to a TRIPS waiver extension will continue this negative precedent which undermines the crucial innovation that helped the world tackle and recover from the pandemic for the following reasons:

- The COVID-19 IP waiver has not been used since it was introduced and cannot therefore be viewed as fulfilling any purpose as a solution to access.
- As a result of company scale-up efforts, supply of therapeutics exceeds demand, undermining the purported rationale for a waiver.
- Voluntary collaborations on COVID-19 treatments are already in place to support access. The TRIPS waiver extension jeopardises such partnerships and discourages voluntary technology transfer.
- There is no globally agreed definition for what constitutes a 'COVID-19 therapeutic'. This means that a TRIPS waiver extension could have significant ramifications or unintended consequences on a broad range of products, disincentivising investment into crucial research and development efforts. This could have significant effects on future global health and pandemic preparedness.
- An extension complicates global regulatory processes, adding unnecessary burden on national regulatory authorities by creating a complicated landscape which must then be mapped to ensure effective global pharmacovigilance.

¹³⁶⁸ <https://geneva-network.com/research/5-five-reasons-the-trips-waiver-should-not-be-expanded-to-covid-therapeutics/>.

¹³⁶⁹ <https://ifpma.org/insights/is-an-extension-of-the-trips-waiver-needed-for-covid-19-tools/>.

¹³⁷⁰ <https://geneva-network.com/research/5-five-reasons-the-trips-waiver-should-not-be-expanded-to-covid-therapeutics/>.

¹³⁷¹ <https://ifpma.org/insights/is-an-extension-of-the-trips-waiver-needed-for-covid-19-tools/>.

¹³⁷² <https://www.merck.com/news/the-medicines-patent-pool-mpp-and-merck-enter-into-license-agreement-for-molnupiravir-an-investigational-oral-antiviral-covid-19-medicine-to-increase-broad-access-in-low-and-middle-income-countries/>.

WTO members should instead concentrate on creating multilateral solutions to help eliminate trade barriers and establish the logistical and health system frameworks needed to enhance country readiness for global public health emergencies. These include removing the trade barriers on products/inputs required for the manufacturing and distribution of COVID-19 therapeutics; strengthening health workforces; increasing public awareness regarding COVID-19 medical countermeasures; improving logistical processes for treatments; and supporting voluntary licensing.

Finally, if the TRIPS waiver is extended, there is a high chance that this negative precedent will spread to other areas of industrial policy and innovation, such as climate change and green technology.

The ABPI encourages all governments to ensure that their position on the TRIPS waiver extension is evidence-based and we are pleased to see this effort by the US ITC to gather data and evidence on the potential impact of the TRIPS waiver extension. The voice of the U.S. is crucial in this debate, and we hope that the U.S. Government opts to support a growing number of countries in opposing the TRIPS waiver extension.

Bayh-Dole Coalition

The Bayh-Dole Coalition is a diverse group committed to protecting the landmark Bayh-Dole Act of 1980, which has enabled transformative U.S.-led technologies and economic growth. Collectively, the coalition is concerned that an expanded waiver under the WTO TRIPS Agreement would undermine the Bayh-Dole system, which relies on strong intellectual property protections. The waiver decision will have a profound impact on U.S. innovation and determine whether our nation will remain at the forefront of cutting-edge research and development.

The Bayh-Dole system, which allows universities and nonprofits to own their inventions, patent them and license the IP rights to private-sector partners, has proved its reliability during the Covid-19 pandemic. Life science companies, research universities, and federal laboratories were able to work together to develop lifesaving Covid-19 vaccines, treatments, and diagnostics in record time.

Suspending IP rights would destroy confidence in the Bayh-Dole system and undermine incentives for companies to license new scientific research from university researchers. The investment calculus is clear: Developing just one successful medicine costs around \$2 billion and up to 10 years to develop, and only 12 percent of those entering clinical trials ultimately receive FDA approval for patient use.¹³⁷³

¹³⁷⁴ ¹³⁷⁵

While the government plays a vital role in supporting university-led research, private firms shoulder the cost burden of developing licensed discoveries and bringing new drugs to market. They spend three times more on drug development than the National Institutes of Health (NIH), and account for nearly 70 percent of total medical and health R&D funding in the United States.¹³⁷⁶

But no firm will license a university's patented technology and dedicate billions of dollars towards its further development and commercialization if the government could seize patent rights on a whim. The pipeline for promising, but risky, areas of research would dry up quickly.

¹³⁷³ <https://csdd.tufts.edu/csddnews/2018/3/9/march-2016-tufts-csdd-rd-cost-study>

¹³⁷⁴ http://www.fdareview.org/approval_process.shtml

¹³⁷⁵ <https://www.cbo.gov/publication/57126>

¹³⁷⁶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9440766/>

This wholly unnecessary suspension of a landmark global agreement -- TRIPS -- ignores the real sources of uptake challenges and will not increase access to Covid-19 products around the world. The current TRIPS vaccine waiver was proposed as a way to address low vaccination rates in some developing countries, despite no evidence of IP-related supply shortages. The core problems were hesitancy and logistical challenges on the ground, none of which had to do with IP protections. The same situation applies for Covid-19 treatments and diagnostics, with supply now exceeding demand and IP enabling -- rather than hindering -- product availability.

Expanding the TRIPS waiver would not only jeopardize U.S. leadership in producing new medicines, but it would also enable competitors such as Russia and China to steal our technology and pilfer our research. This would set a dangerous precedent and open the door for the same strategy to be used for energy, environmental, and other critical technologies our rivals want to copy.

The United States must reject efforts to weaken our innovative ecosystem by expanding the TRIPS waiver. Our ability to defeat the crises of today and tomorrow -- for people around the world -- depends on it.

Biotechnology Innovation Organization (BIO)

Through the collective research efforts of the global innovative biotechnology community, there have been over 800 independent therapeutic R&D programs initiated since the beginning of the pandemic. The global IP framework has enabled this lifesaving innovation and provides a reliable legal foundation for companies to enhance research collaborations and explore voluntary technology transfer and licensing arrangements around the world. Existing voluntary research and manufacturing agreements for COVID-19 therapeutics have contributed to a scenario where supply of therapeutics exceeds global demand.

As innovative therapeutics have become available, breakdowns in health system infrastructure around the world impeding the efficient delivery of COVID-19 therapeutics have become more apparent. Proponents of an IP waiver myopically point to IP rights as the barrier to access while ignoring genuine public health challenges that frustrate the distribution of therapeutics. Modernizing health system infrastructure, eliminating trade barriers, improving regulatory frameworks, and ensuring robust testing and therapeutic procurement initiatives are measures that can promote global public health without undermining the IP rights system.

With news of the WHO declaring the end of the COVID-19 public health emergency on May 5, 2023 and with global supply of therapeutics far exceeding demand, a waiver is wholly unnecessary. Nevertheless, proponents of the waiver continue to point to IP as a barrier to access. Countries like India and China, which actively compete with the U.S. for biotech leadership and investment dollars, are predictably supportive of this IP waiver -- a scenario which makes U.S. support for this policy all the more baffling. Proponents' incessant pursuit and prioritization of the waiver demonstrates a lack of concern with improving public health bottlenecks affecting the distribution of existing therapeutics. Rather, proponents are keen on leveraging the pandemic to achieve a goal that has been decades in the making -- the radical undermining of the existing global IP rights system.

U.S. support of a policy which points to IP rights as a barrier to the access of COVID-19 therapeutics around the world undermines the American biotech sector and compromises U.S. leadership in the life

sciences. This would be a disservice to science and the ecosystem that enables cutting-edge R&D around the world. It also has significant ramifications to the U.S. economy and workers.

Due to the inherent risk brought on by the waiver, companies will receive less private investment in a shrinking market, while being incentivized to scale back R&D programs – threatening American jobs and the pipeline of U.S.-driven biotech innovation. This disruption of the existing investment and research landscape will have a particularly acute impact on U.S.-based SMEs, which account for over 87% of COVID-19 therapeutic development programs. Collectively, the U.S. biotech sector employs, directly and indirectly, approximately 12.5 million people resulting in a \$2.9 trillion impact to the U.S. economy. The sector, and the IP underpinnings which enable its success, should therefore be viewed as critical components for economic recovery in the eventual post-pandemic context.

In conclusion, a waiver is unnecessary and only succeeds in emboldening U.S. competitors, undermining U.S. leadership, and jeopardizing future pandemic preparedness efforts.

Cámara Argentina de Especialidades Medicinales (CAEME)

1. Introduction

The COVID-19 pandemic has exposed vulnerabilities in global healthcare systems, requiring the evaluation of existing international agreements to improve access to medicines. The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), established by the World Trade Organization (WTO), has been criticized for potentially impeding access to essential medical treatments during the crisis. However, a closer examination shows that this agreement eased the transfer of technology necessary for tackling down the challenges posed by the pandemic as well as that the TRIPS Agreement did not create barriers to medicines during the COVID-19 pandemic.

The TRIPS Agreement promotes the development of new pharmaceutical products and processes.

2. TRIPS and Public Health Emergencies

The TRIPS Agreement incorporates several provisions that allow governments to respond to public health emergencies (i.e.: compulsory licenses).

Argentina incorporates compulsory license provisions in its Patent Law. Also, COVID19 triggered a health emergency declaration in Argentina, which would have allowed the grant of compulsory licenses. However, not a single petition for compulsory license has ever been filed in relation to COVID-19.

Moreover, there has not been a single case in Argentina during the COVID-19 pandemic where any Intellectual Property Right (IPR) has been considered as a barrier for the treatment and/or access to medicines or treatments.

3. Voluntary Technology Transfer

Contrary to claims that the TRIPS Agreement hindered technology transfer, several pharmaceutical companies voluntarily shared their intellectual property and technology with other manufacturers to accelerate the production of COVID-19 vaccines and treatments.

In Argentina several tech transfer agreements were entered into during the COVID-19 pandemic, but two agreements stand from the rest. The most relevant agreement was entered in August 2020 between AstraZeneca and mAbxience, a local biotechnology company, for the production of the main component of AstraZeneca's vaccine.¹³⁷⁷ Also, Laboratorios Richmond, a local generic laboratory, entered into an agreement with Gamaleya Institute for manufacturing Sputnik vaccine.¹³⁷⁸

4. Main problems related to access to medicines during COVID-19

The problems in terms of access to medicines during COVID-19 were mainly related to: (i) Supply Constraints, (ii) Logistical Challenges, and (iii) Export restrictions. In this respect, Argentina suffered as a consequence of export restrictions imposed by the US, which caused a significant delay in the production and distribution of AstraZeneca's vaccine.¹³⁷⁹

5. Conclusion

Contrary to the assertions that the TRIPS Agreement created barriers to access to medicines during the COVID-19 pandemic, it is evident that the agreement's flexibilities, voluntary technology transfer, global collaboration, and protection of intellectual property rights have fostered the development, production, and distribution of life-saving treatments and vaccines. While challenges undoubtedly remain in ensuring universal access, the TRIPS Agreement has played a significant role in facilitating global cooperation and addressing the health needs of nations during this unprecedented crisis.

Cámara Industrial de Laboratorios Faarmacéuticos Argentinos

Supply-chain disruptions, inadequate manufacturing capabilities, and limited technology transfer were the primary barriers to accessing COVID-19 vaccines, therapeutics, and diagnostics. While IP was not a significant barrier during the initial stages, it could become a severe limitation in the future. Specific abuses of the patent system such as patent thickets, evergreening, and product-hopping among other unfair practices are a serious matter of concern.

¹³⁷⁷ Ministerio de Relaciones Exteriores, Comercio Internacional y Culto, (August 15, 2020) "El presidente Alberto Fernández anunció que Argentina producirá la potencial vacuna COVID-19," from <https://cancilleria.gob.ar/es/actualidad/noticias/el-presidente-alberto-fernandez-anuncio-que-argentina-producira-la-potencial> (translation: "President Alberto Fernández announced that Argentina will produce a potential COVID-19 vaccine". (last visited May 4, 2023).

¹³⁷⁸ <https://www.argentina.gob.ar/noticias/sputnik-v-el-instituto-gamaleya-aprobo-el-primer-lote-de-dosis-producidas-en-la-argentina>.

¹³⁷⁹ <https://www.cronista.com/economia-politica/demoradas-las-vacunas-de-alberto-y-su-par-de-mexico-llegarian-entre-abril-y-mayo/>.

CILFA acknowledges the unprecedented collaboration between governments and industry that drove the development of COVID-19 treatments, with IP protection playing a secondary role. Cooperation between governments and private sector companies through advanced purchase agreements, public funding for development/testing/production, supply chain corrections, and expediting regulatory authorities' approval processes has been essential in developing medical technologies to address the COVID-19 pandemic.

Considering Argentina's successful utilization of TRIPS flexibilities, CILFA recognizes the importance of balancing IP regulations and safeguarding such flexibilities, which could be further clarified and expanded. Intellectual Property is not an end in itself but only an instrument among many others to promote development and public welfare. TRIPS "flexibilities" are legal instruments that countries can apply according to their national development plans and within the mandatory rules of international instruments. This "margin of maneuver" ensures a balance between intellectual property and the public good, all in light of the objectives and principles provided for in Articles 7 and 8 of the TRIPS Agreement.

Therefore, CILFA supports the extension of the June 17, 2022, WTO Ministerial Decision on the TRIPS Agreement to include COVID-19 therapeutics and diagnostics. Intellectual Property is and will be a barrier to access to COVID-19 therapeutics and diagnostics, affecting mainly the least developed and developing countries. This extension will help ensure access to these crucial treatments for all those in need.

Campaign for Access to Medicines, Diagnostics and Devices, India (CAMD-India)

WHO continues to highlight that COVID-19 response in developing countries remains hobbled as they are unable to provide diagnostics and therapeutics to their populations most in need because these are either unavailable or unaffordable, and this the primary driving force of COVID-19 transmissions.¹³⁸⁰

Some argue that demand is low, but demand is linked to treatments and diagnostics being readily available and affordable which requires production to be diversified and supply options expanded. COVID-19 therapeutics are either widely patented or have multiple pending patent applications. Many of the patents are on new use or new forms of old re-purposed drugs, a "patent evergreening" strategy often used by Big Pharma to extend their monopolies. Diagnostic companies also typically file many patents, with patent thickets being a key concern. This situation hinders generic competition, and consequently availability of affordable COVID-19 pharmaceuticals.

Developing countries with manufacturing capacity have the ability to supply other developing countries to address their needs. However, as patents on existing and potential COVID-19 diagnostics and therapeutics proliferate, compulsory license (CL), a critical TRIPS flexibility has to be used to address patent barriers and enable production and supply of generic versions.

A major challenge in using CL is the constant pressure from trading partners especially the US. After the grant of CL for a kidney cancer drug that reduced the cost of treatment by 97% and saved many lives,

¹³⁸⁰ See pg. 4 <https://www.who.int/publications/i/item/WHO-WHE-SPP-2022.1> and [https://www.who.int/news/item/30-01-2023-statement-on-the-fourteenth-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-coronavirus-disease-\(covid-19\)-pandemic](https://www.who.int/news/item/30-01-2023-statement-on-the-fourteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic).

India was placed on US' Priority Watch List, while the Special 301 Report stated that the US will closely monitor CL developments in India. In another instance, India considered CL to promote access to dasatinib, a leukaemia drug that Bristol-Myers Squibb priced at \$108 per day, in a country with GNI per capita of \$1,570. The USTR was widely reported to have pressured India and the license was blocked.¹³⁸¹ These types of action are inconsistent with WTO rules, jeopardise the ability of developing countries to protect public health, and especially disastrous when responding to health emergencies.

These actions by the US discourage the use of CL in countries with manufacturing capacity, affecting public health in India and beyond, although CL is a legitimate TRIPS flexibility which the US itself relies on regularly to address its national needs.

While more recently, the USTR has acknowledged the right of all countries to use CL, it has to do much more to eliminate political and trade pressures that undermine the use of TRIPS flexibilities especially CLs and instead to encourage their use in support of equitable access. A first step would be for the US to support extending the TRIPS Decision to therapeutics and diagnostics.

Waiver of Article 31(f) is a key feature of the TRIPS Decision which is time-bound and only for developing countries. It offers a better solution than Article 31bis of TRIPS, which is subject to a labyrinth of procedures, that deters generic manufacturers from supplying other developing countries. The Decision also contains useful clarification with respect to Article 39.3 of TRIPS.

Center for Medicine in the Public Interest

The Center for Medicine in the Public Interest (CMPI) is a nonprofit, nonpartisan research and educational organization that seeks to advance the discussion and development of patient-centered health care. CMPI strongly opposes the proposed extension of the intellectual property waiver – under the TRIPS Agreement – to include Covid-19 diagnostics and therapeutics. The TRIPS waiver is inconsistent with long-standing commitments to promoting innovative solutions that advance medical progress, reduce health disparities, extend life and make health care more affordable, preventive, and patient-centered.

The waiver rests on a fundamental misunderstanding of the causes of access issues for Covid-19 vaccines, therapeutics, and diagnostics. IP, quite simply, did not – and does not – restrict patient access to lifesaving medicines.

On the contrary, strong IP protections incentivize the costly research, development, and global distribution of cutting-edge medicines of all stripes. New medicines can require upwards of \$3 billion in private capital to go from discovery to FDA approval. When life science companies commit these sums to a promising candidate, they do so with the surety – provided by the United States' strong IP legal system – that they will be able to recoup their investment. If this surety is undermined by a misguided waiver, medical innovation – and patients here in the United States and around the world – will face a hostile, uncertain future.

The pandemic provides an illustrative case study. Moderna and Pfizer, working with BioNTech, synthesized their mRNA vaccine candidates just two days after Chinese researchers published the

¹³⁸¹See, https://www.msf.org/sites/msf.org/files/doha_11-2001.pdf.

genetic sequence of Covid-19. It took less than a year for life science firms to get shots in the arms of the most vulnerable among us, and by April 2021 nearly everyone had access to cutting-edge American vaccines. The speed at which American life science firms were able to deliver Covid-19 vaccines testifies to the confidence provided by the United States' iron-clad commitment to IP protections. As researchers and policymakers around the globe observed, access to lifesaving Covid-19 vaccines was hampered by logistical challenges – not IP protections. Severe supply chain roadblocks alone nearly derailed the rollout, as shortages and scaling difficulties restricted manufacturing capacity. Export-import controls and tariffs were key factors in the early scale-up, too, given that Covid-19 vaccines were assembled from hundreds of components sourced internationally.

Once vaccines cleared customs and were ready to be unpacked from cold-storage, "last-mile" distribution challenges reared their ugly head – particularly in rural and underserved regions. Doctors, nurses, and technicians were also forced to confront endemic vaccine hesitancy in their patients.

Distribution and hesitancy proved to be the determinative limitations to access, not IP protections. Rather, biopharmaceutical firms followed a long-established, salutary precedent in engaging with voluntary licensing and technology transfer for Covid-19 vaccines. The life sciences industry inked more than 370 separate manufacturing and licensing deals to expand access to lifesaving medicines in low and middle-income countries.

The bottom line is clear. IP has not driven access disparities, and undermining U.S. commitments to a reliable legal system for medical innovation and distribution will decrease global patient access to medicines materially.

Christine McDaniel and Alden Abbott - George Mason University

We argue that there is no evidence that IP protections have limited the availability of COVID-19 vaccines and medicines. Accordingly, a waiver of TRIPS IP protections applicable to COVID-19 medicines would be unnecessary. Furthermore, such a waiver would impose harm by reducing incentives for the investment needed to innovate new treatments for COVID-19 and other diseases. In sum, we submit that granting a TRIPS IP waiver for COVID-19 medicines would be unsound public policy.

We raise two key points for the U.S. International Trade Commission's consideration. First, the case of harm due to TRIPS IP protections for COVID-19 medicines has not been proven. For example, there is no evidence that COVID-19 patentees have unreasonably refused licenses to their IPs, or that more facilities could have manufactured a vaccine in short order if they had the IP. Consistent with the nature of these constraints on vaccine availability, there is no evidence that any unmet demand for COVID-19 diagnostics and therapeutics is due to lack of access to patented technology. Instead, the evidence suggests something quite different: key factors explaining the low vaccination rates in developing countries and associated harm from lack of access to vaccines were due to misinformation about COVID-19 and limitations on logistics, transportation, storage (e.g., refrigeration needed to store vaccines), and production (e.g., limitations due to the challenges inherent in producing complex biologics and pharmaceuticals). Hence, there is no case for a TRIPS waiver of IP protection for COVID-19 medicines.

Second, there is substantial evidence that a TRIPS waiver for COVID-19 medicines would impose harm on companies, future innovation, and the provision of healthcare and therapies in both developing countries and industrialized countries, including the United States. As highlighted in the 2020 report by the Council of Economic Advisers, the role of the US patent-based incentive system is essential in bringing forth pharmaceutical products that benefit the entire world, and this role is threatened by foreign price controls. A TRIPS waiver of pharmaceutical patent rights is the ultimate form of underpricing, because it would give third parties access to the costly development of technology *for a price of zero*. Zero pricing would do great damage by reducing incentives for the costly R&D needed to develop future lifesaving innovative vaccines and drugs. Once an unexpected waiver for a major class of drugs and vaccines is granted, the longstanding TRIPS-based understanding that IP rights on future pharmaceutical innovations will be protected is effectively shattered. The inevitable result will be a slowdown in new treatments and cures, to the detriment of patients around the world.

Consumers Association of Penang

Ensuring access to COVID-19 diagnostics and therapeutics heavily relies on their availability and affordability, which are in turn influenced by intellectual property (IP) including patents, as IP impacts supply, prices, and distribution. Across various diseases, generic manufacturing can take place in areas where IP is not a barrier, enabling affordable supply and scaling up of testing and treatment. For example, in the case of HIV, the entry of generic competition led to a significant drop in prices from US\$10,000 per person per year (pppy) to less than US\$100pppy, making treatment affordable and facilitating scale-up. Similarly, there has been scale-up of hepatitis C treatment in developing countries where affordable generic access has been enabled in the absence of patents (e.g., Egypt), or where the patent barriers have been overcome through the use of compulsory licenses (CL) (e.g., Malaysia). Claims by the pharmaceutical industry that there is a lack of demand or that “last mile” factors such as registration, delivery and distribution are the main challenges, are an attempt to downplay the impact of IP on access. Scale-up of HIV and HCV treatments through generic competition reinforces the importance of addressing IP barriers to ensure access.

The TRIPS Agreement and the Doha Declaration on TRIPS and Public Health recognize the potential misuse of the IP system and its impact on access, and thus provide for appropriate measures to be taken. In the case of patents, CL remains a critical public health tool, irrespective of voluntary licenses (which suffer from many limitations including exclusion of many developing countries from supply). The use of CLs has led to significant drops in treatment prices in several cases of more than 90%,¹³⁸² allowing governments to roll out tests and treatments without affecting the sustainability of their public health systems. Developed countries such as the US frequently use CLs for various purposes, including to address COVID-related access needs.¹³⁸³

However, developing countries face challenges in using CLs, such as pressure from trading partners (e.g. from the US, Switzerland, EU) discouraging their use, and the restriction on exports under Article 31(f) of

¹³⁸² See https://www.twn.my/title2/intellectual_property/info.service/2023/ip230202.htm.

¹³⁸³ See Compilation of various materials including articles, case reports and press releases on the use of CL in US, Europe, South and Central America and the Caribbean, Asia Pacific and America at <https://www.keionline.org/cl>; Also see <https://www.keionline.org/wp-content/uploads/KEI-Briefing-Note-2022-2-FAR-52.227-1-SEC-exhibits.pdf> and <https://www.keionline.org/bn-2022-1>.

TRIPS, which hinders the effective use of CL by smaller economies and those with insufficient manufacturing capacity. With respect to the latter point, the solution contained in Article 31bis of TRIPS is cumbersome to use, and thus ineffectual.

Therefore, extending the TRIPS Decision of 17th June 2022 to diagnostics and therapeutics is a crucial step forward in addressing these challenges. It also usefully clarifies that Article 39.3 of TRIPS does not prevent the rapid approval for use of the product produced under the Decision.

Council for Innovation Promotion (C4IP)

The Council for Innovation Promotion is a bipartisan coalition dedicated to promoting strong and effective intellectual property rights that drive innovation, boost economic competitiveness, and improve lives everywhere.

C4IP wholly supports the ITC as a forum for fact-finding. And, on the TRIPS Agreement, the facts are clear. Extensive consultations with relevant experts — and a wealth of data on market dynamics — reveal that extending the current intellectual property waiver on Covid-19 vaccines to diagnostics and therapeutics would prove enormously counterproductive.

More rapid and equitable deployment of COVID-19 products has only ever been limited by logistical, regulatory, and infrastructure challenges. No IP-induced shortages exist. In fact, strong IP has enabled an unprecedented pace of research, development, and production to safely occur at qualified facilities around the world. When companies know their discoveries are protected, they are prepared to share their technological know-how with other entities to save lives.

Indeed, Covid-19 therapeutic manufacturers have signed over 400 voluntary licensing and manufacturing agreements to bolster global accessibility of the treatments. Governments and NGOs have “large stockpiles of treatments going unused” as a result. Meanwhile, diagnostics manufacturers have reported “large surpluses of tests available for order.”

Extending the TRIPS waiver will not add more of either product to the global arsenal. An expanded waiver would, however, strike a severe blow to innovation by calling support for fundamental IP rights into question.

Innovators must be able to obtain meaningfully enforceable patents to attract investments into cutting-edge research and development, commercialize their products, and recoup outlays. This is particularly true within sectors, like life sciences, where innovations demand steep initial investments — to the tune of \$2 billion — and can take a decade to reach the market.

Unfortunately, expanding the TRIPS waiver will stunt these life-saving investments. In the absence of IP protections, it would become far harder for innovative companies to earn commensurate returns.

And while diagnostics, therapeutics, and vaccines manufactured for Covid-19 may be the first products impacted by the global weakening of IP protections, they will not be the last. Further extending the TRIPS waiver’s scope would continue us down a perilous path — one on which the investment incentives required to pursue innovative inquiries are squandered, and other countries can insist on a “right” to a vast range of U.S. patented technologies.

Of equal concern, by allowing other countries to appropriate U.S.-developed technologies, the TRIPS waiver expansion would hamper U.S. global economic competitiveness. Strong IP protection is the backbone of America's innovation ecosystem. Today, IP-intensive U.S. research industries create millions of jobs, improve billions of lives, and generate trillions of dollars in economic activity.

Forcing American innovators to give up valuable technology to other countries, especially those considered adversaries, remains unwise. Any one of them could exploit the technology to further their own objectives at the United States' expense.

The United States imprudently backed the original TRIPS waiver for Covid-19 vaccines, even though no IP-induced shortages existed then either. Let us not make the same mistake twice.

Development Alternatives with Women for a New Era (DAWN)

The Feminists for a People's Vaccine Campaign, hosted by DAWN, is a network of CSOs working in the global South. In our statement, we make a strong case for extending the TRIPS Decision to facilitate timely access to COVID-19 diagnostics and therapeutics, using the example of Brazil.

COVID-19 will remain a serious public health threat in the near future, in Brazil and elsewhere in the world, as it relentlessly churns out new immune-evading variants. As a result, there will be surges in infection and a continuous high death toll. In the last three weeks of March this year, cases and deaths of Severe Acute Respiratory Syndrome across all states in Brazil were rising. 48% of these cases and 83.3% of deaths are attributed to COVID-19. However, tests and treatments continue to remain a challenge.

Voluntary licenses are unable to address the needs of the Latin American region and developing countries. The Medicines Patent Pool (MPP) paxlovid voluntary license excludes 47% of the world's population; countries like Argentina, Brazil, Malaysia and Thailand will not be allowed to buy or produce generic versions.

In March 2022, Brazil's Ministry of Health issued an emergency authorization to purchase 50,000 originator paxlovid treatment courses. Arriving 7 months later, they were inadequate to serve the needs of a universal health care policy. In contrast, the US was able to procure 200 million treatment courses in 2022. Private sector stocks of paxlovid and baricitinib are out of reach for a large majority of Brazil's population. Paxlovid is available at USD 700-900, and Baricitinib has an unaffordable price of USD 900. Another therapeutic, Remdesivir's cost to the public exchequer of over USD 5 billion, over the next 5 years, hampered its access to Brazil's universal public health system.

Enabled by patent monopolies, high prices imposed by pharmaceutical companies are one of the biggest barriers to access, hindering the rollout of test and treat programmes in Latin America and other developing countries. This has also been Brazil's experience during the HIV/AIDS pandemic. IP enabled monopoly over essential medicines, like the antiretroviral drug efavirenz, resulting in the lack of timely access to affordable treatment. After Brazil issued a compulsory license in 2007, reducing USD 237 million in treatment costs until 2012, 30,000 more patients were reached by 2011. This CL did not affect Merck's revenues as it continued to innovate and invest in R&D with Brazil (see here and here).

Universal access to COVID-19 diagnostics and therapeutics are key links to complement vaccination. The extension of the TRIPS decision to diagnostics and therapeutics will enable manufacturers to achieve economies of scale, expand affordable supply options, and provide developing countries with an important tool to facilitate access to existing and improved COVID-19 diagnostics and therapeutics.

Duncan Matthews - Queen Mary University of London

As a World Trade Organization (WTO) member since its inception on 1 January 1995, the United States of America has longstanding obligations under international trade law, including those set out in the provisions of the TRIPS Agreement. At the core of the USA's obligations under the TRIPS Agreement are the Objectives and Principles set out in Articles 7 and 8 which provide inter alia that the protection and enforcement of intellectual property rights should be to the mutual advantage of producers and users of technological knowledge, that WTO members should be able to protect public health, and to promote the public interest. These obligations are underpinned by the WTO Doha Declaration of November 14, 2001, in accordance with which all members, including the USA, agree that the TRIPS Agreement does not and should not prevent members from taking measures to protect public health, and affirms that the TRIPS Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all. On June 17, 2022, in response to the ongoing impact of COVID-19, members adopted a Ministerial Declaration on the WTO on the application of the TRIPS Agreement to the current and future pandemics. This Decision includes clarifications and a limited waiver of certain requirements under the TRIPS Agreement concerning the use of compulsory licenses which are already available under Article 31 of the TRIPS Agreement to permit the production of COVID-19 vaccines. The June 17, 2022, WTO Decision on the TRIPS Agreement is far removed from the TRIPS waiver originally proposed by India and South Africa in October 2020 and which would have entailed a waiver of substantive provisions of the TRIPS Agreement, including setting aside WTO Member obligations to enforce copyright, industrial designs, patents, and the protection of undisclosed information across a range of healthcare technologies. Instead, the June 17, 2022, WTO Decision more closely resembles the EU Communication of June 4, 2021, which was proposed as a safe harbor from the proposals of India and South Africa, and emphasized the availability of compulsory licensing provisions as a policy tool that could be used during a pandemic with targeted and limited clarifications about how and when the use of such compulsory licenses is permitted under WTO law. As such, the often-stated negative effects of a TRIPS waiver as originally proposed by India and South Africa (namely undermining the innovation ecosystem and threatening US jobs and investment) are difficult to sustain given the limited nature of the June 17, 2022, Decision. A rigorous evidence base would be required to sustain an assertion that significant adverse effect would be anticipated if and when the June 17, 2022, WTO Decision is extended to diagnostics and therapeutics. In the absence of such an evidence-base, it is evident that there is low risk that the USA's support for the extension of the June, 17, 2022 WTO Decision to diagnostics and therapeutics would have significant adverse effects.

European Federation of Pharmaceutical Industries and Associations (EFPIA)

After more than three years of the pandemic, there is no evidence that IP has been an access barrier for vaccines or therapeutics. In spite of the decline in COVID-19 cases around the world, further research remains critical given the potential for new variants, the risk that resistance may build up to existing treatments, or that certain individuals may not respond well to therapeutic options available. Innovative biopharmaceutical companies need reassurances that their investments in ongoing and future research will not be undermined by an IP waiver extension.

Building on the actions taken by companies to support global access to COVID-19 vaccines, multiple complementary initiatives for equitable access are already in place for therapeutics: over 150 voluntary licencing agreements (VLAs, including via the Medicines Patent Pool), tiered pricing policies and collaborations with international organisations (e.g. UNICEF). In contrast to the waiver and proposed extension, these initiatives support, rather than undermine innovation, and can be expected to aid future pandemic preparedness.

A TRIPS waiver extension undermines IP, which is a key catalyst for both R&D and ramping up therapeutics production, including via VLAs, by reducing incentives for innovation and a predictable framework for collaboration. Pursuing compulsory licencing over VLAs would undermine safeguards in quality standards and patient safety. Moreover, the scope of a waiver for therapeutics will be subject to changes in the future as treatment guidelines evolve, in addition to the fact that many COVID-19 symptoms can be treated with a wide range of existing therapeutic options that were neither researched nor developed for it. A waiver could mean that 464 indications, not originally developed for COVID-19, are potentially in scope. A waiver could aggravate supply chain pressures, as scale economies are reduced and competition for resources increases. From an economic angle, a TRIPS waiver extension can negatively impact innovation-intensive countries while benefiting some generics-intensive countries, meaning a shift in GDP, investments and welfare from the EU and the US to India, Russia, China, and South Africa.

While a TRIPS waiver extension would not address existing barriers to access, a number of meaningful policy solutions are available. These include a strong trade and health agenda that would see governments refrain from imposing export restrictions, lift tariffs on medicines, and a broader trade facilitation agenda. In addition, enhancing LIC and LMIC health system capacities and improving their healthcare systems' absorptive capacities continues to be critical. Finally, increasing regulatory agility and improved demand forecasts would make it possible to better anticipate and target where supplies should be directed to.

It is important to emphasise that: the successful elements of the fight against the COVID-19 pandemic are the result of the EU and US driving R&D efforts and ramping up manufacturing, and that they must remain key allies in the fight against COVID-19. Industry is a key supporter of the transatlantic economic relationship that should be strengthened and not weakened by an initiative like a possible TRIPS Waiver extension.

Foundation for Innovative New Diagnostics (FIND)

As a generalization, individual patents are rarely a primary barrier limiting global access to diagnostics products, unlike the importance of single patents as critical barriers for equal global access to therapeutics and vaccines. Patents are not the only or even the most important form of protected intellectual property (IP) in much of the global diagnostics industry. The second form of IP core to diagnostics is ‘know-how.’ The key COVID-19 diagnostic tests were based on polymerase chain reaction (PCR) and lateral flow; consequently, patent-related barriers to diagnostics access during COVID-19 were minimal. Neither compulsory nor voluntary licenses on diagnostic technologies would have been likely to stimulate innovation or enable local manufacturing of COVID-19 tests in middle-income countries. Nonetheless, patent-related waivers under the TRIPS Articles may one day be applicable to essential diagnostics or future pandemics, such as emerging sensing technologies.

The more relevant TRIPS Articles relate to know-how, and TRIPS provisions on trade secrets (Article 7, Section 39) and technology transfer (Article 66, Section 66.2), which is how barriers in equitable diagnostics access due to trade secrets can be addressed. At present, these provisions offer limited tools to address key barriers. Article 66, Section 66.2 of the TRIPS agreement states that developed countries should incentivize voluntary technology transfer to least developed country members,¹³⁸⁴ a position reaffirmed in the Doha Declaration.¹³⁸⁵ Given the importance of manufacturing technology and know-how to diagnostics, application of the principles in Section 39 and Section 66.2, particularly increased incentives for robust technology transfer, would likely have a significant impact on global diagnostics access, both during pandemics and for essential diagnostics.¹³⁸⁶

Gary Locke - Retired Ambassador

Expanding the Trade Related Aspects of Intellectual Property Agreement (TRIPS) waiver to include Covid-19 diagnostics and therapeutics will not only fail on its own terms but, in the process, will also harm U.S. innovation and economic competitiveness.

There is simply no need for this waiver. Innovators have been actively licensing their Covid-19 technology to expedite worldwide production and distribution. Pfizer, Merck, and other leading therapeutic manufacturers, for instance, have entered into hundreds of voluntary licensing agreements with generic manufacturers to increase Covid-19 antiviral supplies.

Global public health experts have routinely connected access challenges with the need to strengthen medical infrastructure and last-mile distribution systems -- not with weakening intellectual property systems. Unfortunately, too much energy is being spent on an IP waiver that would do nothing to address these obstacles.

¹³⁸⁴ World Trade Organization. Overview: the TRIPS Agreement https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm.

¹³⁸⁵ World Trade Organization. Declaration on the TRIPS agreement and public health. https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm.

¹³⁸⁶ FIND. Policy Brief - Diagnostics & Intellectual Property. www.finddx.org/wp-content/uploads/2022/12/20221201_rep_factsheet_dx_ip_FV_EN.pdf. Accessed 2 May 2023.

As with the TRIPS vaccine waiver, suspending intellectual property protections -- without cause -- creates a dangerous precedent, one that will disincentivize much-needed innovation. However, without reasonable assurances that proprietary discoveries will be protected, future life-saving investments like these will not be made. And that is precisely the pall an expanded TRIPS waiver would drape over research into cancer, HIV, and Alzheimer's going forward.

This research disincentive will also extend beyond the biopharmaceutical industry. Every U.S. sector competing on the leading edge of technology would suddenly find itself on shakier IP -- and therefore financial -- footing. They would notice investors repricing risk and pull back on their most ambitious and potentially valuable research.

Supporting an expanded TRIPS waiver would kneecap critical industries across the United States and sacrifice American jobs -- both now and in the future. Under these conditions -- with IP protections suspended -- investors would no longer dedicate resources to high-risk, research-intensive endeavors. Demand for skilled work in the United States would fall as a result.

Meanwhile, United States' rivals would be eager to get their hands on these technologies to grow their own industries. Should they succeed, "any one of them could leverage such mRNA-based innovations to achieve its diplomatic, economic, and even military goals -- at the United States' expense."

However well-intentioned, the proposed TRIPS waiver expansion for Covid-19 diagnostics and therapeutics would do America harm and the world no good.

Gilead

Gilead opposes expanding the TRIPS Waiver to COVID-19 therapeutics like Gilead's Veklury® (remdesivir). As our pre-hearing brief and testimony reflect, patents have not been a barrier to COVID-19 therapies, but essential to innovation and a pre-requisite to access.

Drug development is scientifically and commercially risky. Recent studies suggest over 90% of drug candidates fail in clinical development.¹³⁸⁷ That failure often comes after many years, with massive sunk costs. Innovators must use their few successes to recoup the costs of successes and failures and support future research. The global IP system fosters innovation by affording innovators a period of exclusivity to commercialize their inventions.

Global IP protection is particularly important for Gilead as we invest in researching and treating emerging viruses, where it may be unclear, at time of development, if such viruses would ever materialize as public health threats and which countries would be impacted. The global IP system was important in Gilead's investment in inventing and developing remdesivir. The foundational work on remdesivir began in the late 2000s, when Gilead began investigating its potential to treat a range of emerging viruses. When COVID-19 emerged, Gilead already knew that remdesivir had activity against coronaviruses. That foundational research enabled us to start COVID-19 clinical trials in February 2020— a month before the WHO declared a pandemic. Data from those clinical trials supported the FDA's Emergency Use Authorization by May and full approval as Veklury® in October 2020. In 2020 alone, Gilead invested \$1 billion and increased manufacturing capacity for remdesivir 400 -fold. With our

¹³⁸⁷ Why 90% of clinical drug development fails and how to improve it?

partners and licensees, Gilead has been fulfilling real-time global demand since October 2020, making remdesivir available for over 13 million patients to date. The U.S. Patent Office recognized Gilead’s innovation and rapid response to the pandemic with a “Patents for Humanity” award.¹³⁸⁸

The remdesivir story confirms that patent protection does not hinder, but enhances access. Building on our worldwide network from fighting HIV and hepatitis, Gilead voluntarily licensed remdesivir to vetted generic manufacturers in India, Pakistan, and Egypt to make this medicine available to 127 low- and lower-middle-income countries and upper-middle-income countries with limited access to healthcare. Gilead partnered with licensees, sharing technology and know-how. As a result, remdesivir was made available to over 8 million patients in the developing world, without a report of a Gilead licensee unable to meet demand. These agreements have been royalty-free, reflecting Gilead’s commitment to enabling broad patient access.

In contrast, the proposed TRIPS Waiver seeks to encourage broad-scale compulsory licenses that may include unvetted manufacturers. Compulsory licensees do not rely on know-how and other support to scale up production of safe and effective medicines. Data shows that compulsory licenses result in fewer treated patients than do voluntary licenses.¹³⁸⁹ None of that helps patients.

Pandemics demand global cooperation, and Gilead is proud to cooperate. IP is not the problem, so a TRIPS waiver is not the answer. In fact, U.S. support for a TRIPS Waiver would signal that U.S. leadership in breakthrough medical innovation and pandemic preparedness is no longer a priority.

Global Colon Cancer Association

The Global Colon Cancer Association is the voice for millions of colon cancer patients worldwide. We advocate for patient-centered policy around the globe to ensure increased awareness and screening, access to quality medical treatments, and help our member organizations collaborate, innovate and leverage the full potential of effectuating change.

The question of “whether to extend flexibilities under the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights to COVID-19 diagnostics and therapeutics” is critically important for patients and the future of medical innovation.

The TRIPS Agreement established minimum standards of protection that WTO member nations must extend to each other with regard to each nation’s intellectual property, such as copyrights, trademarks, and patents. Thanks to the strong and enforceable global IP protections guaranteed by TRIPS, in the nearly three decades since its enactment, the biopharmaceutical industry has invested heavily in research and development – bringing hundreds of breakthrough therapies to patients.

Consider how, for over thirty years, one drug – fluorouracil – was the primary treatment available to colon cancer patients. But beginning in the mid-1990s – around the same time as the TRIPS waiver came into force – drug researchers started to make major treatment breakthroughs. Today, over 30 FDA-approved drugs are available for the treatment of colorectal cancer. And the death rate is half of what it was in 1992.

¹³⁸⁸ Patents for Humanity: COVID-19 category award recipients.

¹³⁸⁹ Gilead Testimony: Transcript of USITC Hearing Re: Inv. No. 332-596 on March 29, 2023, 208.

Of course, colon cancer patients aren't the only ones to benefit from strong, IP-backed life sciences innovation. Since the early 1990s, improvements in cancer treatment overall have helped slash the disease's death rate by 33%, saving an estimated 3.8 million lives. Meanwhile, between 2010 and 2019, medical advancements helped cut the national heart disease death rate by 10.4%.

And the hard work continues with over 8,000 drugs currently in the development pipeline, globally. This innovation is not the result of chance. Rather, it's thanks to our strong and predictable IP system that gives drug researchers the security they need to take on inherently risky and expensive projects. They know that – should their candidate beat the odds – they'll have a period of temporary exclusivity in order to recoup upfront development costs and re-invest in additional research.

But IP is a convenient scapegoat. Officials worried that IP protections on Covid-19 vaccines – which scientists brought to patients in record time, thanks to decades of underlying research supported by our IP system – would hamper access in developing nations. While these fears proved unfounded – India's Serum Institute, for example, halted production entirely after amassing over 200 million surplus doses – officials nevertheless proceeded to waive IP protections for Covid-19 vaccines under TRIPS.

That decision alone set a dangerous precedent for the future of IP protections and thus, the next generation of medical innovation. Extending the waiver to Covid-19 diagnostics and therapeutics would only compound the damage – halting decades of progress in the life sciences sector, and forcing scientists to put many promising drug candidates on hold. This will keep potentially life-saving cures from reaching the patients who need them most.

Innovation Council

This submission describes the interplay between IP protection, on the one hand, and efforts to build capacity for biomanufacturing and R&D in more regions, on the other. Especially since COVID-19, extending such capacity has become a priority for many national leaders and the global health community. IP protection is an essential enabler of these scale-up efforts in the coming years. For this reason, we do not endorse expanding the TRIPS waiver to apply to a broader range of technologies.

An extended TRIPS waiver will increase uncertainty and make it more complicated for organizations to share COVID-relevant technology and knowledge. It will reduce the likelihood that intellectual assets with application to COVID-19 and other health crises will be further developed and deployed in emerging markets, in particular, where IP systems are relatively less developed, and risk is thus already perceived by innovators to be higher. Overall, an extended IP waiver is unlikely to improve availability of COVID-19 products, while interrupting the extension of biomanufacturing capacity to developing regions.

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

IFPMA and its members have been, and remain, at the forefront of the COVID-19 response. Nearly every medicine and vaccine used against COVID-19 was developed by the innovative companies represented by our organization. IFPMA members rapidly invested and worked with partners to deliver therapeutics and vaccines for COVID-19 to patients in record time, at an unprecedented scale.

IP has been an enabler rather than a barrier to availability of COVID-19 therapeutics and vaccines globally. Had IP protection not been available, the technologies and knowledge that supported the pandemic response would not have existed. The COVID-19 response would have had to start from scratch; as the pandemic gathered momentum, companies and researchers would have been just starting the decades-long R&D to develop foundational technologies like the viral vector and mRNA platforms.

An expanded TRIPS waiver decision would jeopardize the COVID-19 therapeutics pipeline, creating disincentives to invest in the further R&D needed to move candidates to market. Therapeutics for COVID-19 have applications to other diseases. It is virtually impossible once IP protection has been waived to avoid the technology being used instead for non-COVID-19 purposes. This unfairly penalizes companies that have developed solutions that are relevant for COVID-19 using existing technologies, ultimately disincentivizing innovation.

Nearly every license for the manufacture of COVID-19 therapeutics includes technology transfer. Expanding the scope of the TRIPS waiver decision would undermine the many collaborations and voluntary licensing arrangements that are already in place, affecting innovators and their partners alike.

The pandemic response was unprecedented for the rapid pace and scale of innovation and manufacturing. The global health community rapidly created platforms to address the pandemic quickly and equitably, though there were clear shortcomings. The Global Fund raised billions of dollars to facilitate procurement and support healthcare systems in Low-and-Middle-Income Countries (LMICs). UNICEF procured millions of health products at a time when supply chains were highly disrupted. Meanwhile, the WHO created guidelines for the scientific, medical, and policymaking communities, and prequalified COVID-19 products. The Medicines Patent Pool (MPP) was able to quickly extend its mandate to cover COVID-19, playing an important role in ensuring resilience of supply, as manufacturing partners from developing and developed countries worked together in pursuit of this same goal.

Evidence indicates that TRIPS implementation is linked to benefits such as FDI, technology imports, and more scientific research. Often, Geneva-based negotiators negate these benefits, calling instead for WTO Members to enact lower levels of IP protection. For many years, certain countries have worked to advance an anti-IP agenda at the WTO, to further their own industrial policy goals. The TRIPS waiver re-invigorated this effort, needlessly directing crucial political attention and resources that should have been focused on dismantling the real bottlenecks to the pandemic response towards IP instead.

Looking to the future, IFPMA urges WTO Members to direct their attention to the many documented trade-related challenges that complicated the COVID-19 response – such as border measures, inadequate trade facilitation, and export restrictions.

Initiative for Social and Economic Rights (ISER)

The Initiative for Social and Economic Rights (ISER) is a nonprofit organization that works to advance social economic rights in Uganda and within the African region. ISER has drawn attention to how the failure to take all measures to ensure broad global access to and democratic production of COVID-19 healthcare technologies –vaccines, testing and treatment products – constitutes a violation of states' obligations under human rights treaties they have ratified.

The U.S. government should support the adoption of the ‘Decision text on extension of the 17 June 2022 Ministerial Decision to COVID-19 Therapeutics and Diagnostics’ (WT/GC/W/860;IP/C/W/694) presented in the WTO by a group of developing countries in 2022.

Patents, and other forms of intellectual property, have an adverse effect on prices and supply of COVID-19 diagnostics and therapeutics. Even when supplies do become available, high prices based on monopoly control mean developing countries simply cannot afford to provide their populations with access to key COVID tests and treatments.

Patents artificially suppress demand by restricting supply to a few monopolies. The tiered pricing schemes used by pharmaceutical corporations in direct sales in developing countries still result in untenably high prices. Pfizer has charged more than \$500 for each course of Paxlovid in some developed countries and \$250 in some developing countries, multiple times higher than the price negotiated by the Clinton Foundation for generic Paxlovid (\$25/course-of-treatment) and much higher than \$15.08 estimated cost-of-production plus profit analysis produced by Harvard Researcher Melissa Barber. Developing countries struggling with high debt payments, vast demands for social protection amidst the ongoing economic decimation are unable to afford this for their population.

Countries are then left to depend on donations which are adhoc and limited. Covid 19 vaccine donations reached African countries when the wealthier countries met their needs and sometimes shortly before expiry. Donations of therapeutics like Paxlovid only reached Africa in December 2022 when a few thousand doses of Paxlovid were delivered to Zambia as one of only ten African countries that will receive these drugs through the Medicines Patent Pool. Almost all of the first six months of production of Paxlovid was committed to developed countries. In April 2022, WHO cautioned that it is “extremely concerned” that developing countries “will again be pushed to the end of the queue when it comes to accessing treatment.”

Yet timely access to affordable therapeutics and diagnostics is critical to limit the damaging health and economic effects of COVID-19 which continues to evolve unpredictably particularly in low and developing countries that often have under resourced health systems.

Failure to Take Measures to Ensure Equitable Global Access to and Distribution of Lifesaving COVID-19 Vaccines and Other Healthcare Technologies Entrenches Racial Discrimination

Both the UN Committee on the Elimination of Racial Discrimination (CERD) and the UN Special Rapporteur on Contemporary Forms of Racism, racial discrimination, anti-Semitism, xenophobia and related intolerance found that patents on lifesaving vaccines and COVID-19 technologies by resulting in unequal distribution within and between countries replicating slavery and colonial-era racial hierarchies perpetuate racial discrimination.

Jayashree Watal

The TRIPS waiver of Article 31(f) under the MC12 Decision for COVID-19 vaccines (WT/MIN(22)/30) is an addition to two earlier TRIPS-legal provisions that allow for exports under a compulsory licence (CL), namely Articles 31 (f) and 31bis. While Art. 31(f) has no product restriction, Art. 31bis covers

pharmaceutical products, explicitly including active ingredients and diagnostics, and implicitly including vaccines.

The MC12 Decision, which once again waives Art. 31 (f), does have new elements, such as not requiring prior efforts to get a voluntary licence before a CL is authorised. But, overall, the advantageous elements are mostly gratuitous clarifications, while others are either detrimental to developing countries' interests or cause confusion. Unlike Art. 31(f) or Art. 31bis, the MC12 Decision is limited in scope and limits exporters only to developing countries, paradoxically excluding China.

The sweeping waiver proposals made by South Africa and India in 2020 and 2021, and supported by many in the WTO, would also not have immediately helped developing countries in urgently obtaining pandemic-related products (PRPs) during COVID-19 any better than existing TRIPS-legal avenues, especially for complex technologies such as the mRNA-based vaccines. That the South African mRNA Vaccine Technology Transfer Hub has been unable to distribute its own mRNA COVID-19 vaccine almost two years after its establishment proves this point. India and China also took three years to develop their own mRNA-based COVID-19 vaccines. Thus, neither compulsory licences nor TRIPS waivers are the immediate solutions needed during a pandemic.

Nevertheless, even if the system under Article 31bis was only used once, the very existence of Art. 31 and Art. 31bis in the TRIPS Agreement probably played an important role in originator pharmaceutical companies deploying donations, voluntary licensing and differential pricing of vaccines and therapeutics in developing countries during the COVID-19 pandemic.

Regarding COVID-19 diagnostics, the markets seem to have become competitive quite quickly, after the initial supply-related roadblocks were cleared and governments, including in developing countries, could deploy tests as needed. With respect to therapeutics, WHO advisories kept changing, but one of the most effective medicines against the Delta variant, dexamethasone, was long off-patent, and a newer WHO-recommended one, Pfizer's Paxlovid™, was licensed to the Medicines Patent Pool end-2021 and within a year a WHO-approved generic version was available for sale in 95 countries covering over half of the world's population.

In my view, for greater legal clarity, the US should agree to amend Article 31bis in exchange for abandoning the MC12 Decision and further process:

- 1) to additionally waive Article 31(b) for both the exporting and importing Members; and
- 2) delete the requirement given in TRIPS Annex paragraph 2 (b) (1) to export 100% of production under the CL so that any portion beyond the non-predominant part of production can be exported.

Rapidly correcting inequities in the supply of PRPs during future pandemics primarily requires global political will in ensuring adequate, early funding and incentivising the rapid, wide-spread voluntary licencing and to ensure the simultaneous deployment of PRPs everywhere.

Just Treatment

Aasiya Versi welcomes the opportunity to provide written comments on the Commission's investigation on COVID-19 diagnostics and therapeutics, market dynamics, supply and demand, price points, the relationship between testing and treating, and production and access. Just Treatment is an organization

is a UK based patient led organisation that leads national and international grassroots campaigns, and have led a COVID equity campaign for the past 18 months.

The testimony of Aasiya Versi on behalf of Just Treatment shows the impact of lack of access to COVID 19 treatments and diagnostics which has irrevocably changed lives and caused loss of loved ones. Policy decisions are often made by a small group of people with very little input from people who have been impacted.

Each patient story highlighted in this testimony showed how lack of access is life altering and painful and how each patient is at the mercy of prices dictated by the pharmaceutical industry.

This testimony listed patient stories from Tanzania, Iraq and the UK who lost loved ones or whose lives have been grossly impacted because of lack of access beyond their borders,

The patient leaders whose stories were featured were Sakina Dattoo and Imtiaz Somji who lost family members in Tanzania, Rasha Sikafi who lost her grandmother in Iraq, Izzie Jani Friend and Melanie Duddridge who are clinically vulnerable patients based in the UK still shielding three years from the start of the pandemic.

The health outcomes of others around the world has an impact on everyone. Health is a collective global responsibility and not just a national one. This testimony seeks to highlight the human impact of an often technical debate around intellectual property rights of medicines.

Licensing Executives Society

“The Licensing Executives Society (USA & Canada), Inc (“LES”) is an independent, non-profit, non-partisan, professional association devoted to the global commercialization of intellectual property through education, networking, standards development, and certification. LES opposes additional exceptions to IP protections under the TRIPS Agreement for Covid-19 diagnostics and therapeutics. This would diminish global innovation, and adversely affect U.S. innovators and our economy. Our concerns speak to central questions presented by the USITC to the public on this issue.

The very premise is flawed. IP is not an obstacle to access to Covid-19 diagnostics and therapeutics. Instead, IP has been an essential element in the development, production, and distribution of Covi-19-related technologies. IP forms the foundation on which cross-border collaborations and technology sharing agreements have been formed to efficiently utilize diverse resources and capabilities to create vaccines, diagnostics, and therapeutics, and to make them available around the world.

Many manufacturers of Covid-19 technologies have voluntarily licensed their technology to the Medicines Patent Pool, allowing qualified generic producers to make and sell those technologies in low and middle-income countries. These and other voluntary networks have now over-produced, and global supply exceeds demand. Expanding exceptions to the TRIPS Agreement – and unraveling a carefully orchestrated regime of global IP rights – will do nothing to increase supply or enhance access.

However, enlarging the IP exceptions to the TRIPS Agreement would have an adverse effect on innovation and investment. Not least, it would increase risk and discourage investment in technologies to fight the next pandemic. It would signal to innovators and investors everywhere that their intellectual property rights are not reliable, and their return on investment is at greater risk.

Intellectual property rights encourage investment in life science research and development. They offer protection against theft of the fruits of our mental labors. Removing those protections creates a perverse incentive – to misappropriate rather than innovate. Investors will conclude that, without a global system of respect for intellectual property, their investments in healthcare will not produce a return comparable to the risk. They will not back expensive, long-term R&D projects, and we will be left without the tools needed to fight the next pandemic.

From its inception, the United States recognized the importance of intellectual property protection. We have consistently been at the forefront of efforts to enable all countries to innovate their way to prosperity through IP protection. The U.S. boasts one of the best patent systems in the world, and this provides a compelling basis for inventing and investing in America. Today, most of the world’s new drugs originate in American laboratories, and U.S. pharmaceutical companies employ – directly or indirectly – nearly 4.5 million Americans.

LES is deeply concerned about the proposed new exceptions to IP protections under the TRIPS Agreement, and the overall weakening of international intellectual property protection. We urge the U.S. to oppose diminishment of intellectual property rights. Instead, the U.S. should return to its traditional role as a leading advocate for innovation and intellectual property protection the world over.”

Médecins Sans Frontières (MSF)

Excluding diagnostics and therapeutics from the WTO MC12 Ministerial decision (WT/MIN(22)/30) was a mistake. Diagnostic testing is the entry point for medical care, and therapeutics are needed to respond and control disease outbreaks, such the COVID-19 pandemic. There is significant existing capacity and potential in low and middle-income countries (LMICs) for the production of diagnostics and therapeutics should IP barriers be removed.

Therapeutics and IP barriers

MSF has analyzed four priority COVID-19 therapeutics – nirmatrelvir/ritonavir, molnupiravir, tocilizumab and baricitinib.

Patents

Pfizer has applied for patents on nirmatrelvir in the majority of developing countries.¹³⁹⁰ If granted, the patent will stand until at least 2041.

Merck has been granted or has pending patents on molnupiravir in at least 25 developing countries.¹³⁹¹ These patents, when granted, would stand until 2035-2038.

¹³⁹⁰ [https://www.medspal.org/?product%5B%5D=Nirmatrelvir+\(PF07321332\)%2BRitonavir+300%2B100+mg&page=1](https://www.medspal.org/?product%5B%5D=Nirmatrelvir+(PF07321332)%2BRitonavir+300%2B100+mg&page=1)

¹³⁹¹ [https://www.medspal.org/?product%5B%5D=Molnupiravir+\(formerly+MK-4482\)+200+mg&page=1](https://www.medspal.org/?product%5B%5D=Molnupiravir+(formerly+MK-4482)+200+mg&page=1).

Roche holds primary and secondary patents on tocilizumab, mostly on formulation of tocilizumab as a monoclonal antibody and the method of use tocilizumab in treatment, in nearly 30 developing countries, which expire between 2022-2028.¹³⁹²

Eli Lilly holds patents on baricitinib in more than 50 LMICs.¹³⁹³ The patents will only start to expire in 2029.

Voluntary licenses

Pfizer and Merck have signed voluntary licenses with the Medicines Patent Pool (MPP) on nirmatrelvir/ritonavir and molnupiravir, respectively. However, both voluntary licenses exclude many developing countries – including most Latin American countries – with robust generic manufacturing capacity. The voluntary license signed by Merck also contains a harmful clause which deprives parties of the right of challenging the validity of patents on molnupiravir.^{1394,1395}

Roche has not signed voluntary license nor engaged other forms of collaboration that could accelerate expanding supply of tocilizumab. Eli Lilly signed bilateral voluntary licenses with Indian generic companies on baricitinib to supply only the Indian market.

Compulsory license

Compulsory licenses have not been issued on any of the four priority therapeutics but there are requests pending in some Latin American countries.¹³⁹⁶ Beyond the four therapeutics, compulsory licensing has been used by some governments, including Hungary, Israel and Russia, on other COVID-19 therapeutics.¹³⁹⁷

Diagnostics and IP barriers

IP on diagnostic tools may include patents on reagents, instruments, methods and software. Despite the cost of filing for and upholding patents, developers prioritise this to discourage competition, attract investors, and support an ‘exit strategy’ of being purchased by a larger company.¹³⁹⁸ Know-how and trade secrets are of particular concern for diagnostic production in LMICs.¹³⁹⁹

¹³⁹²

<https://www.medspal.org/?product%5B%5D=Tocilizumab++162+mg%2F0.9ml&product%5B%5D=Tocilizumab++20+mg%2Fml&page=1>.

¹³⁹³ <https://www.medspal.org/?product%5B%5D=Baricitinib+1+mg&page=1>.

¹³⁹⁴ <https://msfaccess.org/msf-response-license-between-pfizer-and-medicines-patent-pool-new-covid-19-treatment-paxlovid>.

¹³⁹⁵ <https://www.doctorswithoutborders.org/latest/msf-merck-and-medicines-patent-pool-license-new-covid-19-drug>.

¹³⁹⁶ <https://www.keionline.org/37066https://www.keionline.org/37066>.

¹³⁹⁷ https://msfaccess.org/sites/default/files/2021-05/COVID_TechBrief_MSF_AC_IP_CompulsoryLicensesTRIPSWaiver_ENG_21May2021_0.pdf.

¹³⁹⁸ https://msfaccess.org/sites/default/files/2021-07/IP_IssueBrief_Local-diagnostics-local-health-needs_ENG_13.7.2021.pdf.

¹³⁹⁹ https://msfaccess.org/improve-local-production-diagnostics?utm_source=Advocacy&utm_medium=email&utm_campaign=LocalProdDiag.

In November 2021, the Spanish National Research Council offered an antibody test technology to the WHO C-TAP and MPP.¹⁴⁰⁰ In May 2022, NIH offered 4 diagnostic technologies to WHO C-TAP as another positive step.¹⁴⁰¹ However, none of these licenses will be sufficient to address patent thickets nor the issues of trade secrets in diagnostics. One license from one technology owner remains insufficient to open up the platform to alternative developers.¹⁴⁰²

Overall, we reiterate that a meaningful IP waiver should extend to all types of relevant IP, all medical tools and their underlying technologies, components and materials, and be applicable to all countries.¹⁴⁰³

Medicines Law & Policy

On 17 June 2022, World Trade Organization (WTO) Members adopted a Ministerial Decision outlining flexibilities in the WTO's Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement that countries could use to access Covid-19 vaccines. A decision on whether and how to extend the scope of the decision was tabled for a later date. As part of the decision-making process, the US Trade Representative has commissioned a study to determine the case for extending the Decision.

Medicines Law & Policy is a research group that brings together experts working at the nexus of international law, intellectual property, medical technology and public health, and is a leading voice on access to countermeasures for Covid-19 and other health emergencies. We recommend that an extension to the Decision:

- **Ensure access to all pandemic countermeasures** including vaccines, diagnostics, therapeutics and any other health technologies needed to prevent, address and/or recover from a health crisis.
- **Ensure preparedness for future pandemics** by making the Ministerial Decision applicable to any emerging or declared health emergency in the future.
- **Ensure an easy pathway for countries to opt back into TRIPS Art. 31bis.** In 2003, many countries opted out of using Art. 31bis (compulsory licensing for export). With increasing concentration of pharmaceutical manufacturing, those countries may find themselves in need of this provision, in particular in a crisis situation.
- **Ensure waivers on market and data exclusivity are available** so that effective implementation of a compulsory licence is not delayed by lack of access to information needed for regulatory purposes.

Since 2001, ML&P has been tracking the use of TRIPS flexibilities for public health in our TRIPS Flexibilities Database (TFD). We see that TRIPS Flexibilities are:

- **Widely used.** The TFD currently documents 172 instances, of which 122 concern compulsory licensing, 3 exceptions to patent rights, 46 the least developed country (LDC) extension and 1 parallel import.

¹⁴⁰⁰ <https://www.who.int/news/item/23-11-2021-who-and-mpp-announce-the-first-transparent-global-non-exclusive-licence-for-a-covid-19-technology>.

¹⁴⁰¹ <https://www.who.int/initiatives/covid-19-technology-access-pool/us-nih-licenses>.

¹⁴⁰² <https://msfaccess.org/msf-welcomes-first-open-license-covid-19-test-who-covid-19-technology-access-pool>.

¹⁴⁰³ <https://msfaccess.org/msf-position-scope-and-duration-trips-waiver-covid-1>.

- **Effective even when not executed.** The TFD notes 27 instances between 2001 and 2023 where compulsory licences were proposed but not executed. Of those, 16 resulted in an access measure by a company - either a voluntary licence, a price decrease, or a declaration not to enforce rights.
- **Useful in a pandemic.** The TFD shows that since 2020 there have been 10 instances of compulsory licensing that concerned products needed to prevent or treat Covid-19. Five of these instances were in high-income countries and four were executed.
- **Useful in high-income countries.** Of 122 compulsory licence instances in the databases, 23 were for the use in high-income countries.

TRIPS flexibilities have an important role in ensuring access to medicines in general, and access to countermeasures in the case of public health emergencies in particular. The Ministerial Decision has the opportunity to ease their use to ensure a more effective response to Covid-19 and future pandemics. WTO Members should take the recommendations above to extend the Ministerial Decision and work to incorporate TRIPS flexibilities into their national legislation. They should also seek to avoid actions that make it more difficult to use TRIPS flexibilities, including opting out of Art. 31bis, agreeing to or demanding so-called 'TRIPS-plus' provisions, or engaging in political pressure against the use of TRIPS flexibilities.

Medicines Patent Pool (MPP)

The Medicines Patent Pool (MPP) works through voluntary licensing of intellectual property rights and technology transfer to increase access to innovative medicines and other health technologies in low and middle-income countries (LMICs). It takes a transparent, non-exclusive, and public health-oriented approach to negotiate and manage licenses with a focus on stimulating a competitive generic market to ensure availability and affordability in LMICs.

During the COVID-19 pandemic, MPP secured licenses for three patent-protected COVID-19 therapeutics, namely molnupiravir, nirmatrelvir, and ensitrelvir from Merck, Sharp & Dohme (MSD), Pfizer, and Shionogi & Co., Ltd respectively. The molnupiravir licence covers 106 LMICs including all of Sub-Saharan Africa, all low-income countries, most lower-middle income countries and 20 upper-middle income countries. The nirmatrelvir licence covers 95 LMICs including all low-income countries, all lower-middle income countries, upper-middle income countries (UMICs) that transitioned to UMIC status over the preceding 5 years, and most of the UMICs in Sub-Saharan Africa. MPP's licence agreement with Shionogi covers 117 countries including all low-income countries, almost all lower-middle income countries, 35 upper-middle income countries, and all countries in Sub-Saharan Africa. Each licence includes LMICs accounting for more than 50% of the world population with progressively greater coverage for people living in the lower bands of World Bank's gross national income (GNI) per capita categorization as well as Least Developed Countries listed by the UN. A total of 119 countries with aggregate population of over 4.35 billion people (56% of the world population) are covered by at least one MPP COVID-19 therapeutics licence.

As at the end of the first quarter of 2023, a total of eight MPP sublicensees had either filed or obtained approval for a COVID-19 antiviral. Development of quality assured generics happened in record time enabling procurement by LMIC governments. Rapid development was supported by the transfer of

know-how and the sharing of innovator reference listed drug to enable companies to undertake the needed studies to show bioequivalence.

MPP has demonstrated that licensing of intellectual property, especially when done earlier in the research and development process, and technology transfer can be applied to ensure equitable access to medical countermeasures in a pandemic. Building on the experience and lessons learnt, the network of sublicensees that has been developed in the context of COVID-19 could be strengthened as a manufacturing network for equitable access to therapeutics in future health emergencies.

Melissa Barber- Harvard PhD in Population Health Science

I welcome the opportunity to provide written comments on the Commission's investigation on COVID-19 diagnostics and therapeutics, market dynamics, supply and demand, price points, the relationship between testing and treating, and production and access. I am a health economist (PhD defended at Harvard University May 2023). I have published extensively on pharmacoconomics and have served as a consultant on pharmaceutical policy for WHO, Médecins Sans Frontières, the Clinton Health Access Initiative, the Global Fund to Fight AIDS, Tuberculosis, and Malaria, and the World Bank. I represent only myself in this submission.

I am writing to follow up on some points raised in the hearing and to provide information requested by the commissioners.

1. Cost of production of COVID-19 therapeutics:

The Commissioners requested further information on the cost of production for COVID-19 therapeutics. I am hopeful that manufacturers will be transparent with the Commission on this question of great public health importance. I have submitted a brief estimating the costs of production for COVID-19 therapeutics.

The methods used in this working paper have been extensively peer-reviewed and validated across over a dozen publications, and the data used is publicly available. Detailed information on assumptions and methods can be found in the submitted brief. Table 1 contains a summary of results. Should commissioners have further inquiries, including questions about cost of production methods and their application, I am available to support as may be helpful.

Table 1 Cost of production and estimated cost-based generic prices for investigational COVID-19 therapeutics

Drug	Treatment Course	Cost of production (\$US)	Estimated cost-based generic price (cost of production + 10% profit margin, and 27% tax on profit) (\$US)
<i>baricitinib</i>	14 day course - 1x4mg baricitinib, 1x daily ⁱ	\$1.83	\$2.06
<i>molnupiravir</i>	5 day course 4x200mg molnupiravir, 2x daily ⁱⁱ	\$7.64	\$8.61
<i>nirmatrelvir/ritonavir</i>	5 day course of 2x150mg nirmatrelvir + 1x100mg ritonavir twice daily for 5 days ⁱⁱⁱ	\$15.81	\$17.82
<i>remdesivir</i>	200mg remdesivir day 1, 100mg days 2-5 ⁵	\$7.01	\$7.90

ⁱ WHO Therapeutics and COVID-19 living guidance. <https://app.magicapp.org/#/guideline/nBkO1E/rec/E5AOaN>

ⁱⁱ <https://clinicaltrials.gov/ct2/show/NCT04575597>

⁵ <https://www.fda.gov/media/155050/download>

2. The interactions between the TRIPS limited exception and 31bis

Several commissioners requested technical analysis explaining how the TRIPS limited exception related to 31bis. I am submitting as a written submission *Flowchart- How do the TRIPS agreement, Article 31bis provisions, and 2022 “TRIPS waiver” interconnect in determining generic access pathways*, which may be helpful.

Merck

Merck & Co., Inc. (“Merck”) is the co-developer and manufacturer of molnupiravir, an investigational oral COVID-19 antiviral approved or authorized in more than 25 countries. Merck prioritized rapid and equitable global access to molnupiravir by following a three-pronged strategy:

- Ramping up production “at risk” (i.e., prior to receiving regulatory authorization) to ensure ample supply would be available as quickly as possible and entering into advance supply agreements with approximately 40 governments to facilitate rapid availability.
- Engaging early with generic manufacturers to facilitate access in low- and middle-income countries (“LMICs”) through voluntary licenses, including bilateral licenses and with the Medicines Patent Pool, which issued sublicenses to more than 20 generic manufacturers from 10 countries. Combined, Merck’s voluntary licensed territory and local manufacturing partnerships cover approximately 90% of the population in LMICs.
- Reserving supply of its own product for global health programs, Merck made up to 5 million courses (approximately 30% of global supply) available to UNICEF and USAID at our best access price” for distribution in 107 LMICs eligible for donor government funding; Merck also donated 100,000 courses to Direct Relief for distribution to refugee programs.

Despite Merck’s efforts to ensure equitable access to molnupiravir, procurement and distribution by governments and global health organizations have been relatively slow or nonexistent, for reasons unrelated to availability or price.

- Distribution through global health organizations has been slow, with few courses distributed. For example, while UNICEF had access to 3 million courses of molnupiravir since January 2022, it shipped only 60,478 courses to just 10 countries through April 2023.
- Demand from many governments and public health programs has been weak, particularly in Latin America, where many governments have not prioritized the purchase of COVID-19 antivirals as part of their pandemic response.
- Governments have been slow to implement and scale up test-and-treat programs, which can help raise awareness of antiviral availability among health care providers and make it easier for appropriate patients to receive a timely prescription.

Given that there are and have been no supply barriers for molnupiravir and no shortages of funding for therapeutic procurement from ACT-A partners, extending the TRIPS waiver to COVID-19 therapeutics would not improve global access to this treatment. Rather, such an extension may have an adverse impact on global health and access to medicines, by weakening incentives for research-based companies to continue investing in future innovations. Moreover, as therapeutics regularly have multiple uses, it would be impossible to constrain the impact of a TRIPS waiver to a product's COVID-19 use only, putting at risk investments underway to evaluate the potential of current COVID-19 therapeutics as medicines against other viral threats.

Without IP protections, Merck would likely not have been able to invest in the development of molnupiravir as a COVID-19 treatment. Merck urges the U.S. government not to support an extension of the TRIPS waiver to COVID-19 therapeutics and diagnostics, and instead to work with its partners to address the real barriers to access, as detailed in Merck's written submission.

Missing Medicines Coalition

The Missing Medicines Coalition is a coalition of UK-based advocacy organisations with decades of experience in mobilising campaigns, advocacy and research to improve global equitable access to medicines.

As a coalition, we support the original TRIPS waiver proposal tabled by India and South Africa in March 2020, calling for a comprehensive temporary waiver of the TRIPS Agreement for COVID-19 vaccines, tests and treatments. In this context, we therefore support an immediate and unconditional extension of the June 2022 decision to include COVID-19 diagnostics and therapeutics.

It remains stark that whilst 73% of people in high-income countries have received multiple vaccine doses, only 32% of those in low-income countries have received a first dose.¹⁴⁰⁴ Such inequalities are largely due to high prices, shortages when demand is high, partisan bilateral deals that prioritise high-income countries, and the commercial disinterest of pharmaceutical companies to make their tests and medicines available in many low- and middle-income (LMIC) markets.

More specifically, there is clear evidence that affordable, timely and sustainable access to tools to both test and treat COVID-19 patients is an ongoing issue in LMICs. Research found that high-income countries account for over 70% of courses via identified supply deals of all existing COVID-19 treatments, with the US responsible for procuring nearly 50% of available treatment courses in 2021.¹⁴⁰⁵

¹⁴⁰⁴ <https://ourworldindata.org/covid-vaccinations>

¹⁴⁰⁵ <https://launchandscalefaster.org/covid-19/therapeutics>

Those courses that do become available are not priced appropriately or affordably. For example, Pfizer has charged some low-income countries \$250 per single course of its treatment Paxlovid. This is 10 times the price negotiated by the Clinton Initiative¹⁴⁰⁶ for generic Paxlovid, and far above the estimated cost-of-production of \$15.08 as calculated by Melissa Barber.¹⁴⁰⁷

The status quo deployment of intellectual property is a key barrier to access to health technologies currently available and those in the R&D pipeline. While limited, the June 2022 decision on vaccines demonstrated international recognition of this. Furthermore, this contributes to the inequalities in access to COVID-19 diagnostics and therapeutics, and arguably more so than for vaccines. This highlights the need for an urgent decision to extend the June decision. Indeed, between January 2020 and September 2021, over 5,000 patent applications related to COVID-19 were published worldwide.¹⁴⁰⁸ Within this total, there were four times more patent applications for therapeutics than for vaccines.

This decision will affect thousands of lives. We must draw on lessons from the HIV response, and reflect on the stark inequities that were repeated during COVID-19. Now in the fourth year of the pandemic, we are seeing a rise of COVID-19 cases again, even in high-income countries. Current measures to curb the pandemic are evidently insufficient and ensuring timely access to affordable therapeutics and diagnostics are essential to end it. Putting an end to the global pandemic will reduce the risk of new variants, the burden of long-COVID on lives and economies, and mitigate preventable illness and death. To achieve this, WTO member states must urgently agree to an extension of the June 2022 decision to include therapeutics and diagnostics.

Novartis

Novartis is a science-based healthcare company whose purpose is to reimagine medicine to improve and extend people's lives. Our innovative medicines and other novel therapies include the world's first CAR-T therapy, groundbreaking gene therapies, and two of the world's first radioligand therapies. The IP system is an essential enabler of the complex, high-risk R&D that it takes to discover and develop breakthrough treatments like these that address unmet patient needs, and allow us to tackle some of society's greatest healthcare challenges. Contrary to popular narrative, it is also an enabler of, not a barrier to, access.

During the COVID-19 pandemic, IP further played a central role in enabling the fastest, most successful global pandemic response in history. IP supercharged innovation, drove unprecedented levels of collaboration, and enabled a global manufacturing network that allowed supply to meet and exceed global demand in record time. These facts alone demonstrate why further weakening the IP system in relation to pandemics—as would be the result of expanding the TRIPS waiver to therapeutics and diagnostics—would be counterproductive, and severely undermine our ability to prepare for and respond to the next pandemic at the same levels that we did for COVID-19.

But there is also a lot more at stake than may be visible from the tools available to treat COVID-19 today. From the earliest days of the pandemic, in addition to testing our own compounds and medicines

¹⁴⁰⁶ <https://www.devex.com/news/a-new-consortium-plans-to-get-paxlovid-to-lmics-103943>

¹⁴⁰⁷ <https://scholar.harvard.edu/melissabarber/publications/estimated-cost-based-generic-prices-nirmatrelvirritonavir-paxlovid>

¹⁴⁰⁸ <https://www.wipo.int/edocs/pubdocs/en/wipo-pub-1075-en-covid-19-related-vaccines-and-therapeutics.pdf>

for potential efficacy against the virus, and helping our industry peers scale-up their treatments and vaccines, we turned our efforts to developing powerful new classes of antivirals and other technologies that have the potential to target broad swaths of the universe of pathogens that make us sick, including those that may cause the next global health crisis. This includes our ongoing work to develop Mpro-based antivirals, which have the potential to treat the entire family of coronaviruses, from yet-undiscovered pandemic threats, to the ones that cause the common cold. It also includes our work with Swiss biotech Molecular Partners, to develop a new class of genetically engineered proteins called DARPin[®], whose scalability and ability to bind a virus in multiple locations makes them especially well-suited for antiviral therapy. In many cases, the utility of these technologies does not end with infectious diseases, but also includes the capacity to treat other illnesses, including cancer and many more.

Given the broad promise and versatility of these nascent technologies, which extends well beyond COVID-19, weakening the IP rights that have, and will be needed to continue to enable them, threatens to slow or even shut these areas of research down, at a time when we have barely begun to explore their potential, and have never needed them more. Expanding the TRIPS waiver to COVID-19 therapeutics would do just that, chilling investment, diverting research and resources elsewhere, and depriving the world of powerful new technologies that may represent our best chance of preventing or quickly overcoming the next global pandemic, as well as some of the world's other healthcare challenges.

Oxfam America

Oxfam urges U.S. Government support for extending the World Trade Organization (WTO) June 2022 Ministerial Decision.

1. Inequitable access to COVID-19 medical tools is partly due to intellectual property (IP) barriers.

COVID-19 deaths and hospitalizations continue at unacceptable levels while tens of millions of people experience long COVID, costing the economy trillions. Risks for future variants and surges persist.

World Health Organization (WHO) reports identify unaffordable pricing as a challenge for developing country access to diagnostics and therapeutics; such pricing is enabled by IP monopolies that block price-lowering generic competition.

Opponents pointing to limited product orders fail to capture the potential impact of an extension. Instead, consider need for wider access to therapeutics and diagnostics based on how many people could benefit from use of these and future tools. Consider also how order demand may change if products were more affordable. For example, test-and-treat approaches employed in the U.S. could become feasible for more countries, motivating increased demand.

2. This decision impacts potential future tools.

There were massive inequities in the roll out of existing COVID-19 tools; there is little reason to expect a different pattern for future tools. With over 270 treatment and antiviral candidates in clinical development and numerous unaddressed treatment needs, it is vital to consider access to potential future products.

The World Intellectual Property Organization identified 5,293 COVID-19 patent applications published through September 2021. Future COVID-19 therapeutics and diagnostics may well face IP barriers.

3. IP holders' voluntary access measures are insufficient.

Voluntary measures often include restrictions limiting their impact. Consider the Medicines Patent Pool deals for WHO-recommended oral antivirals excluding nearly half the world's population, including dozens of middle-income countries. Some excluded middle-income countries are reportedly charged \$250 per course for Paxlovid, for example – over 16 times higher than the estimated sustainable generic price.

Countries included in voluntary measures are not assured timely equitable access, with major deals with global procurement platforms facing months-long delays.

4. Evidence suggests this extension would not undermine innovation.

Research indicates that compulsory licenses encouraged innovation in the past while overly restrictive IP rules can hamper innovation.

Ultimately this is a time-limited decision that only applies to WTO developing countries for COVID-19. It seems unlikely to significantly impact pharmaceutical company revenues given relatively limited sales by IP holders in developing countries.

5. Developing countries should be supported in efforts to ensure a more appropriate balance between IP protections and access to medical products.

The U.S. has issued numerous compulsory licenses, including in the pandemic. Yet when developing countries consider compulsory licenses, they often face undue industry and political pressure from the U.S. and other wealthy countries in response.

People's ability to access COVID-19 medical tools should not depend on where they live. In a global pandemic that has repeatedly resulted in inequitable access to medical tools, the U.S. should support developing countries to access products that can save lives and control COVID-19 through every avenue. This should include supporting the extension of the Ministerial Decision to COVID-19 diagnostics and therapeutics.

Partnership to Fight Infectious Disease

The Partnership to Fight Infectious Disease (PFID) is a convenor of a diverse group of stakeholders including patients, healthcare providers, community organizations, academic researchers, and industry groups. PFID is concerned with the proposed extension of flexibilities to weaken IP protections under the World Trade Organization TRIPS Agreement.

PFID recognizes that diagnostics and therapeutics are essential in the fight against the COVID-19 pandemic. And ensuring equitable access to these products is a critical global health goal that we share.

Expanding the TRIPS waiver, however, would not advance that goal. Worse, such a policy would have devastating unintended consequences for the future of medical science and our ability to respond to future infectious disease threats.

The implicit assumption behind the proposed waiver is that the intellectual property (IP) protections established by the TRIPS Agreement somehow inhibit access to COVID-19 diagnostics and therapeutics. By suspending these protections, the reasoning goes, the WTO can make these items more readily available, particularly in low-income nations.

But the fact is, there is no evidence that IP protections impede access to any of the tools needed to combat COVID-19. This became clear during the debate over the vaccine waiver. That policy was intended to help countries like South Africa and India ramp up vaccine manufacturing. Yet, within weeks of the waiver's adoption, Aspen Pharmacare's plant in South Africa -- the continent's first vaccine manufacturing facility -- announced it would stop making vaccines due to a lack of demand.

That story is hardly an outlier. Barriers to vaccine access had little to do with manufacturing -- and nothing at all to do with IP protections. Hesitancy and inadequacies in healthcare delivery systems are known to be the greatest barriers to more widespread uptake.

And the same can be said for COVID-19 diagnostics and therapeutics. IP protections have bolstered, not hindered, patient access. Rather, international respect for IP has made possible an extensive network of voluntary licensing and manufacturing agreements around the world.

According to a communication from Switzerland and Mexico to the TRIPS Council last year, "no shortage of therapeutics exists. Instead, large parts of innovators' production capacity remain idle due to a lack of demand." The communication goes on to note that "Global demand for tests has reduced and there is no evidence to suggest that supply is constrained relative to actual demand."

Waiving IP protections on therapeutics and diagnostics will not have a positive effect on the current pandemic. But an expanded waiver would have profoundly harmful consequences for the world's capacity to respond to future public health threats. The innovative biomedical system, with its strong, consistently enforced IP protections, is an indispensable component of the biomedical research ecosystem.

These protections enabled the life-saving COVID-19 innovations, their evolution to keep pace with an evolving virus, and their availability -- all in record time. Undermining those protections will put this entire ecosystem at risk, while providing no real benefit to patients in need around the world.

It is for these reasons that the United States should reject the TRIPS waiver expansion.

People's Vaccine Alliance

Sound public health policy requires sustained supply of affordable tests and medicines for countries to face dangers such as COVID-19. However, this is not available to Lower and Middle Income Countries (LMICs) as pharmaceutical companies have monopoly on knowledge and technology and therefore, they control: supply, allocation, and price.

The monopoly on COVID-19 technologies has resulted in rich countries getting priority to access all the tests and medicines they need while LMICs have to wait for pharmaceutical companies ad hoc charitable actions after satisfying the rich market and securing the highest profit.

Therefore, LMICs cannot rely on arbitrary actions by pharmaceutical companies to implement COVID-19 test and treat strategy. LMICs need to have sustained supply at affordable prices which can be established via local/regional manufacturing of these products. Governments can issue compulsory licensing but the retaliation from companies and High-Income Countries is huge. For example, in 2006 Thailand faced threats of trade sanctions from US and EU.

The experience of HIV medicines is a clear example of the role of generics produced in developing countries in expanding access to Antiretrovirals and setting benchmark prices for newer medicines. The result is that at the end of 2021, over 28 million people are on treatment.

Critical points:

1. Compulsory licensing is an integral part of the TRIPS agreement and it has been used over 55 times by the US government during COVID-19.
2. The WTO June 2022 decision did not waive all intellectual property rules, did not suspend patents but clarified one point in Article 39 related to production for export.
3. Extending the June 2022 decision to medicines and tests would provide the market incentive necessary for generic producers to manufacture COVID-19 tests and treatments enabling sustained supply to LMICs.
4. China has selected to opt out of the June 2022 decision so will not benefit from the extension.
5. The extension is relevant only to COVID-19 tests and medicines. Countries and generic companies would have to abide with this restriction in cases of medicines with multiple use. Pharmaceutical companies' donations, tiered pricing, and voluntary licensing face the same issues regarding medicines of multiple use. The challenge is not unique to the extension of the WTO June 2022 decision.
6. Companies' actions of donations, tiered pricing, and voluntary licensing may provide some doses to some people in some countries. However, they exclude millions of people, they are totally dependent on companies' will for if and which action, for which countries, when, what doses, and other conditionalities.
7. The US played a critical role in the WTO June 2022 decision and in delaying the decision on the extension. This investigation can provide the basis for the final decision for the extension.

The US must act in support of global public health learning from previous and current pandemics. Access to tests and treatments require scaling up production in LMICs- by extending the WTO June 2022 decision to cover tests and treatments.

Pfizer

As the developer of both the first COVID-19 oral antiviral therapeutic, PAXLOVID, and, in partnership with BioNTech, the first COVID-19 vaccine to receive Emergency Use Authorization from the U.S. Food & Drug Administration, Pfizer is uniquely positioned to address the issues before the Commission. Those products were made possible by the global IP system, whose protections enable the long-term risk-taking, collaboration and investments necessary to develop such complex medicines. Expanding the TRIPS waiver would only undermine those protections and weaken the ability of companies to invest in the type of innovation and partnerships that helped us confront the pandemic and will help us respond to future pandemics.

There is also no factual basis for expanding the TRIPS waiver to therapeutics. Pfizer enabled broad and equitable access for PAXLOVID through tiered pricing, a voluntary license agreement with the Medicines Patent Pool, supply agreements with UNICEF and Global Fund and other initiatives. That is why with the MPP, UNICEF, and Global Fund agreements, every low and middle-income country in the world, except China, now has the potential to access PAXLOVID or a generic version through one or more of these pathways (as explained in Pfizer's comments, China has access through other agreements).

Despite these efforts, the principal access challenges for COVID-19 therapeutics remain. They include pandemic fatigue, healthcare professional education, testing capacity, and sustained overall pandemic response financing. Weakening IP rules will not solve any of these challenges. Pfizer is also not aware of any generic manufacturers who have sought a compulsory license for PAXLOVID.

Although there are no benefits from expanding the TRIPS waiver, the costs of doing so would be significant. The patent system enabled Pfizer to build a research infrastructure that allowed us to quickly mobilize and devote the necessary resources, technical knowledge, and know-how to combat the pandemic. That system will fuel the next generation of solutions to tackle any future crisis, while undermining it puts that progress at risk. Moreover, the TRIPS waiver mechanism adopted last June lacks clear guardrails for safety, post-market surveillance and equitable distribution of licenses found in voluntary licenses. WTO Members should instead focus on the steps needed to improve access to therapeutics, including strengthening and maintaining health infrastructure to deliver therapeutics; increasing access to testing; implementing public information campaigns to increase awareness and acceptance of therapeutics; and, importantly, removing trade barriers.

Pharmaceutical Research and Manufacturers of America (PhRMA)

The evidence does not support extending the TRIPS waiver to COVID-19 therapeutics.

First, the evidence shows that governments around the world have access to affordable COVID-19 therapeutics. Supply significantly exceeds demand, even if we were to assume per capita consumption levels dramatically increased to become equivalent to those in the United States. PhRMA members have successfully worked with governments and generic manufacturers in developing countries, as well as with multilateral organizations and mechanisms such as COVAX, the Medicines Patent Pool, Global Fund and UNICEF, to provide access pathways for these innovations to all countries and are fully committed to providing global access to COVID-19 vaccines and therapeutics.

Second, to the extent that patients in some countries may not have the same level of access as here in the United States, this is not due to a lack of affordable doses, but rather to regulatory, last-mile administration and systemic barriers in those markets. With worldwide demand for COVID-19 therapeutics waning and governments and the WHO declaring an end to the public health emergency, the evidence does not support the need to increase supply of COVID-19 therapeutics.

Third, no evidence has been presented to demonstrate that waiving commitments to protect intellectual property (IP) will address the real barriers to accessing COVID-19 therapeutics. On the contrary, without credible and certain IP rights, companies would be unable to justify the significant investments needed to research and develop innovative medicines. Moreover, as demonstrated during the COVID-19

pandemic, IP protections have enabled foundational R&D and partnerships to develop COVID-19 solutions in record time and facilitated hundreds of collaborations globally to manufacture COVID-19 vaccines and therapeutics at scale. While TRIPS already anticipates the use of compulsory licensing, it does so as a limited exception to an innovator's patent rights and seeks to make them a measure of last resort. In practice, compulsory licenses, as demonstrated during the COVID-19 pandemic, are rarely the best mechanism for meaningfully improving patient access, and no evidence has been provided that greater flexibility is needed to grant compulsory licenses for COVID-19 therapeutics.

Finally, even if one were to erroneously assume that extension of the waiver to COVID-19 therapeutics would address patient access, any "benefit" would be significantly outweighed by the harm a waiver extension would inflict on innovation for treating COVID-19 and other medical conditions. U.S. workers supporting biopharmaceutical manufacturing and development would suffer as well. The existing waiver has significant legal and political ramifications and inappropriately signals that IP protections are a barrier that should be waived to address any global crisis. These implications exist even though no government has utilized the waiver on COVID-19 vaccines. Extending the waiver to therapeutics would exacerbate these harms without providing any tangible benefits in terms of patient access.

For these reasons, the innovative biopharmaceutical industry repeats its call for the Administration and all policymakers to reject any expansion of the TRIPS waiver and instead focus on the shared objective of solving challenges to distributing and administering the global surplus of COVID-19 vaccines and therapeutics.

Public Citizen Access to Medicines

The intellectual property provisions of the TRIPS Agreement constrain generic competition and rapid, widespread production of therapeutics and diagnostics. This contributes to inequitable global access to COVID-19 medical tools. Extending the June 17, 2022 World Trade Organization Ministerial Decision on the TRIPS Agreement (the 'TRIPS Decision') to therapeutics and diagnostics would simplify efforts to ensure adequate, affordable supply of these medical tools in the years ahead.

There is massive unmet global health need for COVID-19 therapeutics and diagnostics. The world's failure to quickly scale test-to-treat programming has cost many lives. Yet country orders for these medical tools, and other signals of market demand, were distressingly anemic in 2022. For example, the estimated health need for Paxlovid in low- and middle-income countries (LMICs) exceeded market demand by 8,219,833 courses; only 10% of health need was met by the expressed demand of LMICs in 2022. It is important to understand why.

Global demand for COVID therapeutics and diagnostics is constrained by supply challenges - high prices, opaque purchase agreements, and delayed and unpredictable supply. Many patented tools are unaffordable for LMICs, even with industry's tiered and not-for-profit pricing. The secrecy of supply agreements also complicates country procurement decisions. It is challenging for budget constrained LMICs to compete with high-income countries to purchase products in initially limited and/or unreliable supply. An extension of the TRIPS Decision could help facilitate affordable and reliable generic supply.

In addition to supply challenges, LMICs are faced with other access barriers, making it critically important to ensure that countries are able to access affordable supply of diagnostics and therapeutics. Competing health priorities and strained resources limit the ability of governments to prioritize their

country's COVID-19 response. There are also knowledge gaps regarding the available health technologies and the value of testing and therapeutics.

Without diverse, affordable, and reliable supply, demand for diagnostics and therapeutics will continue to be far less than health need. Or, put differently, supply will be inappropriate: even where raw production numbers appear high, a late supply of expensive, single-source drugs, sold under concealed conditions, does too little for public health. Patent holders' licensing arrangements can mitigate the problems of monopoly supply over time, but they have fallen far short of unleashing the world's capabilities to manufacture and provide timely and affordable medicines. Voluntary licenses typically contain geographic restrictions, resulting in market fragmentation and gaps in access, particularly for upper middle-income countries.

TRIPS flexibilities including compulsory licensing are critical to fill these gaps and are much more easily applied to therapeutics and diagnostics than to vaccines. But TRIPS rules still needlessly complicate compulsory licensing, making it harder to clear paths to expansive, affordable, global supply. Simplifying TRIPS rules, including through the proposed extension, would help clear paths to generic entry and make it easier for health agencies to meet the extreme, ongoing health needs of the COVID-19 pandemic.

Public Services International (PSI)

Frontline health workers needlessly experienced immense suffering from the impact of the COVID-19 crisis, driven by the strict implementation of the TRIPS agreement. To prevent further suffering, we call for action at the World Trade Organization (WTO) to ensure that COVID-19 Diagnostics and Therapeutics are available and affordable everywhere in the world.

The brutal inequality in access to tests, treatments, vaccines, and Personal Protective Equipment (PPE) directly resulting from the stringent application of IPRs is a major factor in the death of thousands of health workers. The WHO and its partners have recognised this fact and are calling on political leaders and policymakers to take the necessary steps to safeguard against healthcare workers' deaths in this pandemic and going forward.

Health and care workers believe it is unfair and counter-productive for world leaders to clap for us and call us frontlines heroes but show no political will to support the protection of health workers. Policymakers need to craft policies that will fill the gaps in health needs between the Global North and the Global South, especially during pandemics, to show that they really care for those who care for us all.

We believe it is impossible to win the fight against COVID-19 under circumstances where some countries can receive Antiviral Drugs for COVID-19 one year before others. Nor is it possible when citizens of low- and middle-income countries have to spend anywhere between five to 21 times their daily wage to do one COVID-19 test. And we know health workers will continue to die needlessly until PPE, vaccines, diagnostics, and treatments become affordable, available, and accessible.

We, therefore, call on this commission to do what is needed. Frontlines healthcare workers in the fight against COVID-19 are calling on you to not dash the hope of millions of people in low- and middle-

income countries. We trust that you will support the extension of the June 2022 TRIPS decision on COVID-19 vaccines to cover tests and treatments.

Below, I provide further evidence of the inability of healthcare workers and all people in and low and middle-income countries to access COVID-19 tests, the unaffordable prices for testing, the orphaning of their children, and the mental trauma they have experienced, no doubt exacerbated by poor access to medical countermeasures.

I would like to underline that, in addition to the evidence that I and others have provided of the continued barriers to accessing COVID-19 test and treatments, there are issues on the ground that cannot be quantified in data. For many health workers in low and middle-income countries, access to COVID-19 tests has been sparse, and access to COVID-19 treatments has been completely absent.

This situation has emerged amid an unprecedented global moment advocating for access to COVID-19 vaccines, tests, and treatments. Put simply, if access is this bad when the world's attention has been on this issue, how much worse will access be for the next generation of COVID-19 treatments and tests, when pharmaceutical companies are not under this sustained pressure?

Rethink Trade

U.S. support for a WTO Decision to temporarily facilitate exports of safe, affordable generic COVID-19 treatments and tests that developing countries have capacity to produce for use in other developing nations would provide access now simply unavailable to billions of people. Extending the WTO COVID Decision would deliver major global health benefits and U.S. geopolitical gain with no downside.

1. There is significant unmet demand for affordable treatments and tests in developing countries, which can be documented using the public health measure of unmet need based on infection rates.

Without affordable supply, countries cannot gear up public health campaigns nor place orders. The lack of orders measures lack of affordable supply, not lack of need.

2. The history of HIV-AIDS and hepatitis shows why the ITC must not limit its study to treatments now on the market. Combination treatments, sometimes not even including those first discovered, have proved most effective in battling viruses. Hundreds of COVID-19 treatments are in the pipeline, many in final trials.

3. There are numerous known IP barriers affecting treatments. Even by September 2021, there were at least 1,465 patent filings for COVID-19 therapeutics with many more to come. A WIPO report also found that 80% of the compounds were repurposed, meaning they required minimal R&D and benefited from a 20-year patent monopoly and significant profits.

4. Control of production and distribution of COVID medical technologies by a limited number of pharmaceutical corporations is enabled by intellectual property monopolies enforced globally by the WTO. This results in pricing that is not affordable in most developing countries. The so-called not-for-profit prices drug monopolists offer in tiered systems are unaffordable. Consider the \$250 Paxlovid offered poor countries, which is multiples higher than the Clinton Foundation's \$25 generic price or the estimated \$15.08 cost-of-production-plus-profit figure produced at Harvard.

5. Neither voluntary licensing nor existing WTO intellectual property rules’ “flexibilities” can facilitate timely production of affordable treatments. Numerous generic producers in developing countries are already producing doses of similar treatments being used today. But, the Medicines Patent Pool and other voluntary license deals empower IP holders to control where medicines can be sold and exclude many nations with large populations. Consider Pfizer’s MPP deal for generic Paxlovid. It allowed sales in only 96 nations but barred sales in 100 countries with 47% of the world’s population and high infection rates. And, existing WTO flexibilities do not facilitate access because they limit compulsorily licensed production to mainly domestic use. This denies prospective generic producers economies of scale, which undermines investment needed to start production. Countries with capacity are not producing treatments like Paxlovid, and not preparing to produce the many more promising treatments in the pipeline.

6. There is no downside to U.S. support for a larger portion of generic medicines that WTO rules already permit to be made to be exported. The generic medicines could only be used in poor nations, so pharmaceutical firms and U.S. workers would see no impact, given their market is for-profit sales in wealthy countries.

Sarah Gabriele – Harvard University

Existing flexibilities or patent waivers are promising legal mechanisms and should be taken advantage of with respect to diagnostic and therapeutics for the screening and treatment of Covid-19. However, exceptions to intellectual property law and their implementation have often proven problematic and ineffective. In this regard, the constant efforts by developing countries to limit the impact of intellectual property rights, resorting to the use of flexibilities, such as compulsory licenses and parallel importation schemes, have been undermined by certain developed countries that have often disfavored the use of such mechanisms, reflecting heightened sensitivity to the interests of pharmaceutical companies. Consequently, the use of flexibilities has failed to be the tool to achieve distributive justice that the international community and, more importantly, low-and middle-income countries had hoped for. This written submission does not address whether flexibilities should be implemented for COVID-19 diagnostics and therapeutics. Given the importance that these technologies, any consideration regarding the need to access them is superfluous. In this regard, there should be no question as to the need to leverage current mechanisms to foster access to these technologies, but instead, we should be focusing on how we can best implement them. My work focuses on highlighting critical priorities such as cooperation with international organizations to ensure that every country has the proper legal framework in place and the responsibility of every nation, including high-income countries, to foster the debate and enable the use of flexibilities or the adoption of a patent waiver.

Under the current framework, member states have the possibility, but not the responsibility, to draft mechanisms to enact in case of health emergencies. The lack of guidance in drafting flexibilities has often led to fragmented patent legislation across WTO Members. At the same time, it has resulted in several low- and middle-income countries still needing more implementation of specific schemes in their national patent legislation. To provide the necessary support in drafting and including flexibilities in national legislation, an international organization such as WIPO, which already supports and plays an essential role in providing developing countries with technical assistance to implement flexibilities, should be tasked with the role of assisting countries not only with the best ways to include exceptions in

national patent legislation but to help with establishing strategies for enforcing them as well. Addressing the existence or fragmentation of flexibilities in national patent legislation, however, does not, alone, provide a solution to the problem of implementing flexibilities. Countries not only face hurdles in incorporating this kind of legislation in their national patent legislation but also struggle to implement it successfully. The application and enforcement of flexibilities is not a tool at the complete discretion of low-income countries, which might fear opposition and retaliation. In this respect, this investigation should be careful at avoiding a hold-up of the negotiations for adopting existing flexibilities or establishing patent waivers, and future negotiations should be mindful of the harm that delaying the implementation of a solution, as happened during the negotiation for the first patent waiver, could cause.

Small Business & Entrepreneurship Council

Expanding the WTO's intellectual property waiver to Covid-19 diagnostics and therapeutics would significantly harm the small businesses that drive pharmaceutical innovation in the United States, leaving patients without access to various lifesaving new medicines and tests, while damaging the U.S. economy and its innovative capacity in the process.

Small businesses are responsible for the lion's share of U.S. pharmaceutical innovation. This is only possible because of our strong and reliable system of intellectual property protections, which provide entrepreneurs and investors an opportunity to earn a return on the time, energy, and capital they have devoted to a risky business venture. Without such an incentive, many startups - which make for inherently high-risk investments - would never get off the ground.

Suspending IP protections on Covid-19 diagnostics and therapeutics would dismantle this incentive structure. Knowing that governments can arbitrarily waive patents on revolutionary inventions, funders and entrepreneurs will question whether to invest in these small businesses -and their innovations - in the future.

That will have ripple effects across the entire economy.

Small firms, which account for over 99% of U.S. businesses and employ nearly half the nation's workforce, are vital to America's economic success. This is particularly true in IP-intensive sectors such as the pharmaceutical industry, where small companies make up 96% of all firms and each innovation generates numerous jobs. For instance, the development of Covid-19 vaccines and treatments alone supported 400,000 American jobs.

Extending the TRIPS waiver would jeopardize future jobs at small firms in IP-intensive industries. While the current waiver proposal focuses on Covid-19 diagnostics and therapeutics, global leaders, including UN Secretary-General António Guterres, have advocated for removing IP constraints in other sectors. If the WTO agrees to the waiver extension, investors across IP-intensive industries may fear their sectors will be targeted next, leading to reduced capital and inhibiting new projects and job creation in multiple industries.

Some might argue that these harmful consequences are simply the price we must pay to promote equal access to Covid-19 treatments and tests throughout the world. However, the fact remains that there is no shortage of Covid-19 diagnostics and therapeutics. That is why, in a November communication to the

TRIPS Council, the governments of Switzerland and Mexico concluded that “we do not face an IP-induced lack of access or a lack of manufacturing capacity of Covid-19 therapeutics and diagnostics.”

Extending the TRIPS waiver will constrain America’s small businesses and entrepreneurs, impose irreparable damage to the economy, and mar our nation’s innovative standing without doing anything to increase access to diagnostics and therapeutics. For these reasons, SBE Council urges the ITC to recommend against a waiver expansion.

Social Watch

Timely affordable access to supplies of pharmaceuticals to test and treat COVID-19 patients has been a constant struggle for developing countries. This serious concern has persistently and repeatedly been highlighted by the WHO and its various expert committees.¹⁴⁰⁹

The WHO’s current guidelines on COVID-19 therapeutics that recommend baricitinib, nirmatrelvir, tocilizumab, sarilumab expressed caution that this recommendation could “exacerbate health inequity” as access to diagnostics and therapeutics are a challenge in many developing countries as they are either unavailable and/or unaffordable, and without concerted effort are likely to remain so. The guidelines also add that “given the demonstrated benefits for patients, it should also provide a stimulus to engage all possible mechanisms to improve global access to these treatments”.¹⁴¹⁰

In December 2022, the WHO Director-General emphasized: “[a]ccess to diagnostics and life-saving treatments for COVID-19 remains unacceptably unaffordable and unequal”, adding that “[t]he burden of post-COVID-19 condition is only likely to increase.” Advocating that WTO Members support the extension of the TRIPS Decision to therapeutics and diagnostics, the WHO Director-General stressed the imperative to “implement all the available tools they have to make local production possible and improve access.”¹⁴¹¹ In 2023, he once again stressed: “[v]accines, therapeutics, and diagnostics have been and remain critical in preventing severe disease, saving lives and taking the pressure off health systems and health workers globally. Yet, the COVID-19 response remains hobbled in too many countries unable to provide these tools to the populations most in need, older people and health workers.”¹⁴¹²

Opponents of the extension argue that the problem is not one of access, but allegedly of low volume of orders placed for treatments and tests. But in fact demand for tests and treatments in developing countries has been artificially suppressed. First, rich countries hoarded initial supplies and big biopharmaceutical and diagnostic manufacturers prioritized higher-priced sales to developed countries.

¹⁴⁰⁹ See, e.g. [https://www.who.int/news/item/12-07-2022-statement-on-the-twelfth-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-coronavirus-disease-\(covid-19\)-pandemic](https://www.who.int/news/item/12-07-2022-statement-on-the-twelfth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic) and https://www.who.int/publications/m/item/act-accelerator-facilitation-council-working-group-report-on-diagnostics-and-therapeutics?utm_source=substack&utm_medium=email.

¹⁴¹⁰ <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1>.

¹⁴¹¹ See <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-who--wipo--wto-joint-technical-symposium-on-the-covid-19-pandemic--response--preparedness--resilience---16-december-2022>.

¹⁴¹² See [https://www.who.int/news/item/30-01-2023-statement-on-the-fourteenth-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-coronavirus-disease-\(covid-19\)-pandemic](https://www.who.int/news/item/30-01-2023-statement-on-the-fourteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic).

Second, absent generic production, the prices for diagnostics and treatments that do become available are not affordable for developing countries.

As Nobel laureate Professor Joseph Stiglitz has noted, test and treat programs in developing countries will be limited no matter how dire the need unless ample supplies of affordable diagnostics and treatments are readily available.¹⁴¹³ Consideration of “unmet demand” should reflect people’s actual needs – based on infection rates (including if and when it accelerates again) and the target populations that would be treated – were testing and affordable courses of treatments readily available. Some examples were provided in our public hearing statement and post-hearing brief e.g. developing countries are only testing at 14% the rate of developed countries.¹⁴¹⁴

The likelihood that improved treatments might be beneficial to treat populations beyond the “highest risk” group is also an important factor for consideration.

Third World Network

TRIPS Decision Should be Extended. Big Pharma Arguments Against Extension are Spurious

TRIPS is premised on IP systems being balanced to ‘the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations.’ It recognizes that governments may need to take measures, to prevent abuse of the IP system and to protect public health. Accordingly, “flexibilities” have been built in to enable WTO Members to take measures to protect public interest.

Unlike Big Pharma’s misleading assertions, the TRIPS Decision of 17th June 2022 does not waive TRIPS or patents. It only waives one condition (Art. 31(f) of TRIPS) on using compulsory license (CL), thereby allowing manufacturers to achieve economies of scale, and to supply other developing countries with insufficient manufacturing capacity. Other elements (paragraph 3 (a), (d) and 4) of the Decision clarify what is allowed by TRIPS.

Concerns proliferated by Big Pharma about the extension are unjustified. The Decision is narrow in scope and time bound (5 years). It is specific to COVID-19 and cannot be used for any other purpose.

A developing country government that intends to use the Decision will have to issue a CL for a specific purpose and duration. Notably Article 31(c) of TRIPS makes clear that “the scope and duration of such use shall be limited to the purpose for which it was authorized”. This means a compulsory licensee will have to operate within the parameters of the license granted. And in situations where the TRIPS Decision is invoked, within the parameters of the Decision.

Further, the use of CL is subject to paragraphs (g), (h), (i) and (j) of Article 31 that require payment of adequate remuneration, and present review options to a patent holder that has concerns about the use of a CL.

Importantly, the Decision is only applicable to ‘developing countries’ Sales of pharmaceutical companies are mostly in developed country markets, and these are not affected. The Decision also prevents re-

¹⁴¹³ <https://www.scientificamerican.com/article/the-international-community-must-prioritize-covid-treatment-and-test-access/>.

¹⁴¹⁴ <https://www.un.org/development/desa/dpad/wp-content/uploads/sites/45/LDC-testing-31-Dec-22.pdf>.

export of products manufactured and imported under the Decision, with WTO Members having to ensure that products are not diverted to their markets inconsistently with the Decision.

In the ongoing COVID-19 pandemic, many countries including developed countries enacted progressive CL provisions to make it easier to use CL, while others such as Israel and Hungary have actually issued CL to address shortages of COVID-19 therapeutics. The US has also relied on the right to use CL in its COVID-19 contracts. These instances have not affected pharmaceutical profits or R&D.

On 5 May 2023, WHO stressed that COVID-19 is claiming “a life every three minutes – and that’s just the deaths we know”. “This virus is here to stay. It is still killing, and it’s still changing. The risk remains of new variants emerging that cause new surges in cases and deaths.”¹⁴¹⁵ Extension of the Decision will strengthen the ability of developing countries to respond to this global health threat.

TWN Trust India

Voluntary licenses are deficient public health tools and not a substitute for compulsory licenses

Voluntary licenses (VL) are inadequate and are not a substitute for compulsory license (CL). By its very nature, VLs are voluntary and thus not guaranteed. For example, in the case of baricitinib, no VL has been granted for supply to developing countries.¹⁴¹⁶ Further, VL terms are determined by the patent holder and often delay access, are anti-competitive, anti-innovation as well as exclude many developing countries from being supplied by the licensees.¹⁴¹⁷ VLs even those by the Medicines Patent Pool (MPP) suffer from these limitations. For e.g. the MPP- Pfizer paxlovid VL prohibits the licensee from supplying many developing countries including most Latin American countries even as Pfizer continues to file additional patents in all of these countries that will last until at least 2041.¹⁴¹⁸ This same VL contains troubling conditions preventing R&D on combination regimens, co-formulation, and even co-packaging that may be helpful to treat COVID-19.¹⁴¹⁹ In the case of the MPP-Merck VL on molnupiravir, developing countries excluded from supply had 30 million infections in the first half of 2021, and 50% of all infections in developing countries.¹⁴²⁰

In 2022, Mexico and Switzerland argued that numerous VLs had been signed, suggesting that affordable generic supply was not an issue. Unfortunately, VLs often provide the illusion of timely access and are often referred to by opponents of TRIPS flexibilities to justify inaction. The reality is quite different. Generic supply only became available in December 2022, one year after the MPP-Pfizer VL was signed, and that as well only from one generic company to supply a limited number of countries. This means that even for countries that may be supplied by the VL sub-licensees, they had to wait at least one year

¹⁴¹⁵ <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing---5-may-2023>.

¹⁴¹⁶ See <https://msf-access.medium.com/jak-inhibitors-promising-treatment-for-people-with-severe-covid-19-illness-2b14e812a434> and <https://www.msf.org.za/news-and-resources/press-release/south-africa-must-urgently-revoke-patents-key-covid-19-treatments>.

¹⁴¹⁷ See <https://msfaccess.org/voluntary-licenses-access-medicines>.

¹⁴¹⁸ <https://msfaccess.org/latin-america-how-patents-and-licensing-hinder-access-covid-19-treatments>.

¹⁴¹⁹ See <https://healthgap.org/pfizerletter/> and <https://infojustice.org/archives/44914>.

¹⁴²⁰ <https://www.twn.my/title2/health.info/2021/hi211101.htm>.

for generic supply to become available. Further as mentioned, many developing countries cannot be supplied under the VLs.

In contrast, CLs allow governments to take immediate action to facilitate access by issuing a license to a third party to exploit the patented invention without the consent of the patent holder, in accordance with Article 31 of TRIPS. Experience shows that use of CLs has positively improved timely access.¹⁴²¹ However, effective use of CLs requires generic supply, a challenge for countries with small economies and insufficient manufacturing capacity due to the Article 31(f) condition of TRIPS, which restricts the amount that may be exported under a CL. Extension of the TRIPS Decision will waive this condition, allowing economies of scale to be achieved and enabling diagnostics and therapeutics from developing countries with manufacturing capacities to be exported to other developing countries in need within the terms of the Decision.

Claims that CLs discourage innovation are spurious. For e.g. analysis from NBER found that when patent rights are too broad, innovation is discouraged, and that CL can indeed encourage innovation.¹⁴²²

U.S. Chamber of Commerce

The Chamber is deeply concerned about proposals to expand the WTO TRIPS Waiver to covid-19 therapeutics and diagnostics. The Chamber believes that an expansion of the TRIPS Waiver will have many negative repercussions.

First, an expansion of the waiver will diminish U.S. leadership on IP policy and endanger U.S. national security. U.S. support for the initial vaccine COVID-19 vaccine waiver in June 2022 marked a radical departure from the U.S. government's long-established position on global IP policy. Support for the waiver not only undermines our leadership on IP-driven biopharmaceutical innovation but also in emerging industries including digital, climate change, and agriculture-related technologies. The existing waiver threatens to force the disclosure of technology and know-how needed to create innovative technologies to America's economic competitors, including China. Expanding the waiver further compounds this threat.

Second, an expansion of the waiver will undermine the U.S. economy. The biopharmaceutical industry supports over 4.4 million U.S. jobs and adds \$14 trillion to the U.S. economy. An extension of the waiver will endanger the jobs and economic contributions sustained by IP-enabled innovation and jeopardize our fragile economic recovery.

Third, an expansion of the waiver will impair the life sciences innovation ecosystem that enabled the rapid response to the COVID-19 pandemic and endanger America's response to future public health crises. IP creates legal certainty that enables high-risk, high-capital investments, like those made into innovative medicines. IP also attracts new actors to the innovation ecosystem—including small biotech companies, academic institutions, venture capital firms, and the government—by providing assurances that their investments will be protected in global markets. An expansion of the waiver to include

¹⁴²¹ See Country experiences in using TRIPS safeguards: Part 1, WHO at <http://apps.who.int/iris/bitstream/handle/10665/272977/Countryexperiences-TRIPS-Part1.pdf?sequence=1&isAllowed=y>.

¹⁴²² https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2712428.

therapeutics and diagnostics would disrupt the innovation ecosystem and jeopardize investment into new treatments and cures, in turn undermining our ability to respond to the next major global public health threat.

Finally, an expansion of the waiver will impede the distribution of and access to pandemic-related technologies for patients who need them. The pandemic demonstrated that stakeholders in countries with strong IP frameworks were able to participate effectively in the innovation ecosystem that developed and delivered solutions, whereas those in countries with weaker IP standards found themselves on the sidelines waiting for solutions to be delivered. Accordingly, the Chamber believes the economic welfare of countries would be better served by measures seeking to enhance—rather than undermine IP standards—as an expansion of the TRIPS waiver will do. Furthermore, at the hearing, the waiver’s proponents clearly stated that an expansion of the waiver is critical to creating a path to access future medicines that will enter the market. However, proponents of the waiver fail to acknowledge that the pipeline of future treatments will not exist without effective IP protection. An expansion of the waiver will jeopardize investment in the innovative pipeline, causing uncertainty about whether new game-changing products will be available in the future.

For all these reasons, the Chamber urges the Commission to carefully consider the negative consequences of any expansion of the WTO ministerial decision to therapeutics and diagnostics.

Vacunas para la Gente

Vacunas para la Gente welcomes the opportunity to provide written comments on the Commission’s investigation on COVID-19 diagnostics and therapeutics, market dynamics, supply and demand, price points, the relationship between testing and treating, and production and access.

Speaking in representation of the Latin American chapter of the People’s Vaccine Alliance, also known as Vacunas para la Gente, a regional alliance made up of more than 40 civil society organizations and networks that have come together to fight unequal access to COVID-19 vaccines, treatments, and diagnostics in the region.

As pointed out in our testimony pharmaceutical companies’ measures to address inequity by licensing generics in low and middle-income countries will do next to nothing for Latin America. The first argument is that the licenses agreed for existing treatments through the Medicines Patents Pool exclude most of Latin America. Despite having 8% of the world population, the region had almost 30% of the total deaths from Covid-19 and the highest excess death figures. The lack of timely access to diagnosis and treatment not only impacts morbidity and mortality but also has an impact on the national health systems of the so-called long COVID, which has hit rural and indigenous populations the hardest.

Our second argument is that there is very little transparency on pricing, with Latin Americans paying ten times more than other developing countries for treatments. The lack of transparency in drug prices has been one of the main recommendations issued by the WHO, yet companies continue to withhold this information and put profits before people’s well-being. The experience of the global deployment of vaccines has shown that depending on negotiations with few pharmaceutical companies, inequality widens not only between countries but also within societies and communities. This increases the probability that people emigrate from their countries in search of better living conditions.

Finally, we argued that improving manufacturing capacity in the Global South is crucial. Extending the TRIPS Decision to diagnostic and therapy countries would make it possible to strengthen and utilize the great capacity that exists in the region for the production of tests and treatments. During the development of Covid-19 vaccines, several Latin American countries proved that they possess the human capital and infrastructure to manufacture life-saving medicines. However, the exclusion of Latin America will be repeated for the next generation of COVID treatments unless intellectual property barriers are addressed.

In conclusion, we highlight the need for pharmaceutical companies to address the inequity in accessing medicines and treatments for low and middle-income countries, particularly in Latin America. The lack of timely access to diagnosis and treatment, the lack of transparency in drug pricing, and the need to improve manufacturing capacity in the Global South are significant issues that need to be addressed. We stresses the importance of support from the United States to ensure a deal for tests and treatments that will benefit all countries, regardless of their economic status.

Washington Council on International Trade

The Washington Council on International Trade is the premier organization advocating for trade and investment policies that increase the competitiveness of Washington State workers, farmers, and businesses. WCIT is concerned that the World Trade Organization is weighing a proposal to extend the current intellectual property waiver to include COVID-19 diagnostics and therapeutics.

Supporters of the proposal assert that it would provide more equitable access to these products across the globe – the same argument advanced in favor of the vaccine waiver. But, once more, their argument is not backed by real-world evidence. In fact, suspending IP protections would *limit* access to these life-saving developments.

Voluntary licensing agreements have proven to be the most effective way to ensure quality medical care for low- and middle-income nations, as demonstrated by the licensing program that enabled Gilead to provide remdesivir to millions of patients in over 100 different countries. Pfizer and Merck have also taken similar tacks with their COVID-19 drugs, Paxlovid and molnupiravir, respectively.

Handing over the recipe for COVID-19 treatments and diagnostics to other nations will not boost global public health. It will, however, punish U.S. scientists, businesses, and workers who spearhead these life-saving breakthroughs in record time.

That's especially true in Washington State. As one of the most innovation-focused economies in the nation, more than one in three Washington jobs are found in industries that are highly dependent on IP protections, such as medical research and pharmaceutical development. More than 100,000 union jobs and \$30 billion in annual impact depend on Washington's thriving life-science sector. That includes tens of thousands of union jobs in the skilled trades – such as plumbers, electricians, and sheet metal workers.

The WTO's decision to waive IP protections for COVID-19 vaccines has already dealt a blow to an innovation ecosystem that made the United States the world's leader in medical innovation. Extending the IP waiver and allowing foreign countries to seize US-discovered and IP-protected COVID-19 diagnostics and treatments would only do further damage. It would send a signal that future research

and development might not be worth the effort. Much of our manufacturing capacity, and the jobs that go with it, would move abroad. After all, the relationship between IP protection and research and development expenditures is inseparable – and this is true in an array of industries. In Washington State, the IP-heavy aerospace, tech, clean energy, and artificial intelligence industries have all helped to make our state’s economy a magnet for talent and investment. Extending the TRIPS waiver would set a dangerous precedent for these industries.

IP protections secure the incentive structure of innovation. The entire development process is undertaken on the guarantee that steep investments can be recouped once a successful product is brought to market. Innovators cannot sink years and fortunes into groundbreaking ventures if they have no assurance that their work will be duly rewarded.

For the sake of economic growth, medical advancement, and job creation in the Evergreen State – and across the nation – this waiver proposal must not move forward.

Written Submissions Without Summaries

The following parties filed written submissions without summaries. Please see EDIS for full submission.

Table D.1 List parties that submitted written submissions without summaries

Name of party with written submission without summaries

60 Plus Association

Adrian Smith Congress of the United States

Advanced Medical Technology Association (AdvaMed)

Alliance for Biosecurity

Alliance for Trade Enforcement (AFTE)

ALLvanza

American Chamber of Commerce to the EU

American Intellectual Property Law Association (AIPLA)

Americans for America (Regina Thomson)

Americans for Tax Reform

Arizona Chamber of Commerce & Industry

Associated Industries of Massachusetts (AIM)

Association of American Universities (AAU)

Association of Women’s Business Centers

BASF

BioNJ

Business Council of New York State

California Life Sciences (CLS)

California Policy Center

Canadian American Business Council (CABC)

Carol Mimura- Assistant Vice Chancellor, IP & Industry Research Alliances at UC Berkeley

Center for Individual Freedom (CFIF)

Center for Innovation and Free Enterprise

Citizens Against Government Waste (CAGW)

Cletus R. Willems- Partner at Akin Gump Strauss Hauer & Feld LLP

Competere

Name of party with written submission without summaries

Consensus for Development Reform
Conservatives for Property Rights (CPR)
CSIS Renewing American Innovation
David S. Levine & Joshua D. Sarnoff- Professors at Elon University and DePaul University
David Winwood- Interim Associate VP at Wake Forest Innovations
Devon Herrick- Health Economist at the Benjamin Rush Institute
Embassy of Bangladesh
Erik Paulsen- Former Congressman from Minnesota
Fred Reinhart- Former Senior Advisor for Technology Transfer at University of Massachusetts Amherst
Freedom Foundation of Minnesota
Fundación Libertad y Progreso
Galen Centre for Health and Social Policy
Geneva Network
Global Alliance for Patient Access
Greater New Haven Chamber of Commerce
Health Advocacy International
Health Global Access Project, Inc.
Health Justice Initiative
Healthcare Leadership Council
Howard Dean- Former Governor of Vermont
IMANI Centre for Policy and Education
Initiative for Medicines, Access & Knowledge (I-MAK)
Institute for Policy Innovation
Institute for Regulatory Analysis and Engagement
Instituto de Ciencia Política Hernán Echavarría Olózaga, Colombia
International Cancer Advocacy Network (ICAN)
INTERPAT
Interpharma
Information Technology & Innovation Foundation (ITIF)
Iowa Association of Business and Industry
James Glassman- Former Ambassador
James Pooley- Former Deputy Director General at WIPO
Japan Pharmaceutical Manufacturers Association (JPMA)
Jeffrey Gold- Family Physician and owner of Gold Direct Care
John A. Fraser- President of Burnside Development and Associates
John Locke Foundation
Jonathan Soderstrom- Chief Licensing Advisor at Wilson Sonsini Goodrich & Rosati
Joseph Crowley- Senior Policy Director at Dentons
Joseph P. Hammang
Judge Susan G. Braden- Former judge of the United States Court of Federal Claims
Karl F. Landegger
Katherine Ku- Former Executive Director of the Office of Technology Licensing at Stanford
Knowledge Ecology International (KEI)
Kentucky Chamber of Commerce
Kristen Osenga- Associate Dean for Academic Affairs at the University of Richmond School of Law
Lamar Smith- Former Congressman from Texas
Lawrence County Chamber of Commerce
Libertad y Desarrollo
Life Science Tennessee (LST)
Life Sciences Acceleration Association
Life Sciences Pennsylvania

Name of party with written submission without summaries

Mackenzie Center for Economic Freedom
ManageHealthCareCosts.com
Mark Allen Cohen- Distinguished Senior Fellow and Director of the Berkeley Center for Law and Technology
Market Access Solutions
Maryland Public Policy Institute
Massachusetts Biotechnology Council (MassBio)
Medical Technology Association of Australia (MTAA)
Michigan Chamber of Commerce
Nashville Area Chamber of Commerce
National Center for Public Policy Research
National Foreign Trade Council
National Puerto Rican Chamber of Commerce
National Small Business Association (NSBA)
Nevada Biotechnological and Health Science Consortium
New Jersey Business & Industry Association (NJBIA)
NewYorkBIO
North Carolina Biosciences Organization (NCBIO)
Ohio Manufacturers' Association
Oxfam America
Pacific Research Institute
Paramadina Public Policy Institute, Indonesia
Personalized Medicine Coalition
Pharmaceutical Industry Labor-Management Association
Property Rights Alliance
Prosperdtx
Rafael Fonseca, the Chief Innovation Officer at the Mayo Clinic in Arizona
Representatives Bradley Scott Schneider (D-IL) and Adrian Smith (R-NE), and Senators Thomas R. Carper (D-DE) and Todd Young (R-IN)
Richard Parrish, a pharmacology and medical education professor at the Mercer University School of Medicine in Georgia
Richard T. Timmer, Senior Patent Agent at Innovators Legal
Richard Wilder, the General Counsel for Coalition for Epidemic Preparedness Innovations
Rio Grande Foundation
Ronald Klink, senior policy advisor at the law firm of Nelson Mullins
Roughrider Policy Center
Ruth Rasor, Associate Vice President of Duke University's Office for Translation & Commercialization
Senator M. Michael Rounds (R-SD)
South Centre
Southwest Public Policy Institute
Switzerland WTO
Switzerland
Texas Association of Manufacturers
Tomas Flores, Libertad y Desarrollo in Chile
Trade Alliance to Promote Prosperity
Trade Justice Education Fund
Universities Allied for Essential Medicines
U.S. Council for International Business
VFA (Germany)
Virginia Chamber of Commerce
Walter G. Copan, vice president for research and technology transfer at Colorado School of Mines
West Virginia Manufacturers Association (WVMA)

Name of party with written submission without summaries

William S. Smith, senior fellow and director of the Life Sciences Initiative at the Pioneer Institute

Wisconsin Alumni Research Foundation (WARF)

Wolfgang Klietmann- Lecturer at Harvard Medical School

Working Group on Intellectual Property of the Brazilian Network for the Integration of Peoples (GTPI/Rebrip) and the Brazilian AIDS interdisciplinary Association

Appendix E

Supplemental Tables for Chapter 3

Patent Status

Table E.1 provides more specific information on patents associated with illustrative examples of relevant COVID-19 therapeutics, to the extent practicable.

Table E.1 Illustrative list of COVID-19 therapeutics and related patent activity

INN = International Nonproprietary Name.

Patent holder	Trade name (INN)	Related patent activity
Pfizer Inc.	Paxlovid (nirmatrelvir (+ ritonavir))	Pfizer identified that it had filed 69 patent applications in 66 jurisdictions.
Gilead Sciences Inc. (Gilead)	Veklury (remdesivir)	Gilead identified that it had 512 patents and applications related to manufacturing and processes and 121 product patents and applications. Gilead indicated it had filed manufacturing and process patents in 119 jurisdictions and product patents in 53 jurisdictions. Gilead listed 13 U.S. patents in the FDA Orange Book.
Merck & Co., Inc.	Lagevrio (molnupiravir)	Merck identified that it had 57 patent applications filed in 27 jurisdictions.
Shionogi	Xocova (ensitrelvir)	Shionogi identified 23 patent applications in 7 jurisdictions.
Vir Biotechnology (Vir) and GSK (formerly GlaxoSmithKline)	Xevudy (sotrovimab)	Vir identified that it owns or co-owns 8 patent families, including 3 granted patents; 3 allowed patent applications; pending patent applications in North and South America, Europe, Asia, Eurasia, the Middle East, and Africa; and 5 pending Patent Cooperation Treaty international applications. Vir's portfolio also includes patents and patent applications it has non-exclusively licensed from Xencor.
Regeneron	REGEN-COV (casirivimab and imdevimab)	Regeneron identified approximately 32 patents and applications associated with casirivimab, imdevimab, and the combination filed in 33 jurisdictions.

Sources: MPP, License Agreement between Pfizer and MPP, November 15, 2021, App. 2; Gilead, 2020 Original Covid-19 Voluntary License Agreement, accessed June 6, 2023; Gilead, written submission to the USITC, May 5, 2023, 5; MPP, License Agreement between Merck and MPP, October 26, 2021, App. 2; MPP, License Agreement between Shionogi and MPP, October 3, 2022, Ex. B; MPP, MedsPaL database, accessed June 2, 2023; industry representative, email message to USITC staff, July 14, 2023.

Notes: The licensor in the MPP agreement for nirmatrelvir is identified as PF Prism Holdings, B.V. (Pfizer). The licensor in the MPP agreement for molnupiravir is identified as Merck Sharp & Dohme Corp. (Merck). There is a lack of clarity on the patents associated with the monoclonal antibodies bebtelovimab and bamlanivimab and etesevimab. GSK's patent portfolio for Xevudy (sotrovimab) also is unknown.

Regulatory Status of Virus-Directed Therapeutics for the Treatment of COVID-19

Highlighted below are tables E.2 through E.5 that focus on the affirmative regulatory status of virus-directed COVID-19 therapeutics around the world.¹⁴²³

¹⁴²³ These drugs could be indicated for either inpatient or outpatient patient settings depending on the regulatory authority. Regulatory statuses not listed in the tables are halted EUA, expedited status, recommended against approval, recommended against use, rejected, rolling review, submitted approval application, withdrawal (applicant decision), or status unknown. These statuses, while informative, just provide status (i.e., submitted for approval) or whether the drug is not available for consumption (i.e., recommended against approval or use). Airfinity, "Regulatory Overview by Treatment," July 11, 2023.

Table E.2 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff as of July 2023

In number of countries. EUA = Emergency Use Authorization; — = not applicable.

Drug	EUA	Approved	Recommended
Ensitrelvir	1	—	—
Bebtelovimab	1	—	—
Bamlanivimab and etesevimab	4	—	—
Bamlanivimab	12	—	—
Molnupiravir	39	—	8
Nirmatrelvir (+ ritonavir)	34	30	—
Casirivimab and imdevimab	11	—	—
Sotrovimab	10	—	—
Total	112	30	8

Source: Airfinity, Science 360, Regulatory, by treatment, July 15, 2023.

Notes: The mode of action of convalescent plasma is unknown, but it currently has 3 EUAs. These counts represent information that is publicly available as of July 15, 2023. Excluded are drugs solely approved as prophylactic for COVID-19, however drugs that are approved for both therapeutic and prophylactic use are included. Data exclude drugs classified as “unknown” with respect to patient setting. If a drug is authorized or approved, or recommended for patient settings, it should be known what and how it can be prescribed for COVID-19 (e.g., prophylactic, inpatient, or outpatient).

Table E.3 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff as of July 2023, by region

In number of affirmative regulatory signoffs. EUA = Emergency Use Authorization; — = not applicable.

Region	EUA	Approved	Recommended
East Asia and Pacific	30	1	—
Europe and Central Asia	21	27	8
Latin America and Caribbean	25	—	—
Middle East & North Africa	19	—	—
North America	7	2	—
South Asia	5	—	—
Sub-Saharan Africa	5	—	—
Total	112	30	8

Source: Airfinity, Science 360, Regulatory, by treatment, July 15, 2023, List of Economies, World Bank.

Notes: Excluded are drugs solely approved as prophylactic for COVID-19, however, drugs approved for both therapeutic and/or prophylactic use are included. Data exclude drugs classified as “unknown” with respect to patient setting. If a drug is authorized or approved, or recommended for patient settings, it should be known what and how it can be prescribed for COVID-19 (e.g., prophylactic, inpatient, or outpatient).

Table E.4 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff as of July 2023, by income level

In number of affirmative regulatory signoffs. EUA = Emergency Use Authorization; — = not applicable; HIC = high-income countries; UMIC = upper-middle-income countries; LMIC = lower-middle-income countries; LIC = low-income countries

Income Level	EUA	Approved	Recommended
HIC	67	28	8
UMIC	26	2	—
LMIC	16	—	—
LIC	3	—	—
Total	112	30	8

Source: Airfinity, Science 360, Regulatory, by treatment, July 15, 2023, List of Economies, World Bank.

Notes: Excluded are drugs solely approved as prophylactic for COVID-19, however, drugs that are approved for both therapeutic and/or prophylactic use are included. Data exclude drugs classified as “unknown” with respect to patient setting. If a drug is authorized or approved, or recommended for patient settings, it should be known what and how it can be prescribed for COVID-19 (e.g., prophylactic, inpatient, or outpatient).

Table E.5 Therapeutics for treatment of COVID-19, virus-directed, with regulatory signoff from WHO and EEA as of July 2023

Granting Authority and total number of granting authorities. EEA = European Economic Area (European Medicines Agency (EMA) and/or European Commission (EC)); WHO = World Health Organization; EUA = Emergency Use Authorization; PQ=prequalification; — = not applicable.

Drugs	EUA	Endorsed	Approved	Recommended
bamlanivimab and etesevimab	—	EEA	—	—
bamlanivimab	—	EEA	—	—
molnupiravir	—	EEA	—	—
nirmatrelvir (+ ritonavir)	EEA	EEA, WHO	EEA	EEA
casirivimab and imdevimab	—	EEA, WHO	EEA	—
sotrovimab	EEA	EEA	EEA	—
Total	2	8	4	1

Source: Airfinity, Science 360, Regulatory, by treatment, July 15, 2023.

Notes: These counts represent information that is publicly available as of July 15, 2023. Excluded are drugs solely approved as prophylactic for COVID-19, however, drugs that are approved for both therapeutic and/or prophylactic use are included. Data exclude drugs classified as “unknown” with respect to patient setting. Nirmatrelvir (+ ritonavir) received approval from both the EMA and EC, accounting for the total of 4 “approved” drugs.

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Appendix F

Methodology for Estimating COVID-19-Related Pharmaceutical Trade

Globally, most HS subheadings are not specific to a COVID-19 diagnostic or therapeutic. Therefore, the trade data reported in chapter 4, even with the methodologies as described therein reflect large basket categories of products not specific to COVID-19. Trade is harmonized globally to the HS 6-digit subheading, and when possible, the Commission included trade specific for relevant countries, using individual country codes to provide more specific data. Data in chapter 4 are export data reported by exporters and trade partners (importers). This appendix summarizes the methodologies for determining global trade of COVID-19-related diagnostics and therapeutics.

Diagnostics

COVID-19-related diagnostics (notably “kits”) tend to fall under a single subheading, 3822.19, and most COVID-19-related diagnostics producing countries only have a single tariff-line code under this subheading (table F.1).¹⁴²⁴ Beyond subheading 3822.19, subheadings 3002.13, 3002.14, 3002.15, 3821.00, and 3822.00 were used in reporting trade in COVID-19-related diagnostics in chapter 4. These subheadings are “basket” categories that encompass inputs for materials in test kits, including test kits not specific to COVID-19.

Table F.1 HS subheadings, with description, that include COVID-19 diagnostics, 2022

HS Subheading	2022 HS Description
3002.13	Immunological products, unmixed, not put up in measured doses or in forms or packings for retail sale
3002.14	Immunological products, mixed, not put up in measured doses or in forms or packings for retail sale
3002.15	Immunological products, put up in measured doses or in forms or packings for retail sale
3821.00	Prepared culture media for development or maintenance of micro-organisms (including viruses and the like) or of plant, human or animal cells
3822.00	Composite diagnostic or laboratory reagents, other than pharmaceutical preparations of heading 3002 or 3006
3822.19	Diagnostic or laboratory reagents on a backing, prepared diagnostic or laboratory reagents whether or not on a backing, whether or not put up in the form of kits, other than those of heading 3006; certified reference materials: Other; Containing antigens or antisera

Source: *Harmonized Tariff Schedule of the United States (HTS)*.

Note: 3002.13, 3002.14, and 3002.15 includes trade of mAbs, while 3821.00 includes trade of viral transport media. Subheading 3822.19 is a new classification as of 2022. Subheading 3822.00 is no longer an active HS subheading as of 2022, the language provided for the description is from the 2021 HS. Trade was still reported under subheading 3822.00 due to how data is collected and reported and this data is included in chapter 4.

Therapeutics

Companies trade bulk APIs and formulated end-use pharmaceuticals across borders to be used by licensees and producers’ affiliates/subsidiaries to manufacture formulated end products and/or to be packaged and labeled for global distribution. Formulated pharmaceuticals are generally classified in HS Chapter 30. By comparison, bulk APIs (and API intermediates) are generally classified in other HS chapters, especially Chapter 29. Chapter 30 has specific subheadings indicating whether the finished pharmaceuticals are mixed, in dosage form, and/or packaged or labeled. The chapters covering the bulk

¹⁴²⁴ India was the one exception; it had two tariff line codes, one for pregnancy tests, and one for all other.

APIs are more general in nature and cover many chemicals, including pharmaceuticals. Chapter 29 (“Organic Chemicals”), for example, with the exception of a few subheadings, generally classifies bulk chemicals and bulk APIs in terms of the products’ chemical structures rather than by end use. Many of the subheadings in Chapter 29 are “basket” subheadings, containing bulk chemicals (including APIs) with similar structures. The trade data presented chapter are from HS subheadings 2933.99, 2934.99, 2935.99 3002.13, 3002.14, 3003.90, and 3004.90 (table F.2). These subheadings are “basket” categories which encompass many pharmaceuticals, including immunological products for conditions other than COVID-19.

Table F.2 HS subheadings, with descriptions that include COVID-19 therapeutics, 2022

HS Subheading	2022 HS Description
2933.79	Heterocyclic compounds with nitrogen hetero-atom(s) only, lactams, other
2933.99	Heterocyclic compounds with nitrogen hetero-atom(s) only, other, other
2934.10	Organo-inorganic compounds, heterocyclic compounds, nucleic acids and their salts, and sulphonamides, nucleic acids and their salts, whether or not chemically defined, other heterocyclic compounds, compounds containing an unfused thiazole ring (whether or not hydrogenated) in the structure
2934.99	Organo-inorganic compounds, heterocyclic compounds, nucleic acids and their salts, and sulphonamides, other, other
2935.90	Sulphonamides, other
3002.13	Immunological products, unmixed, not put up in measured doses or in forms or packings for retail sale
3002.14	Immunological products, mixed, not put up in measured doses or in forms or packings for retail sale
3003.90	Medicaments (excluding goods of heading 3002, 3005 or 3006) consisting of two or more constituents which have been mixed together for therapeutic or prophylactic uses, not put up in measured doses or in forms or packings for retail sale; other
3004.90	Medicaments (excluding goods of heading 3002, 3005 or 3006) consisting of mixed or unmixed products for therapeutic or prophylactic uses, put up in measured doses (including those in the form of transdermal administration systems) or in forms or packings for retail sale; other

Source: *Harmonized Tariff Schedule of the United States* (HTS).

To produce a reasonable estimate of trade in COVID-19 related therapeutics, the Commission used tariff-line codes from countries that produce COVID-related therapeutics specific to the therapeutics produced in that country.¹⁴²⁵ For example, the United States’ exports of nirmatrelvir (+ ritonavir) are classified under individual statistical reporting numbers in HS subheadings 3002.13 and 3002.14, so those exports are included in the estimate, but other tariff lines for other COVID-19 therapeutics that are not produced in the United States (e.g., favipiravir: HS subheading 2933.99) are not included (table F.3).

¹⁴²⁵ Producers of COVID-related diagnostics and therapeutics were taken from Airfinity production data.

Table F.3 Therapeutics manufacturing countries and their relevant tariff-line codes

Country	Therapeutic	Subheading(s)	Individual Country Codes
China	Molnupiravir	2934.99	2934.99.90
		3003.90	3003.90
		3004.90	3004.90.90
China	Nirmatrelvir (+ ritonavir)	3002.13	3002.13.00
		3002.14	3002.14.00
Germany	Molnupiravir	2934.99	2934.99.90
		3003.90	3003.90.00
		3004.90	3004.90.00
Germany	Nirmatrelvir (+ ritonavir)	3002.13	3002.13.00
		3002.14	3002.14.00
India	Casirivimab and imdevimab	3002.13	3002.13.00, 3002.13.10
		3002.14	3002.14.00, 3002.14.10
India	Molnupiravir	2934.99	2934.99.90
		3003.90	3003.90.90
		3004.90	3004.90.99
India	Baricitinib	2935.90	2935.90.90
		3003.90	3003.90.90
		3004.90	3004.90.69
India	Favipiravir	2933.99	2933.99.90
		3003.90	3003.90.90
		3004.90	3004.90.99
India	Nirmatrelvir (+ ritonavir)	3002.13	3002.13.00, 3002.13.10
		3002.14	3002.14.00, 3002.14.10
India	Remdesivir	2934.99	2934.99.90
		3003.90	3003.90.90
		3004.90	3004.90.99
Israel	Nirmatrelvir (+ ritonavir)	3002.13	3002.13.00
		3002.14	3002.14.00
Portugal	Molnupiravir	2934.99	2934.99.90
		3003.90	3003.90.00
		3004.90	3004.90.00
South Korea	Molnupiravir	2934.99	2934.99.9000
		3003.90	3003.90.9000, 3003.90.9900
		3004.90	3004.90.9900
South Korea	Sotrovimab	3002.13	3002.13.0000, 3002.13.9000
		3002.14	3002.14.0000, 3002.14.9000
South Korea	Bamlanivimab	3002.13	3002.13.0000, 3002.13.9000
		3002.14	3002.14.0000, 3002.14.9000
Switzerland	Tocilizumab	3002.13	3002.13.00
		3002.14	3002.14.00
Switzerland	Tixagevimab and cilgavimab	3002.13	3002.13.00
		3002.14	3002.14.00
United Kingdom	Molnupiravir	2934.99	2934.99.90
		3003.90	3003.90
		3004.90	3004.90
United Kingdom	Tixagevimab and cilgavimab	3002.13	3002.13.00
		3002.14	3002.14.00

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Country	Therapeutic	Subheading(s)	Individual Country Codes
United Kingdom	Nirmatrelvir (+ ritonavir)	2933.79	2933.7900 (nirmatrelvir)
		2934.10	2934.1000 (ritonavir)
		3002.13	3002.13.00
		3002.14	3002.14.00
United Kingdom	Remdesivir	2934.99	2934.99.90
		3003.90	3003.90
		3004.90	3004.90
United States	Molnupiravir	2934.99	2934.99.3000
		3003.90	3003.90.0120
		3004.90	3004.90.9207
United States	Remdesivir	2934.99	2934.99.3000
		3003.90	3003.90.0120
		3004.90	3004.90.9207
United States	Nirmatrelvir (+ ritonavir)	3002.13	3002.13.0010
		3002.14	3002.14.0010

Sources: Compiled by the USITC using Airfinity production data and trade data from S&P Global, Global Trade Atlas, accessed May 2, 2023.

Note: Tixagevimab and cilgavimab are the APIs in Evusheld, a prophylactic, however the HS headings that these mAbs are traded under are the same headings as for the other virus-directed mAbs.

Appendix G

Literature Review Sources

Table G.1 Sources cited in chapter 8: literature review

n.a. = not applicable.

Study author(s), year	Section in the literature review, chapter 8	Country coverage	Research methodology
Abrams, 2009	Patent protection	United States	n.a.
Agarwal and Gaule, 2022	Research gaps	Cross-country	n.a.
Arora, Ceccagnoli, and Cohen, 2008	Patent protection and innovation	United States	Structural model
Attaran, 2004	Patent protection and access to medicine	65 developing countries	Descriptive analysis
Attarn and Gillespie-White, 2001	Patent protection and access to medicine	53 African countries	Descriptive analysis
Baten, Bianchi, and Moser, 2017	Introduction, the effects of compulsory licenses	Germany	Reduced-form econometrics
Boldrin and Levine, 2013	Patent protection and innovation	n.a.	n.a.
Bond and Saggi, 2014	The effects of compulsory licenses	n.a.	Theoretical model
Boring, 2015	Patent protection and access to medicine	108 developing countries	Reduced-form econometrics
Borrell, 2005	Patent protection and access to medicine	34 developing countries	Reduced-form econometrics
Borrell, 2007	Patent protection and access to medicine	34 developing countries	Reduced-form econometrics
Bown and Bollyky, 2022	Introduction	Cross-country	n.a.
Brunel and Zylkin, 2022	Patent protection and access to medicine	149 countries	Reduced-form econometrics
Bryan and Williams, 2021	Patent protection and innovation	n.a.	n.a.
Budish, Roin, and Williams, 2015	Patent protection and innovation	United States	Descriptive analysis, reduced-form econometrics, and theoretical
Chadha, 2009	Patent protection and innovation	India	Reduced-form econometrics
Chatterjee, Kubo, and Pingali, 2015	Introduction, the effects of compulsory licenses	India	Reduced-form econometrics
Chaudhuri, Goldberg, and Jia, 2006	Patent protection and access to medicine	India	Structural model
Chen, Yongmin, and Puttitanun, 2005	Patent protection and innovation	64 developing countries	n.a.
Co, 2004	Patent protection and access to medicine	71 countries	Reduced-form econometrics
Cockburn and Long, 2015	Patent protection and innovation	United States	Descriptive analysis
Cockburn, Lanjouw, and Schankerman, 2016	Patent protection and access to medicine	76 countries	Descriptive analysis, reduced-form econometrics
Cohen, Nelson, and Walsh, 2000	Methodologies, patent protection and innovation	United States	Descriptive analysis
Delgado, Kyle, and McGahan, 2013	Patent protection and access to medicine	158 countries	Reduced-form econometrics

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Study author(s), year	Section in the literature review, chapter 8	Country coverage	Research methodology
Duggan, Garthwaite, and Goyal, 2016	Patent protection, patent protection and access to medicine	India	Reduced-form econometrics
Dutta, 2011	Patent protection, patent protection and access to medicine	India	Structural model
Gaessler and Wagner, 2022	Patent protection and innovation	Europe	Reduced-form econometrics
Galasso and Schankerman, 2021	The effects of the Medicines Patent Pool	129 countries	Reduced-form econometrics
Galasso and Schankerman, 2018	Patent protection and innovation	United States	Reduced-form econometrics
Galasso and Schankerman, 2015	Patent protection and innovation	United States	Reduced-form econometrics
Gallini, 2017	Patent protection and innovation	United States	n.a.
Gamba, 2017	Patent protection and innovation	74 countries	Reduced-form econometrics
Gilchrist, 2016	Patent protection and innovation	United States	Reduced-form econometrics
Ginarte and Park, 1997	Patent protection, patent protection and access to medicine	110 countries	n.a.
Graham, Merges, Samuelson, and Sichelman, 2009	Methodologies, patent protection and innovation	United States	Descriptive analysis
Grootendorst, Hollis, Levine, Pogge, and Edwards, 2011	Patent protection and innovation	n.a.	Qualitative analysis
Harabi, 1995	Patent protection and innovation	Switzerland	Descriptive analysis
Hellerstein, 2012	Patent protection and access to medicine	Sample of developing countries	Reduced-form econometrics
Horner, 2014	Patent protection and innovation	India	Qualitative analysis
Islam, Kaplan, Trachtenberg, Thrasher, Gallaher, and Wirtz, 2019	Patent protection and access to medicine	Lower-income countries	n.a.
Ivus, 2010	Patent protection and access to medicine	24 OECD and 55 developing countries	Reduced-form econometrics
Jung, Youn, and Soonman, 2015	Patent protection and access to medicine	35 developing countries	Reduced-form econometrics
Kale and Little, 2007	Patent protection and innovation	India	Qualitative analysis
Kyle and McGahan, 2012	Patent protection and innovation	192 countries	Reduced-form econometrics
Kyle and Qian, 2014	Patent protection and access to medicine	60 countries	Reduced-form econometrics
Kyle, 2022	Patent protection and innovation, patent protection and access to medicine	n.a.	n.a.
Lakdawalla, 2018	Patent protection and innovation	n.a.	n.a.
Lanjouw, 2005	Patent protection and access to medicine	68 countries	Descriptive analysis, reduced form-econometrics

Study author(s), year	Section in the literature review, chapter 8	Country coverage	Research methodology
Lanjouw and Cockburn, 2001	Patent protection and innovation	Cross-country, India	Descriptive analysis, qualitative analysis
Lanthier, Miller, Nardinelli, and Woodcock, 2013	Patent protection and access to medicine	n.a.	n.a.
Levin, Klevorick, Nelson, Winter, Gilbert, and Griliches, 1987	Methodologies, patent protection and innovation	United States	Descriptive analysis
Liu and La Croix, 2014	Patent protection and innovation	66 countries	Reduced-form econometrics
Liu and La Croix, 2015	Patent protection and innovation	154 countries	n.a.
Mansfield, 1986	Methodologies, patent protection and innovation	United States	Descriptive analysis
Mansfield, Schwartz, and Wagner, 1981	Methodologies, patent protection and innovation	United States	Descriptive analysis
Martinelli, Mina, and Romito, 2021	The effects of the Medicines Patent Pool	Cross-country	Reduced-form econometrics
Maskus and Penubarti, 1995	Patent protection and access to medicine	77 countries	Reduced-form econometrics
Morin, Moak, Bubb-Humfryes, Drehle, Lazarus, and Burrone, 2022	The effects of the Medicines Patent Pool	Cross-country	Model-based
Moser, 2013	Patent protection, patent protection and innovation	n.a.	n.a.
Moser, 2016	Introduction, the effects of compulsory licenses	n.a.	n.a.
Moser and Voena, 2012	Introduction, the effects of compulsory licenses	United States	Reduced-form econometrics
Motari, Nikiema, Kasilo, Kniazkov, Loua, Sougou, and Tumusiime, 2021	Patent protection and access to medicine	African countries	Descriptive analysis
Murray and Stern, 2007	Patent protection and innovation	United States	Reduced-form econometrics
Nordhaus, 1969	Patent protection	n.a.	Theoretical model
Park, 2008	Patent protection and innovation	122 countries	n.a.
Prieto and Sacristán, 2003	The effects of compulsory licenses	n.a.	n.a.
Qian, 2007	Patent protection and innovation	26 countries	Reduced-form econometrics
Sakakibara and Branstetter, 2001	Patent protection and innovation	Japan	Reduced-form econometrics
Sampat, 2018	Patent protection	n.a.	n.a.
Sampat and Williams, 2019	Patent protection and innovation	United States	Descriptive analysis, reduced-form econometrics
Scherer and Weisburst, 1995	Patent protection and innovation	Italy	Descriptive analysis, reduced-form econometrics
Scotchmer, 1991	Patent protection	n.a.	Theoretical model
Stavropoulou and Valletti, 2015	The effects of compulsory licenses	n.a.	Theoretical model
Taylor and Silberston, 1973	Patent protection and innovation	United Kingdom	Descriptive analysis

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Study author(s), year	Section in the literature review, chapter 8	Country coverage	Research methodology
Tenni, Moir, Townsend, Kilic, Farrell, Keegel, and Gleeson, 2022	Patent protection, patent protection and access to medicine, the effects of compulsory licenses	n.a.	n.a.
Urias and Ramani, 2020	The effects of compulsory licenses	8 countries	n.a.
Wang, 2022	The effects of the Medicines Patent Pool	Cross-country	Reduced-form econometrics
Watal and Dai, 2019	Patent protection and access to medicine	70 countries	Reduced-form econometrics
World Intellectual Property Organization, 2009	Introduction	n.a.	n.a.
World Intellectual Property Organization, 2023	Introduction	n.a.	n.a.
World Trade Organization, 2001	The effects of compulsory licenses	n.a.	n.a.
World Trade Organization, 2021	Research gaps	n.a.	n.a.

Notes: The “research methodology” column includes information only if the methodology or results from the source are discussed in the chapter 8: literature review. Legal citations are not included in the table.

Appendix H

Countries Covered by Voluntary Licenses by Treatment Type and Income Level

Appendix H: Countries Covered by Voluntary Licenses by Treatment Type and Income Level

Table H.1 Developing countries where products can be offered for sale under voluntary license agreements, by treatment type and income level.

UMIC = upper-middle-income countries, LMIC = lower-middle-income countries, LIC = low-income countries

Treatment type	UMIC	LMIC	LIC
Ensitrelvir fumaric acid	Armenia, Azerbaijan, Belize, Botswana, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, Equatorial Guinea, Fiji, Gabon, Georgia, Grenada, Guatemala, Guyana, Iraq, Jamaica, Jordan, Kazakhstan, Kosovo, Libya, Maldives, Marshall Islands, Mauritius, Moldova, Namibia, Paraguay, Peru, Saint Lucia, Saint Vincent and the Grenadines, South Africa, Suriname, Tonga, Tuvalu	Algeria, Angola, Bangladesh, Benin, Bhutan, Bolivia, Burma, Cabo Verde, Cambodia, Cameroon, Comoros, Congo, Côte d'Ivoire, Djibouti, Egypt, El Salvador, Eswatini, Ghana, Haiti, Honduras, India, Iran, Kenya, Kiribati, Kyrgyzstan, Laos, Lesotho, Mauritania, Micronesia, Mongolia, Morocco, Nepal, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Philippines, Samoa, São Tomé and Príncipe, Senegal, Solomon Islands, Sri Lanka, Tajikistan, Tanzania, Timor-Leste, Tunisia, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Zimbabwe	Afghanistan, Burkina Faso, Burundi, Central African Republic, Chad, Democratic Republic of the Congo, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, North Korea, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Syrian Arab Republic, Togo, Uganda, Yemen, Zambia
Molnupiravir	Belize, Botswana, Cuba, Dominica, Equatorial Guinea, Fiji, Gabon, Grenada, Guatemala, Guyana, Iraq, Jamaica, Libya, Maldives, Marshall Islands, Mauritius, Moldova, Namibia, Paraguay, Saint Lucia, Saint Vincent and the Grenadines, South Africa, Suriname, Thailand, Tonga, Tuvalu	Algeria, Angola, Bangladesh, Benin, Bhutan, Bolivia, Burma, Cabo Verde, Cambodia, Cameroon, Comoros, Congo, Côte d'Ivoire, Djibouti, Egypt, El Salvador, Eswatini, Ghana, Haiti, Honduras, India, Indonesia, Iran, Kenya, Kiribati, Laos, Lesotho, Mauritania, Micronesia, Mongolia, Morocco, Nepal, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Philippines, Samoa, São Tomé and Príncipe, Senegal, Solomon Islands, Sri Lanka, Tajikistan, Tanzania, Timor-Leste, Tunisia, Uzbekistan, Vanuatu, Vietnam, Zimbabwe	Afghanistan, Burkina Faso, Burundi, Central African Republic, Chad, Democratic Republic of the Congo, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, North Korea, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Syrian Arab Republic, Togo, Uganda, Yemen, Zambia

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Treatment type	UMIC	LMIC	LIC
Nirmatrelvir (+ ritonavir)	Armenia, Belize, Botswana, Equatorial Guinea, Gabon, Georgia, Guatemala, Jordan, Kosovo, Moldova, Namibia, South Africa, Tonga	Algeria, Angola, Bangladesh, Benin, Bhutan, Bolivia, Burma, Cabo Verde, Cambodia, Cameroon, Comoros, Congo, Côte d'Ivoire, Djibouti, Egypt, El Salvador, Eswatini, Ghana, Haiti, Honduras, India, Indonesia, Iran, Kenya, Kiribati, Kyrgyzstan, Laos, Lesotho, Mauritania, Micronesia, Mongolia, Morocco, Nepal, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Philippines, Samoa, São Tomé and Príncipe, Senegal, Solomon Islands, Sri Lanka, Tajikistan, Tanzania, Timor-Leste, Tunisia, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Zimbabwe	Afghanistan, Burkina Faso, Burundi, Central African Republic, Chad, Democratic Republic of the Congo, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, North Korea, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Syrian Arab Republic, Togo, Uganda, Yemen, Zambia
Remdesivir	Armenia, Azerbaijan, Belarus, Belize, Botswana, Costa Rica, Cuba, Dominica, Dominican Republic, Equatorial Guinea, Fiji, Gabon, Georgia, Grenada, Guatemala, Guyana, Jamaica, Kazakhstan, Libya, Maldives, Marshall Islands, Mauritius, Moldova, Namibia, Palau, Saint Lucia, Saint Vincent and the Grenadines, South Africa, Suriname, Tonga, Turkmenistan, Tuvalu	Algeria, Angola, Bangladesh, Benin, Bhutan, Bolivia, Burma, Cabo Verde, Cambodia, Cameroon, Comoros, Congo, Côte d'Ivoire, Djibouti, Egypt, El Salvador, Eswatini, Ghana, Haiti, Honduras, India, Indonesia, Kenya, Kiribati, Kyrgyzstan, Laos, Lesotho, Mauritania, Micronesia, Mongolia, Morocco, Nepal, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Philippines, Samoa, São Tomé and Príncipe, Senegal, Solomon Islands, Sri Lanka, Tajikistan, Tanzania, Timor-Leste, Tunisia, Ukraine, Uzbekistan, Vanuatu, Vietnam, Zimbabwe	Afghanistan, Burkina Faso, Burundi, Central African Republic, Chad, Democratic Republic of the Congo, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, North Korea, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Togo, Uganda, Zambia

Source: MPP, "Nirmatrelvir," November 2021; MPP, "Molnupiravir (MOL)," October 2021; MPP, "Ensitrelvir Fumaric Acid," October 2022; Gilead, "2020 Original COVID-19 Voluntary License Agreement," 2020.

Note: Bilateral agreements for the production of baricitinib have expired and are not included in this figure. The geographic scope of the MPP licenses for the production of molnupiravir is the same as the scope of the bilateral agreements; therefore, they are not included in this figure. HICs identified in the remdesivir license also are not included in this figure. Venezuela is included in the remdesivir license; it was classified as a UMIC until July 2021 but its income level is now unclassified by the World Bank. Anguilla, the Cook Islands, and Montserrat are included in the ensitrelvir fumaric acid, molnupiravir, and nirmatrelvir licenses, but their income levels are not classified by the World Bank.

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Gilead. “2020 Original COVID-19 Voluntary License Agreement.” 2020. <https://www.gilead.com/-/media/files/pdfs/other/original-covid-19-voluntary-licence-agreement.pdf>.

Medicines Patent Pool (MPP). “Ensitrelvir Fumaric Acid.” October 2022. <https://medicinespatentpool.org/licence-post/ensitrelvir>.

Medicines Patent Pool (MPP). “Molnupiravir (MOL).” October 2021. <https://medicinespatentpool.org/licence-post/molnupiravir-mol>.

Medicines Patent Pool (MPP). “Nirmatrelvir” MPP. November 2021. <https://medicinespatentpool.org/licence-post/pf-07321332>.

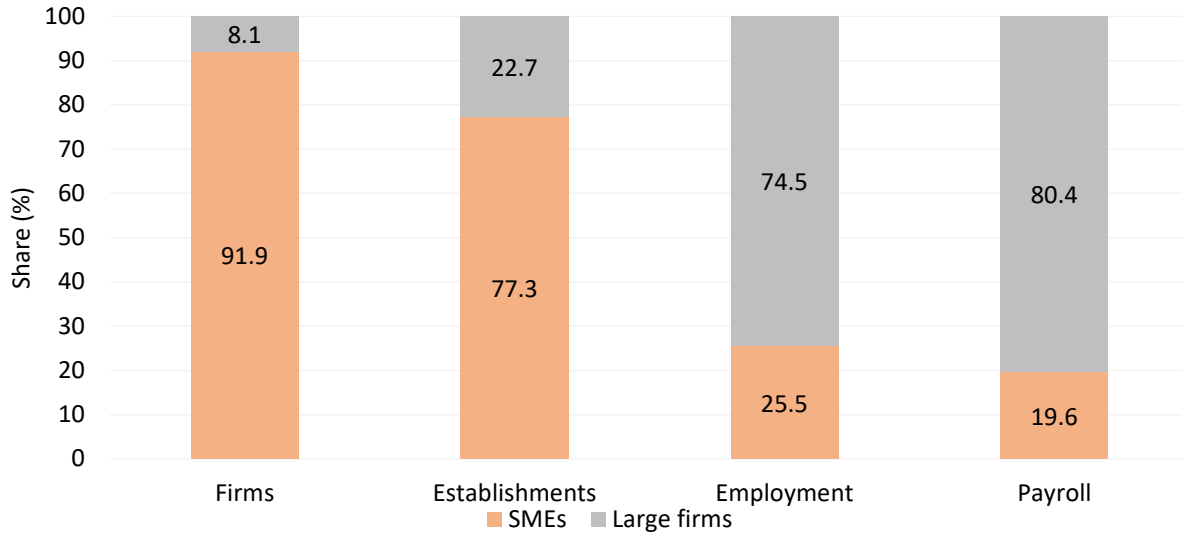
Appendix I

Additional Data on the U.S. Pharmaceuticals Industry and U.S. Pharmaceutical Trade

Data presented in this appendix are from Census and BLS, and present data for North American Industry Classification System (NAICS) code 3254 and the four industry classifications therein: 325411 (medicinals and botanicals), 325412 (pharmaceutical preparations), 325413 (in vitro diagnostic substances), and 325414 (biological products, except diagnostic). The data reported is the most up-to-date data available as of August 2023, but the timeframe of the data is dependent on the source.

Figure I.1 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by business size, 2020

In percentages. SME = small and medium-sized enterprise. Underlying data for this figure can be found in appendix J, [table J.25](#).

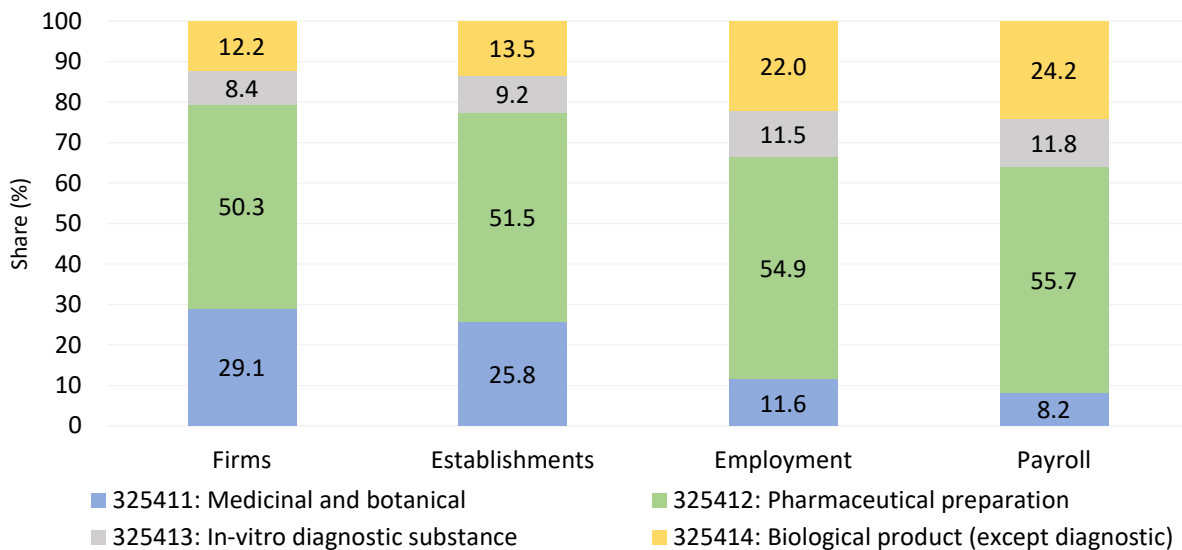


Source: U.S. Census Bureau, Statistics of U.S. Businesses data, NAICS 3254, accessed August 24, 2023.

Note: Business size is based on the size of the enterprise. SMEs have less than 500 employees while large firms have 500 or more employees.

Figure I.2 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by industry classification, 2020

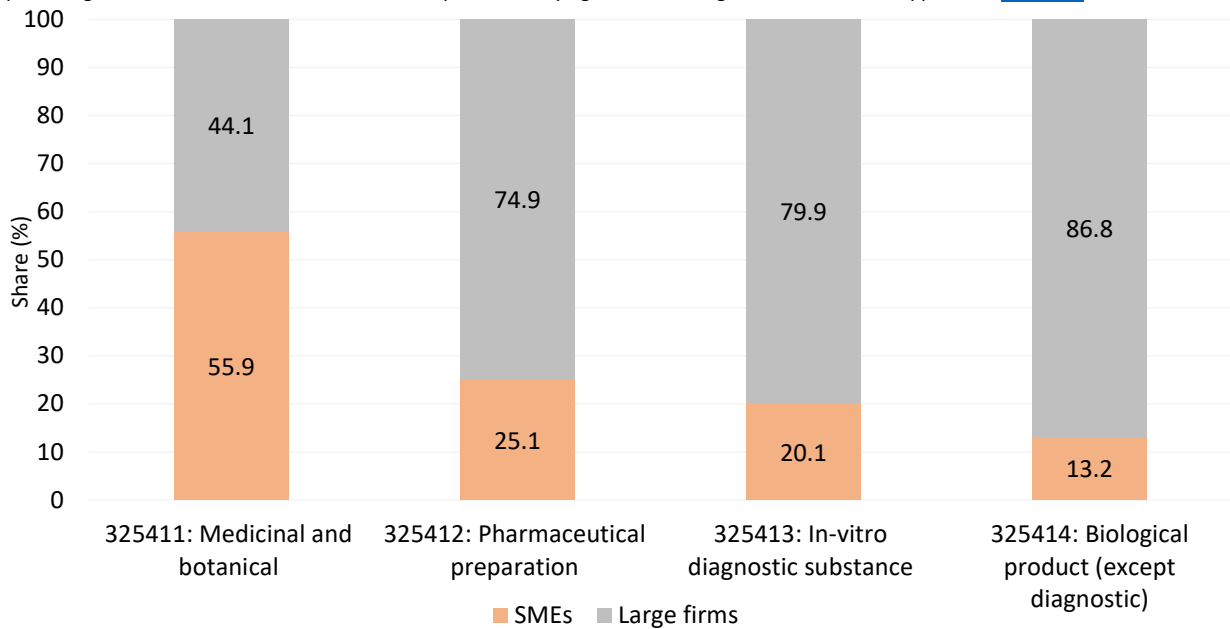
In percentages. Underlying data for this figure can be found in appendix J, [table J.26](#).



Source: U.S. Census Bureau, Statistics of U.S. Businesses data, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Figure I.3 U.S. pharmaceutical employment, by business size and industry classification, 2020

In percentages. SME = small and medium-sized enterprise. Underlying data for this figure can be found in appendix J, [table J.27](#).

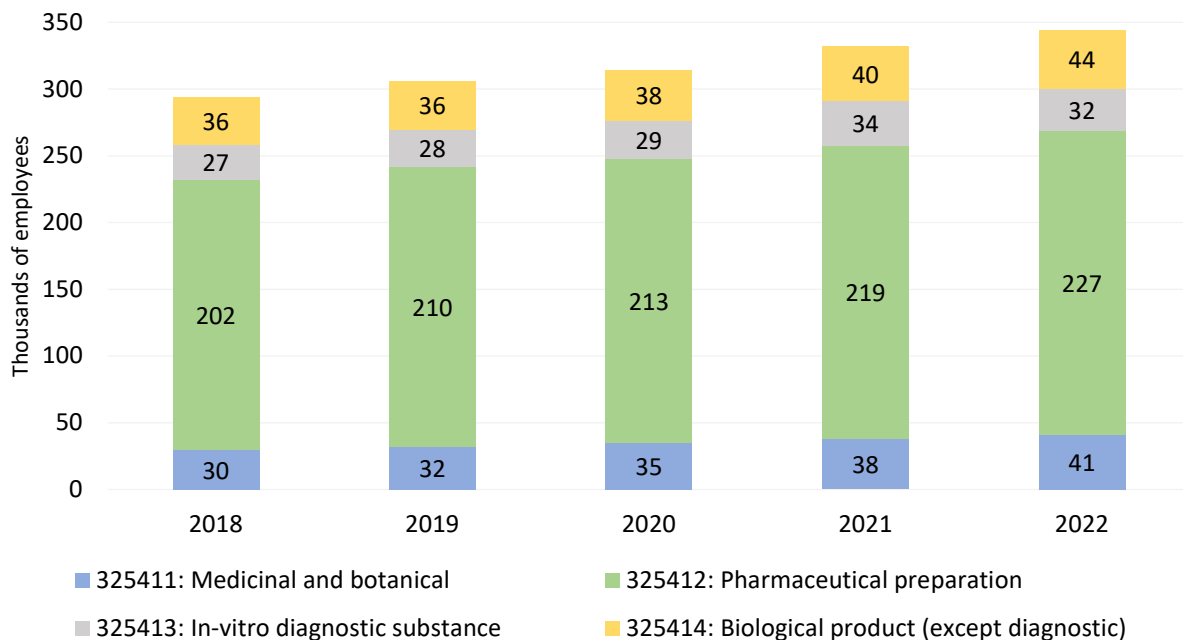


Source: U.S. Census Bureau, Statistics of U.S. Businesses data, NAICS 3254, accessed August 24, 2023.

Note: Business size is based on the size of the enterprise. SMEs have less than 500 employees while large firms have 500 or more employees.

Figure I.4 U.S. pharmaceutical employment by industry classification, 2018–22

In thousands of employees. Underlying data for this figure can be found in appendix J, [table J.28](#).



Source: Bureau of Labor Statistics (BLS), Quarterly Census of Employment and Wages, annual averages, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Table I.1 U.S. pharmaceutical manufacturing employment, by state and industry classification, average October 2022–December 2022

In number of employees.

State	325411: Medicinal and botanical	325412: Pharmaceutical preparation	325413: In-vitro diagnostic substance	325414: Biological product (except diagnostic)	Total, 3254: Pharmaceutical manufacturing
Alabama	0	1,054	0	79	1,133
Arizona	1,046	2,299	0	0	3,345
Arkansas	99	333	0	0	433
California	6,436	28,601	8,767	3,392	47,197
Colorado	2,316	2,355	41	524	5,236
Connecticut	0	1,198	0	0	1,198
Delaware	0	203	0	0	203
Florida	1,671	8,602	584	277	11,133
Georgia	783	2,274	0	0	3,057
Hawaii	0	9	0	0	9
Idaho	0	124	0	0	124
Illinois	2,596	18,171	0	0	20,767
Indiana	98	19,513	2,992	118	22,721
Iowa	957	0	0	2,720	3,677
Kansas	0	2,285	0	804	3,089
Kentucky	443	1,167	249	9	1,868
Louisiana	298	352	0	0	650
Maine	0	0	1,755	236	1,991
Maryland	0	2,198	3,638	0	5,836
Massachusetts	509	6,732	1,595	1,649	10,485
Michigan	928	9,780	47	429	11,183
Minnesota	0	1,985	2,375	0	4,360
Mississippi	0	1,078	0	0	1,078
Missouri	953	3,792	382	1,843	6,970
Montana	400	0	0	323	723
Nebraska	0	708	0	1,266	1,974
Nevada	0	798	0	0	798
New Hampshire	0	413	0	0	413
New Jersey	6,501	18,600	2,009	865	27,974
New Mexico	453	913	0	0	1,366
New York	445	17,215	824	5,939	24,424
North Carolina	319	18,888	54	5,336	24,597
North Dakota	0	11	0	0	11
Ohio	491	5,480	0	0	5,971
Oklahoma	0	792	0	0	792
Oregon	332	670	0	0	1,002
Pennsylvania	852	14,720	738	4,402	20,713
Rhode Island	0	1,333	0	0	1,333
South Carolina	134	5,535	8	76	5,753
Tennessee	577	1,602	0	0	2,179
Texas	951	11,465	322	1,195	13,933

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

State	325411: Medicinal and botanical	325412: Pharmaceutical preparation	325413: In-vitro diagnostic substance	325414: Biological product (except diagnostic)	Total, 3254: Pharmaceutical manufacturing
Utah	2,151	5,013	0	0	7,164
Vermont	28	0	0	0	28
Virginia	324	1,693	0	0	2,017
Washington	443	1,445	492	1,527	3,907
West Virginia	0	709	0	0	709
Wisconsin	1,019	2,428	395	2,830	6,672
Puerto Rico	118	13,334	0	0	13,453
Total	34,670	237,870	27,267	35,839	335,646

Source: Bureau of Labor Statistics (BLS), Quarterly Census of Employment and Wages, October–December 2022, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Note: Alaska, South Dakota, and Wyoming do not have employment in pharmaceutical manufacturing.

Table I.2 U.S. states’ share of total employment accounted for by pharmaceuticals, by industry classification, October 2022–December 2022

In percentages. ** = rounds to zero.

State	325411: Medicinal and botanical	325412: Pharmaceutical preparation	325413: In-vitro diagnostic substance	325414: Biological product (except diagnostic)	Total, 3254: Pharmaceutical manufacturing
Alabama	0.0	0.4	0.0	0.2	0.3
Arizona	3.0	1.0	0.0	0.0	1.0
Arkansas	0.3	0.1	0.0	0.0	0.1
California	18.6	12.0	32.2	9.5	14.1
Colorado	6.7	1.0	0.2	1.5	1.6
Connecticut	0.0	0.5	0.0	0.0	0.4
Delaware	0.0	0.1	0.0	0.0	0.1
Florida	4.8	3.6	2.1	0.8	3.3
Georgia	2.3	1.0	0.0	0.0	0.9
Hawaii	0.0	**	0.0	0.0	**
Idaho	0.0	0.1	0.0	0.0	**
Illinois	7.5	7.6	0.0	0.0	6.2
Indiana	0.3	8.2	11.0	0.3	6.8
Iowa	2.8	0.0	0.0	7.6	1.1
Kansas	0.0	1.0	0.0	2.2	0.9
Kentucky	1.3	0.5	0.9	**	0.6
Louisiana	0.9	0.1	0.0	0.0	0.2
Maine	0.0	0.0	6.4	0.7	0.6
Maryland	0.0	0.9	13.3	0.0	1.7
Massachusetts	1.5	2.8	5.8	4.6	3.1
Michigan	2.7	4.1	0.2	1.2	3.3
Minnesota	0.0	0.8	8.7	0.0	1.3
Mississippi	0.0	0.5	0.0	0.0	0.3
Missouri	2.7	1.6	1.4	5.1	2.1
Montana	1.2	0.0	0.0	0.9	0.2
Nebraska	0.0	0.3	0.0	3.5	0.6
Nevada	0.0	0.3	0.0	0.0	0.2
New Hampshire	0.0	0.2	0.0	0.0	0.1
New Jersey	18.7	7.8	7.4	2.4	8.3
New Mexico	1.3	0.4	0.0	0.0	0.4

Appendix I: Additional Data on the U.S. Pharmaceuticals Industry and U.S. Pharmaceutical Trade

State	325411: Medicinal and botanical	325412: Pharmaceutical preparation	325413: In-vitro diagnostic substance	325414: Biological product (except diagnostic)	Total, 3254: Pharmaceutical manufacturing
New York	1.3	7.2	3.0	16.6	7.3
North Carolina	0.9	7.9	0.2	14.9	7.3
North Dakota	0.0	**	0.0	0.0	**
Ohio	1.4	2.3	0.0	0.0	1.8
Oklahoma	0.0	0.3	0.0	0.0	0.2
Oregon	1.0	0.3	0.0	0.0	0.3
Pennsylvania	2.5	6.2	2.7	12.3	6.2
Rhode Island	0.0	0.6	0.0	0.0	0.4
South Carolina	0.4	2.3	**	0.2	1.7
Tennessee	1.7	0.7	0.0	0.0	0.6
Texas	2.7	4.8	1.2	3.3	4.2
Utah	6.2	2.1	0.0	0.0	2.1
Vermont	0.1	0.0	0.0	0.0	**
Virginia	0.9	0.7	0.0	0.0	0.6
Washington	1.3	0.6	1.8	4.3	1.2
West Virginia	0.0	0.3	0.0	0.0	0.2
Wisconsin	2.9	1.0	1.4	7.9	2.0
Puerto Rico	0.3	5.6	0.0	0.0	4.0
Total	100.0	100.0	100.0	100.0	100.0

Source: Bureau of Labor Statistics (BLS), Quarterly Census of Employment and Wages, October–December 2022, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Table I.3 U.S. states' share of total pharmaceutical employment by industry classification, October 2022–December 2022

In percentages. ** = rounds to zero.

State	325411: Medicinal and botanical	325412: Pharmaceutical preparation	325413: In-vitro diagnostic substance	325414: Biological product (except diagnostic)	Total, 3254: Pharmaceutical manufacturing
Alabama	0.0	93.0	0.0	7.0	100.0
Arizona	31.3	68.7	0.0	0.0	100.0
Arkansas	23.0	77.0	0.0	0.0	100.0
California	13.6	60.6	18.6	7.2	100.0
Colorado	44.2	45.0	0.8	10.0	100.0
Connecticut	0.0	100.0	0.0	0.0	100.0
Delaware	0.0	100.0	0.0	0.0	100.0
Florida	15.0	77.3	5.2	2.5	100.0
Georgia	25.6	74.4	0.0	0.0	100.0
Hawaii	0.0	100.0	0.0	0.0	100.0
Idaho	0.0	100.0	0.0	0.0	100.0
Illinois	12.5	87.5	0.0	0.0	100.0
Indiana	0.4	85.9	13.2	0.5	100.0
Iowa	26.0	0.0	0.0	74.0	100.0
Kansas	0.0	74.0	0.0	26.0	100.0
Kentucky	23.7	62.5	13.3	0.5	100.0
Louisiana	45.8	54.2	0.0	0.0	100.0
Maine	0.0	0.0	88.1	11.9	100.0
Maryland	0.0	37.7	62.3	0.0	100.0

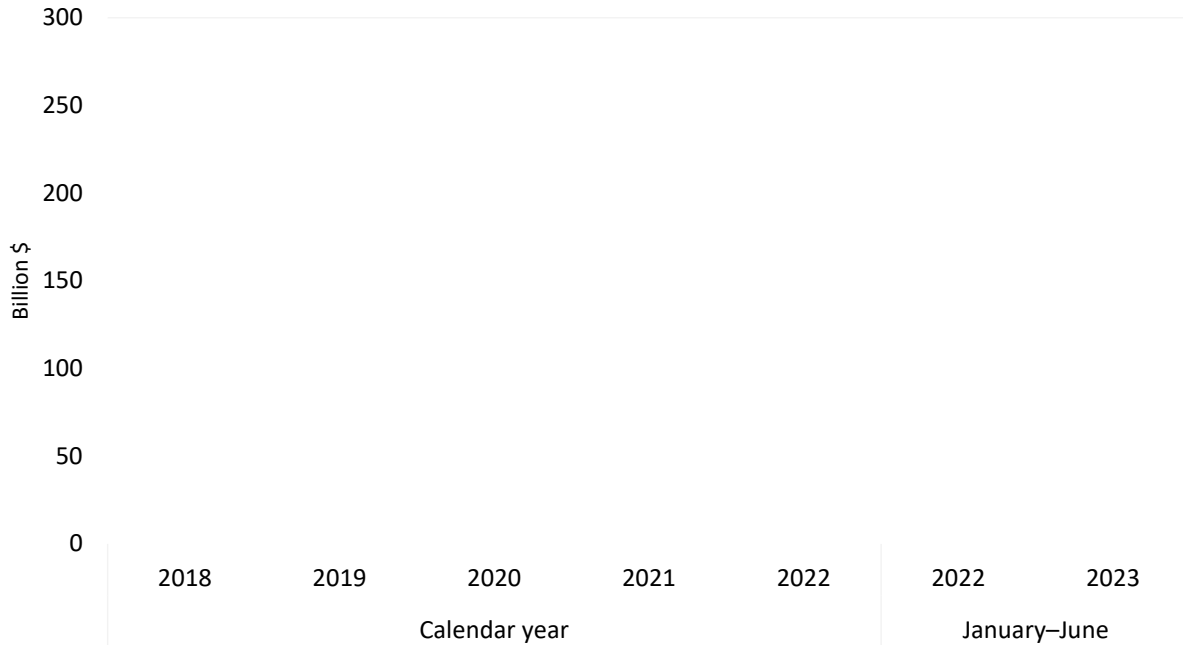
COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

State	325411: Medicinal and botanical	325412: Pharmaceutical preparation	325413: In-vitro diagnostic substance	325414: Biological product (except diagnostic)	Total, 3254: Pharmaceutical manufacturing
Massachusetts	4.9	64.2	15.2	15.7	100.0
Michigan	8.3	87.4	0.4	3.8	100.0
Minnesota	0.0	45.5	54.5	0.0	100.0
Mississippi	0.0	100.0	0.0	0.0	100.0
Missouri	13.7	54.4	5.5	26.4	100.0
Montana	55.3	0.0	0.0	44.7	100.0
Nebraska	0.0	35.9	0.0	64.1	100.0
Nevada	0.0	100.0	0.0	0.0	100.0
New Hampshire	0.0	100.0	0.0	0.0	100.0
New Jersey	23.2	66.5	7.2	3.1	100.0
New Mexico	33.2	66.8	0.0	0.0	100.0
New York	1.8	70.5	3.4	24.3	100.0
North Carolina	1.3	76.8	0.2	21.7	100.0
North Dakota	0.0	100.0	0.0	0.0	100.0
Ohio	8.2	91.8	0.0	0.0	100.0
Oklahoma	0.0	100.0	0.0	0.0	100.0
Oregon	33.1	66.9	0.0	0.0	100.0
Pennsylvania	4.1	71.1	3.6	21.3	100.0
Rhode Island	0.0	100.0	0.0	0.0	100.0
South Carolina	2.3	96.2	0.1	1.3	100.0
Tennessee	26.5	73.5	0.0	0.0	100.0
Texas	6.8	82.3	2.3	8.6	100.0
Utah	30.0	70.0	0.0	0.0	100.0
Vermont	100.0	0.0	0.0	0.0	100.0
Virginia	16.0	84.0	0.0	0.0	100.0
Washington	11.3	37.0	12.6	39.1	100.0
West Virginia	0.0	100.0	0.0	0.0	100.0
Wisconsin	15.3	36.4	5.9	42.4	100.0
Puerto Rico	0.9	99.1	0.0	0.0	100.0
Total	10.3	70.9	8.1	10.7	100.0

Source: Bureau of Labor Statistics (BLS), Quarterly Census of Employment and Wages, October–December 2022, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Figure I.5 U.S. pharmaceutical shipments, 2018–22, January–June 2022, and January–June 2023

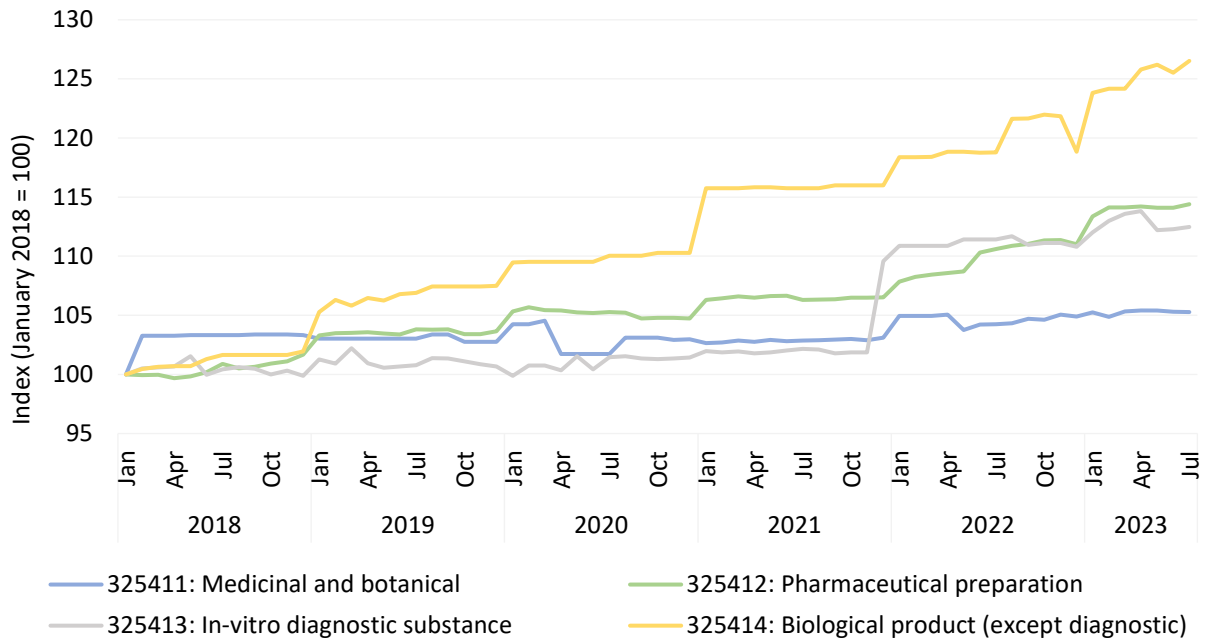
In billions of dollars. Underlying data for this figure can be found in appendix J, [table J.29](#).



Source: U.S. Census Bureau, “Manufacturers’ Shipments, Inventories, and Orders,” Series U25BVS (NAICS 3254), accessed August 24, 2023.

Figure I.6 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023

Index, January 2018=100. Underlying data for this figure can be found in appendix J, [tables J.30–J.33](#).



Source: Bureau of Labor Statistics (BLS), Produce Price Indexes, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Note: Data for April–July 2023 are preliminary.

Table I.4 U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	11,373	11,505	15,026	13,387	16,670	7,243	6,992
325412: Pharmaceutical preparation	82,390	92,414	93,302	97,382	106,060	54,936	52,693
325413: In-vitro diagnostic substance	5,030	5,208	7,250	10,194	28,180	12,714	17,000
325414: Biological product (except diagnostic)	36,775	42,732	51,932	55,551	46,960	24,869	25,439
Total	135,568	151,859	167,510	176,515	197,870	99,762	102,125

Source: USITC DataWeb/Census, general imports, NAICS 3254, accessed August 21, 2023.

Table I.5 Share of value of U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In percentages.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	8.4	7.6	9.0	7.6	8.4	7.3	6.8
325412: Pharmaceutical preparation	60.8	60.9	55.7	55.2	53.6	55.1	51.6
325413: In-vitro diagnostic substance	3.7	3.4	4.3	5.8	14.2	12.7	16.6
325414: Biological product (except diagnostic)	27.1	28.1	31.0	31.5	23.7	24.9	24.9
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 3254, accessed August 21, 2023.

Table I.6 U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In millions of kilograms.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	130	156	221	186	186	107	94
325412: Pharmaceutical preparation	505	433	525	540	609	297	296
325413: In-vitro diagnostic substance	48	48	52	69	113	77	35
325414: Biological product (except diagnostic)	22	19	21	28	30	14	17
Total	704	656	819	823	937	495	441

Source: USITC DataWeb/Census, general imports, NAICS 3254, accessed August 21, 2023.

Table I.7 Share of volume of U.S. imports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In percentages.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	18.5	23.7	27.0	22.6	19.8	21.7	21.2
325412: Pharmaceutical preparation	71.7	66.0	64.1	65.6	65.0	60.0	67.1
325413: In-vitro diagnostic substance	6.8	7.3	6.4	8.4	12.0	15.5	7.8
325414: Biological product (except diagnostic)	3.1	3.0	2.5	3.3	3.2	2.8	3.9
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 3254, accessed August 21, 2023.

Table I.8 U.S. imports of pharmaceuticals, by source, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	35,919	38,743	42,921	42,394	50,230	25,050	23,595
Germany	15,928	17,956	21,053	22,802	18,702	8,164	9,886
Switzerland	14,561	15,903	18,079	21,589	18,105	9,535	8,683
India	6,833	8,043	8,784	9,737	9,608	5,018	5,510
Singapore	7,159	6,464	6,294	8,821	7,058	3,104	7,614
All other sources	55,168	64,750	70,378	71,172	94,167	48,891	46,837
Total	135,568	151,859	167,510	176,515	197,870	99,762	102,125

Source: USITC DataWeb/Census, general imports, NAICS 3254, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.9 Share of U.S. imports of pharmaceuticals, by source, 2018–22, January–June 2022, and January–June 2023

In percentages.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	26.5	25.5	25.6	24.0	25.4	25.1	23.1
Germany	11.7	11.8	12.6	12.9	9.5	8.2	9.7
Switzerland	10.7	10.5	10.8	12.2	9.2	9.6	8.5
India	5.0	5.3	5.2	5.5	4.9	5.0	5.4
Singapore	5.3	4.3	3.8	5.0	3.6	3.1	7.5
All other sources	40.7	42.6	42.0	40.3	47.6	49.0	45.9
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 3254, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.10 U.S. imports of medicinal and botanical manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	6,207	6,669	8,838	7,742	11,245	4,383	2,828
China	1,577	1,257	1,769	2,046	1,892	1,117	834
United Kingdom	809	965	1,141	217	128	53	104
Switzerland	597	391	555	613	617	290	506
Belgium	309	351	721	759	532	334	139
All other sources	1,873	1,871	2,002	2,010	2,256	1,067	2,581
Total	11,373	11,505	15,026	13,387	16,670	7,243	6,992

Source: USITC DataWeb/Census, general imports, NAICS 325411, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.11 Share of U.S. imports of medicinal and botanical manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In percentages.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	54.6	58.0	58.8	57.8	67.5	60.5	40.4
China	13.9	10.9	11.8	15.3	11.4	15.4	11.9
United Kingdom	7.1	8.4	7.6	1.6	0.8	0.7	1.5
Switzerland	5.3	3.4	3.7	4.6	3.7	4.0	7.2
Belgium	2.7	3.0	4.8	5.7	3.2	4.6	2.0
All other sources	16.5	16.3	13.3	15.0	13.5	14.7	36.9
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 325411, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.12 U.S. imports of pharmaceutical preparation manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	16,091	20,496	23,379	19,929	21,763	12,428	10,585
Switzerland	11,991	12,933	12,701	16,154	13,086	6,908	5,741
India	6,484	7,766	8,240	8,981	8,970	4,636	5,295
Germany	8,755	8,262	7,531	8,893	8,686	4,702	3,544
Denmark	4,127	5,919	6,550	6,450	6,591	2,935	2,973
All other sources	34,942	37,038	34,900	36,976	46,964	23,327	24,556
Total	82,390	92,414	93,302	97,382	106,060	54,936	52,693

Source: USITC DataWeb/Census, general imports, NAICS 325412, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.13 Share of U.S. imports of pharmaceutical preparation manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In percentages.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	19.5	22.2	25.1	20.5	20.5	22.6	20.1
Switzerland	14.6	14.0	13.6	16.6	12.3	12.6	10.9
India	7.9	8.4	8.8	9.2	8.5	8.4	10.0
Germany	10.6	8.9	8.1	9.1	8.2	8.6	6.7
Denmark	5.0	6.4	7.0	6.6	6.2	5.3	5.6
All other sources	42.4	40.1	37.4	38.0	44.3	42.5	46.6
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 325412, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.14 U.S. imports of in-vitro diagnostic substance manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	760	820	997	1,283	4,545	768	2,966
Ireland	190	122	191	1,039	5,292	1,805	3,037
Singapore	511	572	481	616	1,724	441	3,058
China	355	213	729	819	4,120	3,586	364
United Kingdom	734	675	753	1,405	1,716	646	1,153
All other sources	2,480	2,808	4,098	5,033	10,783	5,467	6,422
Total	5,030	5,208	7,250	10,194	28,180	12,714	17,000

Source: USITC DataWeb/Census, general imports, NAICS 325413, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.15 Share of U.S. imports of in-vitro diagnostic substance manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	15.1	15.7	13.7	12.6	16.1	6.0	17.4
Ireland	3.8	2.3	2.6	10.2	18.8	14.2	17.9
Singapore	10.2	11.0	6.6	6.0	6.1	3.5	18.0
China	7.1	4.1	10.1	8.0	14.6	28.2	2.1
United Kingdom	14.6	13.0	10.4	13.8	6.1	5.1	6.8
All other sources	49.3	53.9	56.5	49.4	38.3	43.0	37.8
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 325413, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.16 U.S. imports of biological product (except diagnostic) manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	13,431	11,457	10,513	13,685	11,931	6,433	7,146
Germany	6,146	8,567	12,165	12,413	5,276	2,596	3,280
Belgium	2,269	4,429	7,303	5,184	7,711	2,800	1,931
Switzerland	1,937	2,529	4,775	4,758	4,263	2,295	2,276
Netherlands	1,291	2,276	2,273	2,097	2,252	1,504	3,201
All other sources	11,701	13,475	14,905	17,414	15,528	9,240	7,605
Total	36,775	42,732	51,932	55,551	46,960	24,869	25,439

Source: USITC DataWeb/Census, general imports, NAICS 325414, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.17 Share of U.S. imports of biological product (except diagnostic) manufacturing products, by source, 2018–22, January–June 2022, and January–June 2023

In percentages.

Import source	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Ireland	36.5	26.8	20.2	24.6	25.4	25.9	28.1
Germany	16.7	20.0	23.4	22.3	11.2	10.4	12.9
Belgium	6.2	10.4	14.1	9.3	16.4	11.3	7.6
Switzerland	5.3	5.9	9.2	8.6	9.1	9.2	8.9
Netherlands	3.5	5.3	4.4	3.8	4.8	6.0	12.6
All other sources	31.8	31.5	28.7	31.3	33.1	37.2	29.9
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, general imports, NAICS 325414, accessed August 21, 2023.

Note: Top sources include the top five countries by total import value over the period.

Table I.18 U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	2,208	1,995	2,021	2,353	2,644	1,388	2,435
325412: Pharmaceutical preparation	22,908	27,100	24,217	27,193	32,677	16,782	15,496
325413: In-vitro diagnostic substance	7,659	7,818	9,578	11,514	11,646	6,036	5,299
325414: Biological product (except diagnostic)	21,967	22,843	23,126	39,044	35,091	18,093	22,061
Total	54,742	59,756	58,942	80,103	82,058	42,299	45,291

Source: USITC DataWeb/Census, domestic exports, NAICS 3254, accessed August 21, 2023.

Table I.19 Share of value of U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In percentages.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	4.0	3.3	3.4	2.9	3.2	3.3	5.4
325412: Pharmaceutical preparation	41.8	45.4	41.1	33.9	39.8	39.7	34.2
325413: In-vitro diagnostic substance	14.0	13.1	16.2	14.4	14.2	14.3	11.7
325414: Biological product (except diagnostic)	40.1	38.2	39.2	48.7	42.8	42.8	48.7
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 3254, accessed August 21, 2023.

Table I.20 U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In millions of kilograms.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	263	232	237	252	226	129	87
325412: Pharmaceutical preparation	451	422	388	382	444	253	145
325413: In-vitro diagnostic substance	21	19	82	95	97	49	45
325414: Biological product (except diagnostic)	84	76	72	84	85	44	47
Total	819	750	780	812	852	475	324

Source: USITC DataWeb/Census, domestic exports, NAICS 3254, accessed August 21, 2023.

Table I.21 Share of volume of U.S. exports of pharmaceuticals, by industry classification, 2018–22, January–June 2022, and January–June 2023

In percentages.

Industry classification	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
325411: Medicinal and botanical	32.1	31.0	30.4	31.0	26.5	27.1	26.9
325412: Pharmaceutical preparation	55.1	56.3	49.8	47.0	52.1	53.2	44.9
325413: In-vitro diagnostic substance	2.6	2.6	10.5	11.7	11.4	10.4	13.8
325414: Biological product (except diagnostic)	10.2	10.2	9.3	10.3	9.9	9.3	14.4
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 3254, accessed August 21, 2023.

Table I.22 U.S. exports of pharmaceuticals, by market, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	4,894	5,852	6,497	6,221	7,251	3,655	4,604
Netherlands	4,987	5,123	5,473	5,925	7,938	3,979	4,061
Canada	3,577	3,743	4,095	7,746	6,399	3,062	2,320
Japan	3,958	4,131	4,062	5,131	6,365	2,973	2,419
China	3,351	3,758	4,409	4,828	6,375	3,089	2,914
All other markets	33,975	37,149	34,406	50,253	47,730	25,541	28,972
Total	54,742	59,756	58,942	80,103	82,058	42,299	45,291

Source: USITC DataWeb/Census, domestic exports, NAICS 3254, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.23 Share of U.S. exports of pharmaceuticals, by market, 2018–22, January–June 2022, and January–June 2023

In percentages.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	8.9	9.8	11.0	7.8	8.8	8.6	10.2
Netherlands	9.1	8.6	9.3	7.4	9.7	9.4	9.0
Canada	6.5	6.3	6.9	9.7	7.8	7.2	5.1
Japan	7.2	6.9	6.9	6.4	7.8	7.0	5.3
China	6.1	6.3	7.5	6.0	7.8	7.3	6.4
All other markets	62.1	62.2	58.4	62.7	58.2	60.4	64.0
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 3254, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.24 U.S. exports of medicinal and botanical manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
United Kingdom	83	88	61	68	85	49	1,267
Mexico	271	252	229	211	216	109	110
China	147	153	158	250	353	163	149
Canada	215	188	164	179	179	93	90
Netherlands	183	143	153	179	218	130	122
All other markets	1,309	1,170	1,257	1,467	1,593	844	698
Total	2,208	1,995	2,021	2,353	2,644	1,388	2,435

Source: USITC DataWeb/Census, domestic exports, NAICS 325411, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.25 Share of U.S. exports of medicinal and botanical manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In percentages.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
United Kingdom	3.7	4.4	3.0	2.9	3.2	3.5	52.0
Mexico	12.3	12.6	11.3	9.0	8.2	7.9	4.5
China	6.7	7.7	7.8	10.6	13.4	11.7	6.1
Canada	9.7	9.4	8.1	7.6	6.8	6.7	3.7
Netherlands	8.3	7.2	7.6	7.6	8.2	9.4	5.0
All other markets	59.3	58.7	62.2	62.3	60.2	60.8	28.7
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 325411, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.26 U.S. exports of pharmaceutical preparation manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Canada	1,831	2,002	2,088	3,295	2,628	1,291	1,256
United Kingdom	2,074	1,927	1,481	2,465	3,766	2,219	1,017
Japan	1,773	2,335	1,899	2,282	3,197	1,576	819
Netherlands	1,563	1,451	1,466	1,821	3,079	1,691	1,100
China	1,330	1,585	2,072	1,625	2,605	1,348	1,132
All other markets	14,337	17,800	15,211	15,706	17,403	8,657	10,172
Total	22,908	27,100	24,217	27,193	32,677	16,782	15,496

Source: USITC DataWeb/Census, domestic exports, NAICS 325412, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.27 Share of U.S. exports of pharmaceutical preparation manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In percentages.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Canada	8.0	7.4	8.6	12.1	8.0	7.7	8.1
United Kingdom	9.1	7.1	6.1	9.1	11.5	13.2	6.6
Japan	7.7	8.6	7.8	8.4	9.8	9.4	5.3
Netherlands	6.8	5.4	6.1	6.7	9.4	10.1	7.1
China	5.8	5.8	8.6	6.0	8.0	8.0	7.3
All other markets	62.6	65.7	62.8	57.8	53.3	51.6	65.6
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 325412, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.28 U.S. exports of in-vitro diagnostic substance manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	1,278	1,228	1,499	1,524	1,582	831	678
China	936	1,049	1,140	1,248	1,543	715	657
Netherlands	564	622	955	1,105	1,070	577	454
Canada	473	455	652	996	789	425	343
Japan	482	510	512	733	1,062	475	340
All other markets	3,926	3,955	4,820	5,908	5,600	3,013	2,827
Total	7,659	7,818	9,578	11,514	11,646	6,036	5,299

Source: USITC DataWeb/Census, domestic exports, NAICS 325413, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.29 Share of U.S. exports of in-vitro diagnostic substance manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In percentages.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	16.7	15.7	15.7	13.2	13.6	13.8	12.8
China	12.2	13.4	11.9	10.8	13.3	11.9	12.4
Netherlands	7.4	8.0	10.0	9.6	9.2	9.6	8.6
Canada	6.2	5.8	6.8	8.7	6.8	7.0	6.5
Japan	6.3	6.5	5.3	6.4	9.1	7.9	6.4
All other markets	51.3	50.6	50.3	51.3	48.1	49.9	53.3
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 325413, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.30 U.S. exports of biological product (except diagnostic) manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In millions of dollars.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	1,910	2,738	3,295	3,419	4,215	2,073	2,535
Netherlands	2,678	2,907	2,899	2,820	3,571	1,581	2,385
Belgium	2,000	1,717	1,017	2,908	1,504	879	4,265
Canada	1,058	1,098	1,191	3,276	2,803	1,253	632
Italy	2,489	2,413	1,767	1,341	1,428	746	611
All other markets	11,832	11,970	12,957	25,279	21,570	11,561	11,634
Total	21,967	22,843	23,126	39,044	35,091	18,093	22,061

Source: USITC DataWeb/Census, domestic exports, NAICS 325414, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Table I.31 Share of U.S. exports of biological product (except diagnostic) manufacturing products, by market, 2018–22, January–June 2022, and January–June 2023

In percentages.

Export market	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
Germany	8.7	12.0	14.2	8.8	12.0	11.5	11.5
Netherlands	12.2	12.7	12.5	7.2	10.2	8.7	10.8
Belgium	9.1	7.5	4.4	7.4	4.3	4.9	19.3
Canada	4.8	4.8	5.2	8.4	8.0	6.9	2.9
Italy	11.3	10.6	7.6	3.4	4.1	4.1	2.8
All other markets	53.9	52.4	56.0	64.7	61.5	63.9	52.7
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Source: USITC DataWeb/Census, domestic exports, NAICS 325414, accessed August 21, 2023.

Note: Top markets include the top five countries by total export value over the period.

Appendix J

Data for Figures

Table J.1 Examples of different ways to categorize COVID-19 diagnosticsThis table corresponds to [figure ES.1](#).

Type	Subtypes	COVID-19 test
Diagnostic	Molecular	PCR
Diagnostic	Antigen	Rapid tests
Diagnostic	Serology	Antibody
Diagnostic	Other	Breathalyzer
Diagnostic	Other	Genotyping
Immune response	Adaptive response	T cell immune response
Management	Biomarker	Immunoenzymatic assay

Source: Compiled by the USITC.

Note: The tests listed here do not represent an exhaustive list of COVID-19 diagnostics.

Table J.2 Examples of different ways to categorize COVID-19 therapeuticsThis table corresponds to [figure ES.2](#).

Treatment type	Treatment class	Modes of action	Pharmaceutical	Patient setting
Antiviral	Virus-directed	Protease inhibitor	Ensitrelvir	Outpatient
Antiviral	Virus-directed	Protease inhibitor	Nirmatrelvir (+ ritonavir)	Outpatient
Antiviral	Virus-directed	Nucleoside analogue	Molnupiravir	Outpatient
Antiviral	Virus-directed	Nucleotide analogue	Remdesivir	In- and outpatient
Anti-inflammatory	Host-directed	Immune suppression	Dexamethasone	Inpatient
Anti-inflammatory	Host-directed	Inhibitor (e.g., JAK or IL-6)	Baricitinib	Inpatient
Anti-inflammatory	Host-directed	Inhibitor (e.g., JAK or IL-6)	Tocilizumab	Inpatient
Monoclonal antibody (mAb)	Virus-directed	Neutralizing mAb	Casirivimab and imdevimab	In- and outpatient
Monoclonal antibody (mAb)	Virus-directed	Neutralizing mAb	Bamlanivimab and etesevimab	In- and outpatient
Monoclonal antibody (mAb)	Virus-directed	Neutralizing mAb	Sotrovimab	Inpatient
Other	Adjunctive therapy	Secondary (e.g., NSAID, immunomodulator, anticoagulant)	Heparin	Inpatient
Other	Adjunctive therapy	Secondary (e.g., NSAID, immunomodulator, anticoagulant)	Ibuprofen	Outpatient
Other	Adjunctive therapy	Secondary (e.g., NSAID, immunomodulator, anticoagulant)	Vitamin C	Outpatient

Source: Compiled by the USITC.

Notes: The drugs listed here do not represent an exhaustive list of COVID-19 therapeutics. Patient setting refers to the location of the patient being treated (e.g., the drug in question can be prescribed for the treatment of COVID-19 in patients that who are not hospitalized (outpatient) or are hospitalized (inpatient)).

Table J.3 Count of manufacturers of COVID-19 diagnostics and therapeutics

In number of manufacturers. HIC = high-income countries; UMIC = upper-middle income countries, LMIC = lower-middle income countries; LIC = low-income countries. This table corresponds to [figure ES.3](#).

Country income level	Diagnostics	Therapeutics
HIC	580	96
UMIC	290	55
LMIC	30	70

Sources: FIND, accessed June 30, 2023; Airfinity, accessed August 28, 2023.

Note: Additionally, there are 58 manufacturers of serology COVID-19 tests, and 1 manufacturer of a COVID-19 saliva test. For therapeutics, the count of manufacturers only includes manufacturers of drugs that are approved, authorized, and/or recommended for the treatment of COVID-19. Serology tests are not currently relevant for COVID-19 diagnostics.

Table J.4 Courses of COVID-19 therapeutics made available through donation or purchase, by country and region, based on publicly announced supply agreements

In number of courses. — = Not applicable. k = thousand; m = million. This table corresponds to [figure ES.4](#).

Region	Country	Supply	Range for map
Africa	Egypt	70,000	10k–100k
Africa	Morocco	0	Unknown
Africa	South Africa	0	Unknown
Africa	—	100,000	100k–250k
Asia	Brunei	50,000	10k–100k
Asia	China	0	Unknown
Asia	India	1,363,833	1m–5m
Asia	Indonesia	2,033,333	1m–5m
Asia	Israel	160,000	100k–250k
Asia	Japan	6,400,000	5m–10m
Asia	Kuwait	0	Unknown
Asia	Malaysia	260,000	250k–500k
Asia	Pakistan	100,000	100k–250k
Asia	Philippines	4,300,000	1m–5m
Asia	Saudi Arabia	0	Unknown
Asia	Singapore	0	Unknown
Asia	South Korea	1,024,000	1m–5m
Asia	Taiwan	740,000	500k–1m
Asia	Thailand	9,343,669	5m–10m
Asia	United Arab Emirates	0	Unknown
Asia	Vietnam	133,333	100k–250k
Europe	Austria	470,167	250k–500k
Europe	Belgium	45,000	10k–100k
Europe	Bulgaria	0	Unknown
Europe	Cyprus	15,000	10k–100k
Europe	Czech Republic	44,500	10k–100k
Europe	Denmark	90,000	10k–100k
Europe	France	654,500	500k–1m
Europe	Georgia	0	Unknown
Europe	Germany	1,505,833	1m–5m
Europe	Greece	34,700	10k–100k
Europe	Hungary	50,000	10k–100k
Europe	Ireland	220,000	100k–250k
Europe	Italy	670,000	500k–1m
Europe	Luxembourg	20,000	10k–100k
Europe	Norway	50,000	10k–100k
Europe	Poland	50,000	10k–100k

Region	Country	Supply	Range for map
Europe	Portugal	16,666	10k–100k
Europe	Romania	22,500	10k–100k
Europe	Russia	3,500	< 10k
Europe	Serbia	0	Unknown
Europe	Slovakia	50,000	10k–100k
Europe	Slovenia	0	Unknown
Europe	Spain	376,500	250k–500k
Europe	Sweden	1,700	< 10k
Europe	Switzerland	32,840	10k–100k
Europe	Ukraine	850,000	500k–1m
Europe	United Kingdom	5,080,000	5m–10m
Europe	Unknown	4,607,517	1m–5m
North America	Canada	2,273,233	1m–5m
North America	Costa Rica	108,000	100k–250k
North America	El Salvador	100,000	100k–250k
North America	Honduras	0	Unknown
North America	Mexico	430,000	250k–500k
North America	Panama	50,000	10k–100k
North America	United States	35,855,364	10m
Oceania	Australia	1,385,560	1m–5m
Oceania	New Zealand	185,300	100k–250k
South America	Argentina	0	Unknown
South America	Bolivia	0	Unknown
South America	Brazil	2,100,000	1m–5m
South America	Chile	0	Unknown
South America	Colombia	0	Unknown
South America	Ecuador	0	Unknown
South America	Paraguay	0	Unknown
South America	Uruguay	0	Unknown
South America	Venezuela	1,000,000	1m–5m
Global Fund	—	6,000,000	Unknown
UNICEF	—	7,000,000	Unknown
Other PPP	—	270,000	Unknown

Source: Airfinity, accessed August 28, 2023.

Note: These numbers represented announced government procurements, private purchases (including by multilateral organizations), and donations. The data do not reflect confirmed deliveries. Not all supply agreements disclose the country or region.

Table J.5 Economies by World Bank income group

HIC = high-income countries, UMIC = upper-middle income countries, LMIC = lower-middle income countries, LIC = low-income countries. This table corresponds to [figure 1.1](#).

Income level	Country
HIC	Andorra, Antigua Barbuda, Aruba, Australia, Austria, Bahamas, Bahrain, Barbados, Belgium, Bermuda, Br Virgin Is, Brunei, Canada, Cayman Is, Channel Islands, Chile, Croatia, Curacao, Cyprus, Czechia, Denmark, Estonia, Faroe Islands, Finland, France, French Polynesia, Germany, Gibraltar, Greece, Greenland, Guam, Hong Kong, Hungary, Iceland, Ireland, Isle of Man, Israel, Italy, Japan, Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Macau, Malta, Monaco, Nauru, Netherlands, New Caledonia, New Zealand, Northern Mariana Islands, Norway, Oman, Panama, Poland, Portugal, Puerto Rico, Qatar, Romania, San Marino, Saudi Arabia, Seychelles, Singapore, Sint Maarten, Slovakia, Slovenia, South Korea, Spain, St. Kitts and Nevis, St. Martin (French part), Sweden, Switzerland, Taiwan, Trinidad & Tobago, Turks & Caicos Is, United Arab Emirates, United Kingdom, United States, Uruguay, Virgin Islands (U.S.)
UMIC	Albania, American Samoa, Argentina, Armenia, Azerbaijan, Belarus, Belize, Bosnia and Herzegovina, Botswana, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, Equatorial Guinea, Fiji, Gabon, Georgia, Grenada, Guatemala, Guyana, Iraq, Jamaica, Jordan, Kazakhstan, Kosovo, Libya, Malaysia, Maldives, Marshall Islands, Mauritius, Mexico, Moldova, Montenegro, Namibia, North Macedonia, Palau, Paraguay, Peru, Russia, Serbia, South Africa, St. Lucia, St. Vincent and the Grenadines, Suriname, Thailand, Tonga, Turkey, Turkmenistan, Tuvalu
LMIC	Algeria, Angola, Bangladesh, Benin, Bhutan, Bolivia, Burma, Cabo Verde, Cambodia, Cameroon, Comoros, Congo-Brazza, Cote d'Ivoire, Djibouti, Egypt, El Salvador, Eswatini, Ghana, Haiti, Honduras, India, Indonesia, Iran, Islamic Rep., Kenya, Kiribati, Kyrgyzstan, Laos, Lebanon, Lesotho, Mauritania, Micronesia Federated States, Mongolia, Morocco, Nepal, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Philippines, Samoa, Sao Tome & Principe, Senegal, Solomon Is, Sri Lanka, Tajikistan, Tanzania, Timor-Leste, Tunisia, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Zimbabwe
LIC	Afghanistan, Burkina Faso, Burundi, Cen African Rep, Chad, Congo-Kinshasa, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Korea, Dem. People's Rep., Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Syrian Arab Republic, Togo, Uganda, Yemen, Republic, Zambia
Not classified	Venezuela

Source: Hamadeh, Van Rompaey, Metreau, "New World Bank Country Classifications by Income Level," July 1, 2022. Country classifications are for calendar year 2021 or World Bank fiscal year 2023 (FY23).

Notes: Venezuela was classified as a UMIC until July 2021, after which it was recategorized as "not classified" by the World Bank. Although country classifications were updated by the World Bank on July 1, 2023 (resulting in a change in classification for American Samoa, El Salvador, Guinea, Guyana, Indonesia, Jordan, West Bank and Gaza, and Zambia), USITC uses FY23 classifications to maintain consistency with Airfinity data used throughout the report.

Table J.6 COVID-19 pandemic: Timeline of notable events and reported COVID-19 deaths by income level, January 2020–May 2023

In thousands of deaths. WHO = World Health Organization; WTO = World Trade Organization; EUA = Emergency Use Authorization; EUL = Emergency Use Listing; FDA = U.S. Food and Drug Administration. **beta** **delta** **gamma** **omicron**. This table corresponds to [figure 1.2](#).

Month/Year	HIC	UMIC	LMIC	LIC	Notable moment
January 2020	0	213	0	0	SARS-CoV-2 sequence published
February 2020	50	2,625	27	0	None
March 2020	36,087	1,329	3,207	25	WHO declares pandemic; First commercial molecular test granted EUA (FDA)
April 2020	175,216	20,854	7,328	524	1 million cases confirmed (U.S.)
May 2020	87,885	64,572	10,932	804	None
June 2020	40,844	86,906	24,792	1,501	None
July 2020	40,026	105,504	38,583	1,527	None
August 2020	42,192	104,115	46,188	1,321	-variant identified (South Africa)
September 2020	35,254	79,895	52,410	829	None
October 2020	62,916	69,331	47,535	788	-variant identified (India)
November 2020	159,024	75,446	47,974	1,249	Bamlanivimab granted EUA (FDA); -variant identified (Brazil)
December 2020	215,347	105,162	40,876	1,677	COVID-19 mRNA Vx Pfizer and Moderna (granted EUA, FDA); First EUA (FDA) for a rapid antigen self-test
January 2021	251,264	142,861	34,933	2,355	None
February 2021	161,906	113,932	26,193	1,822	None
March 2021	109,023	141,413	29,216	2,205	-surge (India)
April 2021	99,762	180,906	88,263	2,712	None
May 2021	62,216	155,656	162,836	1,829	None
June 2021	30,739	131,089	102,528	4,461	China's Sinovac vaccine granted WHO EUL
July 2021	21,886	140,088	94,243	6,609	None
August 2021	50,164	131,816	114,974	3,209	Global vaccination rate reaches target of 40%
September 2021	78,710	109,281	64,361	2,371	None
October 2021	82,545	85,665	44,928	2,052	None
November 2021	88,128	79,116	47,095	1,101	None
December 2021	109,262	67,129	39,271	1,131	-variant identified (South Africa); Nirmatrelvir approved (FDA)
January 2022	131,723	75,317	34,521	2,125	Bamlanivimab EUA (FDA) rescinded
February 2022	138,118	93,585	45,996	1,413	None
March 2022	100,697	54,368	27,515	1,277	None
April 2022	55,635	21,572	7,599	121	None
May 2022	33,776	13,135	2,164	62	None
June 2022	25,366	14,358	1,192	153	WTO 2022 Ministerial Decision
July 2022	43,894	18,960	3,403	153	None
August 2022	47,226	17,309	6,170	99	None
September 2022	33,065	11,107	3,809	90	None
October 2022	36,616	9,208	3,279	50	None
November 2022	31,389	7,076	4,139	57	None
December 2022	46,736	27,449	1,989	52	USITC receives request letter
January 2023	46,576	73,117	1,242	55	None
February 2023	27,833	11,251	912	48	None
March 2023	17,876	4,899	1,408	29	None
April 2023	15,857	3,439	2,344	26	None
May 2023	2,536	868	628	11	WHO declares end of global health emergency; Nirmatrelvir approved (FDA)

COVID-19 Diagnostics and Therapeutics: Supply, Demand, and TRIPS Agreement Flexibilities

Source: WHO, “WHO Coronavirus (COVID-19) Dashboard,” accessed June 2, 2023; Wellcome, “What Is a Variant? An Expert Explains,” accessed August 10, 2023; Kay and Pandya, “How Errors, Inaction Sent a Deadly Covid Variant,” December 29, 2021; WHO, “WHO Validates Sinovac COVID-19 Vaccine for Emergency Use,” June 1, 2021; KFF, “KFF Global COVID-19 Vaccine Coverage Tool,” July 24, 2023.

Note: WHO data on COVID-19 deaths are an aggregation of data reported by countries, territories, and areas. The income categories shown are defined by World Bank. As discussed in the text, official counts of COVID-19 depend on jurisdictional testing capabilities and reporting standards and records management systems, and may, therefore, be understated for LICs relative to other income categories shown in this figure.

Table J.7 Number of reported cases of COVID-19 in 2020, with key dates in the United States for development and approval of COVID-19 diagnostic tests, by month

Millions of COVID-19 cases, U.S. cumulative. This table corresponds to [figure 2.3](#).

COVID-19 cases		
Month	(millions)	Notable moment
January	0	January 10–12: SARS CoV-2 genomic sequences uploaded to online repositories
February	0	February 4: EUA for CDC COVID-19 test granted
March	0	March 10: First commercial molecular test receives an EUA
April	2	None
May	2	None
June	3	None
July	5	None
August	6	None
September	7	None
October	9	None
November	13	None
December	19	December 15: First EUA for a rapid antigen self-test

Source: WHO, “WHO Coronavirus (COVID-19) Dashboard,” accessed May 13, 2023. CDC, “CDC Museum COVID-19 Timeline.”

Note: WHO listed the first quality-assured SARS-CoV-2 self-test for emergency use, 19 months after the EUA by FDA. <https://extranet.who.int/pqweb/news/who-issues-its-first-emergency-use-listing-sars-cov-2-self-test>.

Table J.8 Number of COVID-19 diagnostics manufacturers by country income class and country as of June 30, 2022

Number of manufacturers. HIC = high-income countries; UMIC = upper-middle income countries; LMIC = lower-middle income countries. This table corresponds to [figure 4.3](#).

Country	Income level	Number of manufacturers
United States	HIC	168
South Korea	HIC	67
Germany	HIC	53
United Kingdom	HIC	52
Japan	HIC	31
Canada	HIC	26
Italy	HIC	25
France	HIC	19
All other HICs	HIC	139
China	UMIC	247
Turkey	UMIC	26
All other UMICs	UMIC	17
India	LMIC	21
All other LMICs	LMIC	9

Source: FIND, “COVID-19 Test Directory.”

Note: Manufacturers are classified by headquarters location; countries’ income classes are based on World Bank classifications.

Table J.9 Diagnostics, including COVID-19 diagnostics: exports and imports by income level of exporter (left) and importer (right), 2022

In billions of dollars. — = Not applicable, HIC = high-income countries; UMIC = upper-middle income countries; LMIC = lower-middle income countries. This table corresponds to [figure 4.4](#).

Income level	HIC (imports)	UMIC (imports)	LMIC (imports)	LIC (imports)	Total
HIC (exports)	197.3	27.7	3.9	0.3	229.3
UMIC (exports)	11.2	1.2	0.5	0.1	13.0
LMIC (exports)	0.3	0.1	0.1	0.0	0.4
Total	208.8	29.0	4.6	0.4	242.7

Source: S&P Global, Global Trade Atlas, accessed June 6, 2023. HS codes include 3821.00, 3822.19, 3002.13, 3002.14, 3002.15.

Note: The figure above only uses 2022 data because the Harmonized System split diagnostics-related codes in 2022, allowing for an analysis that included a higher share of COVID-related diagnostics than in previous years.

Table J.10 COVID-19 virus-directed therapeutics manufacturing, by drug

In number of manufacturers. — = Not applicable. HIC = high-income countries; UMIC = upper-middle income countries; LMIC = lower-middle income countries. This table corresponds to [figure 4.7](#).

Manufacturer	HIC	UMIC	MIC	LMIC	No income classification
Bamlanivimab	3	—	—	—	—
Bamlanivimab + etesevimab	1	—	—	—	—
casirivimab and imdevimab	3	—	—	—	—
Ensitrelvir	2	3	—	4	—
Molnupiravir	3	23	1	52	—
Nirmatrelvir (+ ritonavir)	10	19	—	38	—
remdesivir	4	3	—	21	2
Ritonavir	—	1	—	—	—
Sotrovimab	3	—	—	—	—

Source: Airfinity, “Production,” accessed July 7, 2023.

Note: The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.). In aggregate the deals include API/excipient manufacturing, finished drug product, and fill/finish. Deals that have been noted as inactive (with no production, not “launched”) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. It likely underreports an originators/patent holder’s own production sites for manufacturing. The middle-income production of molnupiravir was an announcement between a UMIC and LMIC country. No income classification refers to Venezuela.

Table J.11 HICs: COVID-19 virus-directed therapeutics manufacturing by production type, as of July 2023

In number of manufacturers. — = Not applicable. HIC = high-income countries. This table corresponds to [figure 4.8](#).

Country	API/excipient	Fill/finish	Finished drug product
United States	2	—	5
South Korea	3	—	3
Portugal	1	—	1
Japan	—	—	1
Italy	—	1	—
Ireland	1	—	—
Hong Kong	—	—	1
Germany	—	1	—
France	1	—	—

Source: Airfinity, “Production,” accessed July 7, 2023.

Note: The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.). In aggregate the deals include API/excipient manufacturing, finished drug product, and fill/finish. Deals that have been noted as inactive (with no production, not “launched”) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. It likely underreports an originators/patent holder’s own production sites for manufacturing.

Table J.12 UMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023

 In number of manufacturers. — = Not applicable, UMIC = upper-middle income countries. This table corresponds to [figure 4.9](#).

Country	API/excipient	Fill/finish	Finished drug product
Venezuela	—	—	2
Thailand	—	—	1
South Africa	1	—	—
Serbia	—	—	1
Russia	—	3	11
Paraguay	—	—	5
Mexico	—	—	1
Jordan	—	—	1
Dominican Republic	—	—	1
China	5	—	13
Belarus	—	—	1

Source: Airfinity, “Production,” accessed July 7, 2023; Hamadeh, Van Rompaey, Metreau, “New World Bank Country Classifications by Income Level,” July 1, 2021.

Note: Deals that have been noted as inactive (either no production or not launched) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic: The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.), which may not capture an originator’s/patent holder’s production sites for manufacturing. Not accounted for is the production of molnupiravir (finished drug product) under a joint arrangement with Jordan (UMIC) and Egypt (LMIC). Venezuela was classified as a UMIC until July 2021; since then, Venezuela has been regulated to “unclassified” by the World Bank.

Table J.13 LMICs: virus-directed COVID-19 therapeutics manufacturing by production type, as of July 2023

 In number of manufacturers. — = Not applicable, LMIC = lower-middle income countries. This table corresponds to [figure 4.10](#).

Country	API/excipient	Finished drug product
Vietnam	—	5
Ukraine	—	2
Philippines	—	1
Pakistan	—	4
Laos	—	3
Kenya	—	1
Indonesia	—	2
India	9	51
Egypt	—	3
Bangladesh	—	27

Source: Airfinity, “Production,” accessed July 7, 2023.

Note: The information presented in this chart is based on publicly available information (i.e., announced deals, press releases, etc.). Deals that have been noted as inactive (with no production, not “launched”) or classified as distribution or commercialization have been excluded. A single producer may produce more than one COVID-19 therapeutic. It likely underreports an originators/patent holder’s own production sites for manufacturing. Not accounted for is the production of molnupiravir (finished drug product) was a joint arrangement for Jordan (UMIC) and Egypt (LMIC).

Table J.14 Exports and imports of HS subheadings that include COVID-19 therapeutics by income level of exporter (left) and importer (right), 2022

In billions of dollars. —=Not applicable, HIC = High-income countries, UMIC = Upper-middle income countries, LMIC = Lower-middle income countries. This table corresponds to [figure 4.11](#).

Income level	HIC (imports)	UMIC (imports)	LMIC (imports)	LIC (imports)	Total
HIC (exports)	95.1	11.6	2.2	0.1	109.0
UMIC (exports)	5.7	0.9	1.1	0.2	6.9
LMIC (exports)	4.8	1.6	1.4	0.6	9.3
Total	105.5	14.1	4.7	0.8	125.2

Source: S&P Global, Global Trade Atlas, accessed May 2, 2023.

Notes: Exporters were selected based on their production of COVID-related therapeutics. See “Methodology” for more detail on selection. High-income exporters in this data include Germany, Israel, Portugal, South Korea, Switzerland United States, and United Kingdom. Brazil and China are the upper-middle-income countries, and India is the only lower-middle-income country.

Table J.15 UMICs, LMICs, and LICs where COVID-19 therapeutics licensed under MPP licenses or BLAs cannot be offered for sale under the terms of those licenses/agreements, by treatment type and income levels

UMIC = upper-middle income countries; LMIC = lower-middle income countries; LIC = low-income countries. This table corresponds to [figure 5.1](#).

Treatment type	UMIC	LMIC	LIC
Ensitrelvir Fumaric Acid	Albania, American Samoa, Argentina, Belarus, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Malaysia, Mexico, Montenegro, North Macedonia, Palau, Russia, Serbia, Thailand, Turkey, Turkmenistan	Indonesia, Lebanon	None
Molnupiravir	Albania, American Samoa, Argentina, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Costa Rica, Dominican Republic, Ecuador, Georgia, Jordan, Kazakhstan, Kosovo, Malaysia, Mexico, Montenegro, North Macedonia, Palau, Peru, Russia, Serbia, Turkey, Turkmenistan	Indonesia, Lebanon	None
Nirmatrelvir (+ ritonavir)	Albania, American Samoa, Argentina, Azerbaijan, Belarus, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, Fiji, Grenada, Guyana, Iraq, Jamaica, Kazakhstan, Libya, Malaysia, Maldives, Marshall Islands, Mauritius, Mexico, Montenegro, North Macedonia, Palau, Paraguay, Peru, Russia, Saint Lucia, Saint Vincent and the Grenadines, Serbia, Suriname, Thailand, Turkey, Turkmenistan, Tuvalu	Lebanon	None
Remdesivir	Albania, American Samoa, Argentina, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Ecuador, Iraq, Jordan, Kosovo, Malaysia, Mexico, Montenegro, North Macedonia, Paraguay, Peru, Russia, Serbia, Thailand, Turkey	Iran, Lebanon, West Bank and Gaza	Syrian Arab Republic, Yemen

Sources: MPP, Nirmatrelvir, “Country List,” <https://medicinespatentpool.org/licence-post/pf-07321332>, accessed June 26, 2023; MPP, Molnupiravir, “Country List,” <https://medicinespatentpool.org/licence-post/molnupiravir-mol>, accessed June 26, 2023; MPP, Ensitrelvir Fumaric Acid, “Country List,” <https://medicinespatentpool.org/licence-post/ensitrelvir>, accessed June 26, 2023; Gilead, Access Partnerships, “2020 Original COVID-19 Voluntary License Agreement,” <https://www.gilead.com/-/media/files/pdfs/other/original-covid-19-voluntary-license-agreement.pdf>, accessed June 26, 2023

Note: Bilateral agreements for the production of Baricitinib have expired and are not included in this figure. The geographic scope of the MPP licenses for the production of molnupiravir is the same as the scope of the bilateral agreements. High-income countries identified in the remdesivir license are not included in this figure. Venezuela is included in the remdesivir license. It was classified as a UMIC until July 2021; its income level is now unclassified by the World Bank. Anguilla, the Cook Islands, and Montserrat are included in the ensitrelvir fumaric acid, molnupiravir, and nirmatrelvir licenses, but their income levels are not classified by the World Bank.

Table J.16 UMICs, LMICs, and LICs where four COVID-19 therapeutics can be offered for sale under MPP licenses and BLAs, by count of treatment types

UMIC = upper-middle income countries; LMIC = lower-middle income countries; LIC = low-income countries. This table corresponds to [figure 5.2](#).

Number of treatments	Countries
No treatments	Albania, American Samoa, Argentina, Bosnia and Herzegovina, Brazil, Bulgaria, China, Colombia, Lebanon, Malaysia, Mexico, Montenegro, North Macedonia, Russia, Serbia, Turkey
1	Belarus, Ecuador, Palau, Peru, Thailand, Turkmenistan
2	Azerbaijan, Costa Rica, Dominican Republic, Iraq, Jordan, Kazakhstan, Kosovo, Paraguay, West Bank and Gaza
3	Armenia, Cuba, Dominica, Fiji, Georgia, Grenada, Guyana, Indonesia, Iran, Jamaica, Kyrgyzstan, Libya, Maldives, Marshall Islands, Mauritius, Saint Lucia, Saint Vincent and the Grenadines, Seychelles, Suriname, Syrian Arab Republic, Tuvalu, Ukraine, Yemen
4	Afghanistan, Algeria, Angola, Bangladesh, Belize, Benin, Bhutan, Bolivia, Botswana, Burkina Faso, Burma, Burundi, Cape Verde, Cambodia, Cameroon, Central African Republic, Chad, Comoros, Congo, Cote d'Ivoire, Democratic Republic of the Congo, Djibouti, Egypt, El Salvador, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Gabon, Gambia, Ghana, Guatemala, Guinea, Guinea-Bissau, Haiti, Honduras, India, Kenya, Kiribati, Lao People's Democratic Republic, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Micronesia, Moldova, Mongolia, Morocco, Mozambique, Namibia, Nepal, Nicaragua, Niger, Nigeria, North Korea, Pakistan, Papua New Guinea, Philippines, Rwanda, Samoa, Sao Tome and Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, South Africa, South Sudan, Sri Lanka, Sudan, Tajikistan, Tanzania, Timor-Leste, Togo, Tonga, Tunisia, Uganda, Uzbekistan, Vanuatu, Vietnam, Zambia, Zimbabwe.

Source: Airfinity, "COVID-19," accessed August 9, 2023.

Note: The four therapeutics are ensitrelvir, molnupiravir, nirmatrelvir, and remdesivir. High-income countries are not included in this map. The World Bank did not include the following countries in their list of income levels therefore they are not included in this figure: Anguilla, Cook Islands, Montserrat, (one therapeutic each), and Venezuela (3 therapeutics).

Table J.17 Number of public health uses of TRIPS Agreement Art. 31 flexibilities since 2001, by execution status in count of Art. 31 flexibilities

In count of Art 31 flexibilities. This table corresponds to [figure 5.3](#).

Execution	Count
Executed	79
Non-executed	28
Pending	14

Source: ML&P, The TRIPS Flexibilities Database, accessed July 12, 2023.

Note: Excludes studies with terminated, suspended, unknown, or withdrawn statuses.

Table J.18 Number of public health uses and attempts to use TRIPS Agreement Art. 31 flexibilities since 2001, by countryIn number of CL uses and attempts. This table corresponds to [figure 5.4](#).

Number of instances Art. 31 used	Country
1	Argentina, Azerbaijan, Belarus, Cameroon, Canada, Dominican Republic, Ethiopia, Georgia, Germany, Ghana, Guatemala, Guinea, Guinea Equatorial, Guyana, Hungary, Israel, Kazakhstan, Liberia, Mongolia, Myanmar, Norway, Pakistan, Papua New Guinea, Romania, São Tomé and Príncipe, Sudan (Government of Sudan), Swaziland, Switzerland, Taiwan (Chinese Taipei), Tajikistan, Zambia
2	Chile, China, Malaysia, Mozambique, Peru, Philippines, Russia, South Africa, Ukraine
3	Colombia, Congo, Cuba, Gabon, Honduras, Italy, Ivory Coast, Korea, United Kingdom
4	Brazil, Kenya, United States of America, Zimbabwe
5	India, Indonesia
8	Thailand
9+	Ecuador

Source: ML&P, The TRIPS Flexibilities Database, accessed July 12, 2023.

Note: While the Medicines Law and Policy database from which this map is derived is thorough in its coverage, it is not an exhaustive list of all CL uses or attempts to use a CL. Due to the differences in national IP laws, the rules regarding TRIPS Agreement reporting requirements, and the role of private actors in potential CL uses through litigation, among other factors, certain actions may be omitted. Additionally, certain included actions might not be characterized as a CL or attempt to use a CL by some parties, including the government in question. Subsequently, the database should be treated as an informative resource and not an authoritative summation of all relevant measures or attempts to implement measures.

Table J.19 COVID-19 average daily testing rates, quarterly by country income class

Tests per 1,000 people, — = not applicable. Q1 = January – March; Q2 = April – June; Q3 = July – September; Q4 = October – December; HIC = high-income countries; UMIC = upper-middle income countries; LMIC = lower-middle income countries; LIC = low-income countries. This table corresponds to [figure 6.1](#).

Year/Quarter	HIC	UMIC	LMIC	LIC
2020/Q1	0.1610	0.3045	0.0079	0.0014
2020/Q2	0.6963	0.4889	0.0644	0.0201
2020/Q3	1.5439	0.6052	0.2778	0.0421
2020/Q4	3.0028	0.9755	0.4441	0.0420
2021/Q1	4.4137	1.0564	0.3573	0.0477
2021/Q2	4.4827	1.2766	0.7679	0.0498
2021/Q3	4.5754	1.4458	0.7884	0.0792
2021/Q4	5.9635	1.3995	0.6125	0.0818
2022/Q1	7.1896	1.4633	0.6405	0.0807
2022/Q2	2.7691	0.5147	0.3647	0.0421
2022/Q3	1.7823	0.8808	0.1982	0.0290
2022/Q4	1.6212	1.4650	0.1022	0.0193
2023/Q1	0.7991	1.7961	0.0775	—
2023/Q2	0.4965	0.0964	0.0893	—

Source: FIND, "COVID-19 Test Tracker." FIND also has data on average daily testing rate per 1000 people broken out by income group for countries. Data stopped being updated in April 2023 COVID-19 Test tracker - FIND (finddx.org).

Note: There was no testing rate data for LICs after 2022/Q4.

Table J.20 Select price ranges for COVID-19 therapeutics by country income groups

Pricing in dollars. HIC = high-income countries; UMIC = upper-middle income countries; LMIC = lower-middle income countries. This table corresponds to [figure 6.2](#).

Therapeutic	Income level	Low price	High price
Bamlanivimab	HIC	1,250.00	1,250.00
Baricitinib	HIC	395.40	2,326.38
Baricitinib	UMIC	506.29	577.69
Baricitinib	LMIC	6.67	626.78
Molnupiravir	HIC	653.00	705.88
Molnupiravir	UMIC	221.00	297.09
Molnupiravir	LMIC	14.40	98.60
Nirmatrelvir (+ ritonavir)	HIC	280	1392.78
Nirmatrelvir (+ ritonavir)	UMIC	280	280
Nirmatrelvir (+ ritonavir)	LMIC	6	190
Remdesivir	HIC	390	533
Remdesivir	UMIC	55	55
Remdesivir	LMIC	65	65
Ronapreve	HIC	1,500	2,435
Ronapreve	LMIC	821	821
Sarilumab	HIC	876	3,827
Sotrovimab	HIC	2,100	2,100
Tocilizumab	HIC	411	5,304
Tocilizumab	UMIC	429	1,197
Tocilizumab	LMIC	777	1,207

Source: Airfinity, "COVID-19," accessed August 9, 2023.

Note: Baricitinib excludes data for a dosage of 2 mg and Tocilizumab excludes dosages of 162 mg subcutaneous and 400 mg infusions. Ronapreve pricing is based on 2 different dosages – LMICs had a dosage of 1200 mg infusion while HICs were 2400 mg infusion doses.

Table J.21 UMICs where COVID-19 therapeutics cannot be offered for sale under voluntary license agreements or procured through multilateral programs according to MPP or Gilead’s access partnerships

This table corresponds to [figure 6.3](#).

Country
Albania
American Samoa
Argentina
Bosnia and Herzegovina
Brazil
Bulgaria
China
Mexico
Turkey

Source: MPP, Nirmatrelvir, "Country List," <https://medicinespatentpool.org/licence-post/pf-07321332>, accessed June 26, 2023; MPP, Molnupiravir, "Country List," <https://medicinespatentpool.org/licence-post/molnupiravir-mol>, accessed June 26, 2023; MPP, Ensitrelvir Fumaric Acid, "Country List," <https://medicinespatentpool.org/licence-post/ensitrelvir>, accessed June 26, 2023; Gilead, Access Partnerships, "2020 Original COVID-19 Voluntary License Agreement," <https://www.gilead.com/-/media/files/pdfs/other/original-covid-19-voluntary-license-agreement.pdf>, accessed June 26, 2023; Source: Airfinity, "COVID-19," accessed August 9, 2023.

Table J.22 Countries where COVID-19 therapeutics were offered through multilateral programs, as of 2022GF = Global Fund. This table corresponds to [figure 6.4](#).

Therapeutic	Country
nirmatrelvir + ritonavir (UNICEF)	Armenia and West Bank and Gaza
molnupiravir (UNICEF)	Seychelles
nirmatrelvir + ritonavir (GF)	Azerbaijan, Belarus, Colombia, Costa Rica, Dominican Republic, Ecuador, Kazakhstan, Lebanon, Malaysia, Montenegro, Nauru, Peru, Republic of North Macedonia, Romania, Russia, Serbia, Thailand, Turkmenistan
nirmatrelvir + ritonavir (UNICEF & GF)	Georgia, Jordan, Kosovo, Kyrgyzstan, Ukraine
molnupiravir (UNICEF) and nirmatrelvir + ritonavir (GF)	Cuba, Dominica, Fiji, Grenada, Guyana, Iraq, Jamaica, Libya, Maldives, Marshall Islands, Mauritius, Paraguay, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Tuvalu
nirmatrelvir + ritonavir and molnupiravir (UNICEF) & nirmatrelvir + ritonavir (GF)	Afghanistan, Algeria, Angola, Bangladesh, Belize, Benin, Bhutan, Bolivia, Botswana, Burkina Faso, Burma, Burundi, Cambodia, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo, Cote d'Ivoire, Democratic Republic of the Congo, Djibouti, Egypt, El Salvador, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Federated States of Micronesia, Gabon, Gambia, Ghana, Guatemala, Guinea, Guinea-Bissau, Haiti, Honduras, India, Indonesia, Iran, Kenya, Kiribati, Laos, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Moldova, Mongolia, Morocco, Mozambique, Namibia, Nepal, Nicaragua, Niger, Nigeria, North Korea, Pakistan, Papua New Guinea, Philippines, Rwanda, Samoa, São Tomé and Príncipe, Senegal, Sierra Leone, Solomon Islands, Somalia, South Africa, South Sudan, Sri Lanka, Sudan, Syria, Tajikistan, Tanzania, Timor-Leste, Togo, Tonga, Tunisia, Uganda, Uzbekistan, Vanuatu, Venezuela, Vietnam, Yemen, Zambia, Zimbabwe

Source: Airfinity.

Table J.23 Per capita annual health care expenditure, by income group, 2021In dollars per person. HIC = high-income countries; UMIC = upper-middle income countries; LMIC = lower-middle income countries; LIC = low-income countries. This table corresponds to [figure 6.5](#).

Income level	Dollars per person
HIC	3,289
UMIC	524
LMIC	137
LIC	39

Source: World Health Organization, per capita health care expenditure, accessed May 31, 2023.

Table J.24 Regulatory approvals by country for relevant COVID-19 therapeutics

In number of approvals. This table corresponds to [figure 6.6](#).

Number of approvals	Countries
1	Argentina, Austria, Belgium, Bolivia, Bulgaria, Cambodia, Chile, Colombia, Croatia, Cyprus, El Salvador, Estonia, Ethiopia, Finland, French Guiana, Greece, Guyana, Iran, Iraq, Ireland, Jordan, Latvia, Liechtenstein, Lithuania, Netherlands, Norway, Oman, Peru, Poland, Portugal, Romania, Slovakia, Slovenia, Solomon Islands, Spain, Turkey, Uruguay, Zambia
2	Bangladesh, Costa Rica, Denmark, Egypt, Guatemala, Hungary, Luxembourg, Morocco, Paraguay, Qatar, Rwanda, Saudi Arabia, South Africa, Sri Lanka
3	Bahrain, China, France, Indonesia, Pakistan, Sweden, Switzerland
4	Czech Republic, Germany, Israel, Kuwait, Malaysia, New Zealand, Panama, Philippines, Singapore, South Korea
5	Hong Kong, Thailand, United Arab Emirates
6	Canada, India, Italy, Mexico, Russia, Taiwan
7	Brazil
8	Australia
9	Japan, United Kingdom
10	None
11	None
12	United States

Source: Airfinity, Regulatory approval by country, August 9, 2023.

Table J.25 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by business size, 2020

In percentages. SME = small and medium-sized enterprise. This table corresponds to [figure 1.1](#).

Business size	Firms	Establishments	Employment	Payroll
SMEs	91.9	77.3	25.5	19.6
Large firms	8.1	22.7	74.5	80.4

Source: U.S. Census Bureau, Statistics of U.S. Businesses data, NAICS 3254, accessed August 24, 2023.

Note: Business size is based on the size of the enterprise. SMEs have less than 500 employees while large firms have 500 or more employees.

Table J.26 U.S. pharmaceutical industry: Firms, establishments, employment, and payroll, by industry classification, 2020

In percentages. This table corresponds to [figure 1.2](#).

Industry classification	Firms	Establishments	Employment	Payroll
325411: Medicinal and botanical	29.1	25.8	11.6	8.2
325412: Pharmaceutical preparation	50.3	51.5	54.9	55.7
325413: In-vitro diagnostic substance	8.4	9.2	11.5	11.8
325414: Biological product (except diagnostic)	12.2	13.5	22.0	24.2

Source: U.S. Census Bureau, Statistics of U.S. Businesses data, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Table J.27 U.S. pharmaceutical employment, by business size and industry classification, 2020

In percentages. SME = small and medium-sized enterprise. This table corresponds to [figure 1.3](#).

Industry classification	SMEs	Large firms
325411: Medicinal and botanical	55.9	44.1
325412: Pharmaceutical preparation	25.1	74.9
325413: In-vitro diagnostic substance	20.1	79.9
325414: Biological product (except diagnostic)	13.2	86.8

Source: U.S. Census Bureau, Statistics of U.S. Businesses data, NAICS 3254, accessed August 24, 2023.

Note: Business size is based on the size of the enterprise. SMEs have less than 500 employees while large firms have 500 or more employees.

Table J.28 U.S. pharmaceutical employment by industry classification, 2018–22In thousands of employees. This table corresponds to [figure I.4](#).

Industry classification	2018	2019	2020	2021	2022
325411: Medicinal and botanical	30	32	35	38	41
325412: Pharmaceutical preparation	202	210	213	219	227
325413: In-vitro diagnostic substance	27	28	29	34	32
325414: Biological product (except diagnostic)	36	36	38	40	44
Total	294	306	314	332	344

Source: Bureau of Labor Statistics (BLS), Quarterly Census of Employment and Wages, annual averages, NAICS 325411, 325412, 325413, 325414, accessed August 24, 2023.

Table J.29 U.S. pharmaceutical shipments, 2018–22, January–June 2022, and January–June 2023In billions of dollars. This table corresponds to [figure I.5](#).

Metric	2018	2019	2020	2021	2022	Jan–Jun 2022	Jan–Jun 2023
U.S. shipments (billions)	209.3	221.2	228.4	248.4	276.7	132.8	144.8

Source: U.S. Census Bureau, “Manufacturers’ Shipments, Inventories, and Orders,” Series U25BVS (NAICS 3254), accessed August 24, 2023.

Table J.30 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023Index, January 2018 = 100. — = not applicable. This table corresponds to [figure I.6](#).

Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2018	100.0	103.3	103.3	103.3	103.3	103.3	103.3	103.3	103.4	103.4	103.4	103.3
2019	103.0	103.0	103.0	103.0	103.0	103.0	103.0	103.4	103.4	102.8	102.8	102.8
2020	104.2	104.2	104.5	101.7	101.7	101.7	101.7	103.1	103.1	103.1	102.9	103.0
2021	102.6	102.7	102.9	102.8	102.9	102.8	102.9	102.9	102.9	103.0	102.9	103.1
2022	105.0	105.0	105.0	105.0	103.7	104.2	104.2	104.3	104.7	104.6	105.1	104.9
2023	105.2	104.9	105.3	105.4	105.4	105.3	105.3	—	—	—	—	—

Source: Bureau of Labor Statistics (BLS), Produce Price Indexes, NAICS 325411, accessed August 24, 2023.

Note: Data for April–July 2023 are preliminary.

Table J.31 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023Index, January 2018 = 100. — = not applicable. This table corresponds to [figure I.6](#).

Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2018	100.0	99.9	100.0	99.7	99.8	100.2	100.9	100.5	100.7	100.9	101.1	101.7
2019	103.3	103.5	103.5	103.6	103.5	103.4	103.8	103.8	103.8	103.4	103.4	103.7
2020	105.3	105.7	105.4	105.4	105.3	105.2	105.3	105.2	104.7	104.8	104.8	104.7
2021	106.3	106.4	106.6	106.5	106.6	106.7	106.3	106.3	106.4	106.5	106.5	106.5
2022	107.8	108.2	108.4	108.6	108.7	110.3	110.6	110.9	111.0	111.3	111.4	111.0
2023	113.4	114.1	114.1	114.2	114.1	114.1	114.4	—	—	—	—	—

Source: Bureau of Labor Statistics (BLS), Produce Price Indexes, NAICS 325412, accessed August 24, 2023.

Note: Data for April–July 2023 are preliminary.

Table J.32 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023

Index, January 2018 = 100. — = not applicable. This table corresponds to [figure I.6](#).

Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2018	100.0	100.5	100.6	100.7	101.5	100.0	100.4	100.6	100.5	100.0	100.3	99.9
2019	101.3	100.9	102.2	100.9	100.6	100.7	100.8	101.4	101.3	101.1	100.9	100.7
2020	99.9	100.8	100.8	100.4	101.5	100.4	101.5	101.5	101.3	101.3	101.3	101.4
2021	102.0	101.9	101.9	101.8	101.9	102.0	102.2	102.1	101.8	101.9	101.9	109.6
2022	110.9	110.9	110.9	110.9	111.4	111.4	111.4	111.7	111.0	111.1	111.1	110.8
2023	112.0	113.0	113.6	113.8	112.2	112.3	112.5	—	—	—	—	—

Source: Bureau of Labor Statistics (BLS), Produce Price Indexes, NAICS 325413, accessed August 24, 2023.

Note: Data for April–July 2023 are preliminary.

Table J.33 U.S. producer price index for pharmaceuticals, by industry classification, January 2018–July 2023

Index, January 2018 = 100. — = not applicable. This table corresponds to [figure I.6](#).

Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2018	100.0	100.4	100.6	100.7	100.7	101.3	101.6	101.6	101.6	101.6	101.6	101.9
2019	105.3	106.3	105.8	106.5	106.3	106.8	106.9	107.4	107.4	107.4	107.4	107.5
2020	109.5	109.5	109.5	109.5	109.5	109.5	110.0	110.0	110.0	110.3	110.3	110.3
2021	115.7	115.7	115.7	115.8	115.8	115.7	115.8	115.8	116.0	116.0	116.0	116.0
2022	118.4	118.4	118.4	118.8	118.8	118.8	118.8	121.6	121.7	122.0	121.8	118.8
2023	123.8	124.2	124.2	125.8	126.2	125.5	126.5	—	—	—	—	—

Source: Bureau of Labor Statistics (BLS), Produce Price Indexes, NAICS 325414, accessed August 24, 2023.

Note: Data for April–July 2023 are preliminary.

