ADDRESSING DRUG SHORTAGES: EMERGENT CHALLENGES, STRUCTURAL FACTORS, AND POTENTIAL POLICY REFORMS

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U.S. House of Representatives Committee on Energy and Commerce, Subcommittee on Health
Legislative Proposals to Prevent and Respond to Generic Drug Shortages

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ONE PAGE SUMMARY OF REMARKS

1. Measures in the proposed *Stop Drug Shortages Act* to raise prices on certain classes of medicines by exempting them from rebates are inefficient and poorly targeted policy instruments to address shortages.
   1.1 Analysis of the drivers of shortages, and therefore potential solutions, is severely limited by gaps in the data.
   1.2. The root causes and proximate determinants of shortages are complex and heterogeneous.
   1.3. Not all shortages are equal in terms of public health importance.
   1.4. Generic sterile injectables comprise the majority of generic drugs that are in shortage. Price decreases for generic sterile injectables have not been found to be predictive of shortages.
   1.5. Raising the price of medicines in shortage, medicines with supply chain issues, and sterile injectable medicines is not likely to incentivize manufacturers to invest in improving quality and building resilience into their supply chains.
   1.6. Exempting medicines in shortage from inflation rebates creates perverse incentives for investments in quality and supply stability.
   1.7. Wording in the proposed legislation is ambiguous and should be more carefully defined.
   1.8. The "more than one supplier" condition for exemptions from inflation rebates or 340b coverage may not be correctly targeted.
   1.9. There is significant public interest in creating a healthy market for generics, which includes offering manufacturers a fair price. However, it is important to keep in mind that these price-inflation rebates were put in place due to a trend of sharp year-on-year increases in the prices of a significant number generic drugs in the United States.
2. Congress should consider other more targeted policy instruments to address the root causes of shortages.
   2.1. Federal agencies such as CMS and the FDA should have more transparent oversight of the supply chain.
   2.2. Case-by-case review of exemptions from inflationary rebates (e.g. as the result of unavoidable supply chain challenges from natural disasters) is a more targeted and appropriate approach than exempting wider classes of drugs from these rebates.
   2.3. CMS and FDA could consider lowering the burden of generic drug user fees under the Generic Drug User Fee Act (GDUFA) to incentivize new generic manufacturers to enter the market.
   2.4. CMS could consider writing contracts with a "failure to supply" penalty clause.
   2.5 DHHS should establish a single point of responsibility for drug shortages to work across federal agencies more effectively.
   2.6. Congress should target pricing interventions to incentivize manufacturers to strengthen the resilience of their supply chains.
3. The proposed legislation includes many important first steps in improving the transparency of API markets. These measures should be further strengthened.
   3.1. There is no systematically collected data on API manufacturing and markets.
   3.2. Many generic medicines are at risk of shortage because API is manufactured in just one facility.
   3.3. Existing powers in CARES should be expanded to further improve API transparency.
4. Sec. 506. New domestic facility inspection pilot program
   4.1. The faster review timeline created by this provision would create a significant incentive for manufacturers, which should be coupled with requirements ensuring supply chain resilience
   4.2. New requirements on the FDA for faster review will likely require additional funding.
   4.3. It is important to note that on-shoring of pharmaceutical manufacturing is important as a question of industrial policy, but in terms of health policy, domestic manufacture is not necessarily associated with higher quality.
5. Sec. 502. Incentive for shelf-life extension studies
   5.1. The proposed 1-month extension would apply only to new products, which are unlikely to make up a significant proportion of the drugs commonly affected by shortages.
   5.2. The proposed granting of an additional 1 month of exclusivity for the conduct of shelf-life extension studies would add significant costs for CMS and likely overcompensate, at least by a factor of 60, the costs incurred by manufacturers in conducting relevant studies.
   5.3 There is a clear need for shelf-life extension studies to be mandated for all new drug approvals, and for a mechanism to ensure that shelf-life extension studies are undertaken for key generic medicines.
6. Leveraging and strengthening research and industrial capacity in the United States
   6.1. Grant-making and organizations with significant research capacity like the National Institutes of Health (NIH) and Biomedical Advanced Research and Development Authority (BARDA) should invest in process manufacturing research.
   6.2. Public manufacturing should be considered for drugs in shortage.

The work of this Committee and the proposed legislation respond to an important and long-standing threat to the supply of essential drugs in the United States. We commend the work of members of the Health Subcommittee in putting forward concrete proposals to address the issue through targeted legislation.

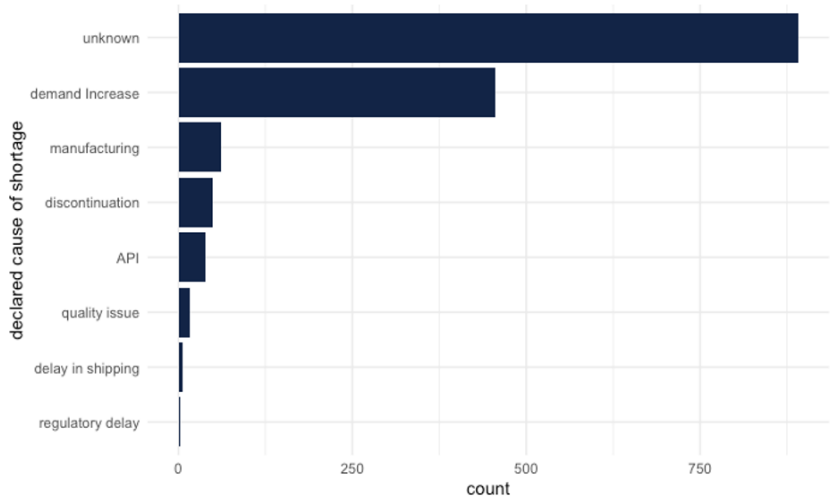
In this written testimony, I will outline recommendations for changes or additions to the proposed legislation. The objective of these recommendations is to design targeted legislative interventions for avoiding and mitigating shortages, while limiting unnecessary increases in drug expenditures to the Centers for Medicare and Medicaid Services (CMS) and other unintended negative effects on the US generic drugs market.

1. Measures in the proposed *Stop Drug Shortages Act* to raise prices on certain classes of medicines by exempting them from rebates are inefficient and poorly targeted policy instruments to address shortages.

1.1 Analysis of the drivers of shortages, and therefore potential solutions, is severely limited by gaps in the data.

It is important to contextualize the available literature on shortages within data limitations. Manufacturers report shortages to the FDA, but there are no standardized shortage reporting codes, nor are manufacturers obligated to give detailed information on the cause of the shortage. More than half (59%) of current (June 2023) shortages did not have a declared cause (Fig 1).

Fig 1. Current shortages reported to the FDA by declared cause[1]



Both academics and agencies such as the Government Accountability Office (GAO) have studied the causes of shortages, but analyses are limited by incomplete data. Of shortages with reported causes, the majority (72%) were due to increased demand, followed by manufacturing delays or issues (10%), discontinuation (8%), issues with the active pharmaceutical ingredient (API) (6%), quality issues (3%), shipping delays, (<1%), and regulatory delays (<1%).

Thus, while this testimony outlines some key findings within the literature on causes of shortages, it does so from a position of some uncertainty - academics and policymakers alike do not have the data. In order to improve analysis of these important issues, Congress should consider compelling more detailed disclosure by manufacturers, as well as adequately resourcing and empowering the FDA to analyze and act on this data.

[1] Center for Drug Evaluation and Research. (n.d.). Current Drug Shortages. U.S. Food and Drug Administration. Shortages data retrieved July 3, 2023, from https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages. There are no standardized codes for shortages; data were manually recoded using any information provided in the record. Shortages were filtered to include unique company, generic name, and presentation (formulation) combinations.

1.2. The root causes and proximate determinants of shortages are complex and heterogeneous.

Shortages for some medicines - in particular, for generic sterile injectables- have been attributed by some to prices that are too low. Price is always a factor in questions of supply, and an FDA analysis on the "root cause of shortages" estimated that half of the 163 drugs that went into shortage from 2013-2017 "may have had inadequate financial incentives to market the product or invest in ensuring manufacturing capability and capacity prior to the shortage."[2] However, studies of shortages of generic sterile injectables suggest that manufacturing issues rather than price declines, are more predictive of shortages. Sec. 101, 201, and 301 of the proposed *Stop Drug Shortages Act*, which would increase the prices paid for these drugs by exempting them from inflationary rebates, will likely result in considerable increased expenditures including for CMS without changing incentives for manufacturers to invest in areas that are key to preventing shortages: robust manufacturing processes, quality assurance and control, and a resilient upstream supply chain.

1.3. Not all shortages are equal in terms of public health importance.

The definition of a shortage is complicated. Generally, it is used to refer to a situation where supply does not meet demand for a given formulation. However, not all shortages meeting this definition affect individual health, population health, or medical care provision, as in many cases therapeutic substitutes exist. Drugs also vary in terms of public health

[2] USFDA. Drug Shortages: Root Causes and Potential Solutions. Retrieved September 12, 2023, from https://www.fda.gov/media/131130/download?attachment

importance: policymakers should consider the relative importance of drugs and prioritize efforts on those most critical to public health.

A list of priority drugs has been formulated by FDA in response to an August 2020 Executive Order 13944.[3] The drugs identified by the FDA are those "that are most needed for patients in U.S. acute care medical facilities," as well as FDA-regulated products that meet the definition of a "medical countermeasure" and may be needed to respond to "future pandemics epidemics, and chemical, and biological, and radiological/nuclear threats."[4]

1.4. Generic sterile injectables comprise the majority of generic drugs that are in shortage. Price decreases for generic sterile injectables have not been found to be predictive of shortages.

Of particular concern are generic sterile injectables, which comprise the majority of generic drugs (and thus, of all drugs) that are in shortage.[5] Of 138 generic medicines currently recorded as being in shortage by the FDA, 68% are injectables, 16% are tablets or capsules, and 16% are other formulations (e.g. oral, topical, suppositories).[6] Generic sterile injectable products play a critical role in the treatment of patients across healthcare facilities, including in outpatient clinics, emergency departments, hospital inpatients, intensive care units, and operating rooms. Commonly used generic sterile injectable products such as saline, diluting

[3] U.S. Food and Drug Administration. (2020). *Criteria For Identifying Human Drug and Biologic Essential Medicines, Medical Countermeasures, and Critical Inputs for the List Described in Section 3(c) of the Executive Order (EO) 13944.* [online] Available at: https://www.fda.gov/media/143407/download?attachment.
[4] U.S. Food and Drug Administration. (2020). *Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs.* [online] Available at: https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs
[5] Center for Drug Evaluation and Research. (n.d.). Current Drug Shortages. U.S. Food and Drug Administration. Retrieved July 6, 2023, from https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages
[6] Shortages data downloaded from https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages on 3 July 2023. There are no standardized codes for formulation type; I recoded the data manually using any information provided in the record. Shortages were filtered to include generic name.

agents, morphine, as well as lifesaving or life-prolonging cancer treatments are currently in shortage, significantly compromising patient care. For example, shortages of norepinephrine, a first-line vasopressor injectable for septic shock, were associated with greater hospital mortality.[7]

Perhaps the most comprehensive report on shortages of sterile injectable drugs is a 2016 report by the Government Accountability Office (GAO), which used a range of data sources including drug shortage data from the University of Utah Drug Information Service, drug sales data from a commercial database (IMS Health), FDA data including warning letters from inspections and data on prioritized reviews, and qualitative data from interviews with officials at FDA.[8] One focus of the report was analyzing factors associated with shortages of sterile injectable drugs. In the period of study (2007-2013), GAO found that the number of warning letters issued annually by the FDA to manufacturers of sterile injectable drugs increased from 1% in 2007 to 5% in 2010 and 2011.[9] GAO found that seven sterile injectable drug manufacturing establishments receiving warning letters from fiscal year 2010 - 2012 reduced or stopped production.[10] Warning letters for six of the seven facilities receiving them were for issues that were of considerable concern to patients, for example "glass shards or metal shavings in vials of injectable drugs," and for the seventh endotoxin, a bacteria that can cause fever and death. [11]

[7] Vail, E., Gershengorn, H. B., Hua, M., Walkey, A. J., Rubenfeld, G., & Wunsch, H. (2017). Association between US norepinephrine shortage and mortality among patients with septic shock. JAMA, 317(14), 1433. https://doi.org/10.1001/jama.2017.2841

[8] Government Accountability Office. (2016). *DRUG SHORTAGES | Certain Factors Are Strongly Associated with This Persistent Public Health Challenge*. [online] Available at: https://www.gao.gov/assets/gao-16-595.pdf.

[9] ibid

[10] ibid

[11] ibid

According to the FDA, this reduction in supply led to widespread shortage of sterile injectable drugs.[12] The shutdown of just one facility "led to the actual or potential shortage of more than 100 drugs."[13] Four of these facilities had receive warning letters for the same manufacturing violation, suggesting systemic issues in maintaining good quality manufacturing.[14]

GAO concluded that the two most predictive factors of shortages were a) a decline in the number of suppliers and b) the failure of at least one establishment making a drug to comply with manufacturing standards resulting in a warning letter. Sales of a generic version were also predictive, but **price decline was not found to be strongly associated with shortages of drugs in this study (See Table 1).**

Table 1: Estimated Percentage Point Increase in Probability of a Drug Shortage in the Presence of Certain Factors, for Sterile Injectable Anti-infective and Cardiovascular Drugs, 2012-2014[15]

[12] ibid
[13] ibid
[14] ibid
[15] ibid

The estimated mean probability of a shortage predicted for all drugs in our study by the model is 60.7 percent.

Factors	Estimated percentage point increase in the probability of a shortage[a]
Decrease in suppliers, previous 2 years	16.8**
Sales of a generic version, previous year	12.3**
Failure to comply with manufacturing standards resulting in a warning letter, previous 2 years	8.1**
Price decline, previous 2 years	0.7

Source: GAO analysis of data from IMS Health, the Food and Drug Administration, and the University of Utah Drug Information Service | GAO-16-595.

Notes: Our multivariate logistic regression model uses a 3-year panel data file that contains shortage measures for 118 sterile injectable anti-infective and cardiovascular drugs from 2012 through 2014 and measures of market structure (whether there was a decrease in suppliers), compliance with FDA manufacturing standards (whether there was a failure to comply with manufacturing standards resulting in a warning letter for at least one establishment that manufactured the drug), drug characteristics (whether sales of a generic version), and price and volume of sales (whether the price declined) from 2010 through 2013.

[a]The estimated percentage point increase in the probability of a shortage is calculated as the difference between (1) the probability of a shortage if the factor is present for all drugs and the other three factors remain unchanged and (2) the mean probability of a shortage predicted for all drugs in our study by the model (60.7 percent). To compute the predicted probability of a shortage when the characteristic is present, we set the value of the variable to one, left the values of the other explanatory variables unchanged, and then calculated the probability using the coefficients estimated from our 3-year repeated measures logistic regression model. To compute the mean probability of a shortage predicted for all drugs in our study by the model, we first computed the predicted probability of a shortage for every drug and every year in our study by using the estimated coefficients from the model and the data for each drug. We then computed the mean of the 354 predicted values (118 drugs and 3 years), which was 0.607, or 60.7 percent.

** indicates that the estimated probability is based on a coefficient estimate that was significant at a level of 0.01 or better, based on our logistic regression model results.

1.5. Raising the price of medicines in shortage, medicines with supply chain issues, and sterile injectable medicines is not likely to incentivize manufacturers to invest in improving quality and building resilience into their supply chains.

Since 1990, manufacturers are required to provide statutory rebates to Medicaid state programs for outpatient drugs reimbursed by Medicaid. For branded drugs, Medicaid rebates are calculated as the sum of a base rebate, which is the greater of 23.1% average manufacturer price or the best discount provided to any entity, and an inflationary component, which penalizes post-launch increases in prices above inflation. For generic drugs, Medicaid rebates are calculated as the sum of a base rebate of 13% of average manufacturer price and a similarly calculated inflation rebate. After the passage of the Inflation Reduction Act (IRA), manufacturers are also required to pay inflation penalties for drugs reimbursed by Medicare Part B and D. Part D rebate provisions begin in 2022, with

the starting point for measuring drug price increases starting in 2022. Part B rebate provision takes effect in 2023. Mandatory inflation rebates are also triggered for single source generics or generic drugs with only one manufacturer when the average Medicare price per patient is more than $100. To prevent drug shortages, the IRA allows CMS to reduce or waive inflation rebates for Medicare Part B biosimilars and single source Part D generics that experience supply chain disruptions, for both current and future shortages.[16]

Research undertaken by the FDA analyzing shortages found that supply disruptions for drugs in shortage persist even after some price increases.[17] This suggests that it is unlikely that exempting inflation rebates would play a major role in averting generic drug shortages. Furthermore, inflation rebates are only triggered by increases in drug prices above inflation: it is unlikely that generic products that go into shortage due to decreased profit margins are subject to inflation rebates, as they would not have taken increases in prices above inflation (most likely, they would have seen decreases in prices since launch).

Increasing the prices of medicines through inflation rebate exceptions may incentivize new manufacturers to enter the market (though we expect this effect to be low or negligible, as price competition with a 'race to the bottom' will remain, as argued above). Nevertheless, this measure is poorly targeted because manufacturers would not be incentivized to invest in improving quality and building resilience into their supply chains – on the contrary, they will continue to be incentivized to *reduce* investments in these areas in order to cut costs and increase their margins. For this reason, increased prices through rebate exception are not a

[16] Wosińska, M. (2023). *Drug shortages and IRA inflation rebates: Considerations for CMS*. [online] Brookings. Available at: https://www.brookings.edu/articles/drug-shortages-and-rebates/.
[17] USFDA. Drug Shortages: Root Causes and Potential Solutions. Retrieved September 12, 2023, from https://www.fda.gov/media/131130/download?attachment

well-targeted instrument for achieving the intended aim of improved supply chain robustness.

We recommend, instead, that any new financial incentives reward manufacturers for taking proactive steps to prevent manufacturing disruptions, such as employing good risk management practices, investing in back-up manufacturing capabilities, and ensuring robust supply chains for key manufacturing inputs. In addition to this incentive, we recommend the creation of penalties for failure to take appropriate steps to modernize their equipment and facilities to ensure a robust and reliable supply. At present, there are no such penalties

1.6. Exempting medicines in shortage from inflation rebates creates perverse incentives for investments in quality and supply stability.

The purpose of shortage notifications should be to a) provide regulators advanced warning to triage supply – for example, by prioritizing applications for new entrants for a given medicine, and b) to provide medical professionals time to develop guidelines for potential substitution policies, and to be sure that these are clearly communicated to patients.

There are many problems associated with tying drug prices to shortage notifications, the most important being that it creates perverse incentives for companies that have not made investments to improve manufacturing quality to nevertheless benefit from price increases that outpace inflation. But the problem is also procedural and pragmatic: advanced warning of a shortage is a probabilistic endeavor, not a strict binary. To avert a shortage, at least 6-18 months' notice is necessary to scale up quality-assured production at new facilities; there is a wide range in the length of needed notice as the complexity of pharmaceutical

manufacturing varies across product types. As an example, consider a manufacturer of a sterile injectable product: The manufacturer marketing the drug in the United States is a fill-and-finish facility, and relies on an active pharmaceutical ingredient (API) manufactured by a different company in a different facility. The sterile injectable manufacturer receives notice from the API manufacturer that in one year, the factory is closing down the production line for the given API. This is exactly the situation in which policymakers should hope that manufacturers would report a potential shortage, so relevant stakeholders can organize and ideally locate new API sources to avert the shortage altogether.

Risk mapping generates useful signals for when shortages are likely, but by the time a shortage is certain, notification is of little use in averting the shortage.[14] In practice, the best-prepared manufacturers test resilience by running regular risk simulations to understand the effects on production should any of their supply nodes be compromised. Such 'stress tests' are essential in prioritizing where redundancy might be best deployed. 'Stress tests' are standard practice in many industries, including banking, for which stress tests are conducted annually by the Federal Reserve Board.[18] FDA should require manufacturers of priority drugs to conduct and publicly report the results of similar 'stress tests' to demonstrate that their supply chains are resilient to increases in demand or disruptions in supply of materials.

The challenges I have highlighted above illustrate the practical challenges of the proposed exemptions from inflation rebates. **I strongly urge legislators to remove these provisions, and instead target resources to policy instruments more likely to address both proximate and distal causes of shortages. Should these provisions remain,**

[18] Board of Governors of the Federal Reserve System. (n.d.). *Federal Reserve Board - Stress Tests and Capital Planning.* [online] Available at: https://www.federalreserve.gov/supervisionreg/stress-tests-capital-planning.htm.

legislators should consider more carefully articulating how shortages are defined for the purpose of the proposed exemptions from inflationary rebates. For example, do exemptions apply for drugs already in shortage? If so, the incentive is too late. Do exemptions apply for drugs with challenges in the supply chain that will likely to lead to shortages? How are 'supply chain issues' defined, how likely does the shortage need to be given the severity of the supply chain issue, to what degree should manufacturers be held to account if supply chain issues are due to issues within their control and the result of underinvestment, and who provides adjudication and oversight in reviewing these applications?

Additionally, in constructing policy interventions to address shortages, Congress should consider the experience of countries where similar provisions are in place. Recent experiences in Europe show that shortages can be created artificially to obtain leverage in negotiating for higher prices, resulting in harm to patients.[19]

1.7. Wording in the proposed legislation is ambiguous and should be more carefully defined.

Section 301(c) in the proposed Bill would prohibit the Department of Health and Human Services (DHHS) from setting a limit on how many days a shortage must last before the drug in question is eligible for an inflation rebate waiver. In the extreme example, this would allow a shortage lasting only 1 day to trigger the waiver of a rebate. In that example, despite a

[19] For example, see the findings by the Italian Competition Authority in its 29 September 2016 decision on the case concerning the drug manufacturer Aspen. Van Bael & Bellis. Italian Competition Authority fines Aspen € 5 million for excessive pricing. 30/09/2016. Available from: https://www.vbb.com/insights/competition/abuse-of-dominance/italian-competition-authority-fines-aspen-5-million-for-excessive-pricing.
See also Bea Perks. Drug shortages and ensuring the quality of medicine. 2013. Available from: https://ppme.i2ct.eu/ejop_article/drug-shortages-and-ensuring-the-quality-of-medicine

shortage lasting for 1 day, the rebate waiver would be in force over nearly 5 quarters (1 year and 3 months), tapering over this duration (Section 301(a) of the proposed Bill).

It is not obvious why a prohibition on DHHS setting a (lower) limit of shortage duration to trigger the rebate exceptions is necessary.

Enactment of this prohibition would open the rebate exception mechanism to abuse by unscrupulous actors, where companies could notify the FDA of a shortage limited to a few days, and resume regular supply without losing significant revenue but while benefiting from rebate exemptions. A lower limit on the shortage duration required to trigger the rebate exemption would help limit the potential for such abuse.

1.8. The "more than one supplier" condition for exemptions from inflation rebates or 340b coverage may not be correctly targeted.

In some cases, multiple suppliers of an interchangeable finished drug will use the same supplier for the API. This means that drugs that appear to have a robust multi-source supply chain may in fact be reliant, upstream, on one or a few API manufacturers and may thus be less resilient than is apparent.

A recent study found that approximately one-third of generic APIs produced for use in the United States market between 2020 and 2021 were manufactured by a single facility; an additional third was manufactured by two or three facilities.[20] The same study found that "23.0 percent of markets had upstream vulnerabilities to the supply chain because a robust

[20] Socal, M. P., Ahn, K., Greene, J. A., & Anderson, G. F. (2023). Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs*, 42(3), 407–415. https://doi.org/10.1377/hlthaff.2022.01120

level of competition among finished drug manufacturers obscured a fundamentally uncompetitive market of three or fewer API producers."[21]

1.9. There is significant public interest in creating a healthy market for generics, which includes offering manufacturers a fair price. However, it is important to keep in mind that these price-inflation rebates were put in place due to a trend of sharp year-on-year increases in the prices of a significant number generic drugs in the United States.

Ensuring fair prices on medicines, such that margins are high enough to incentivize good quality and robust supply chains, but not so high as to waste limited public resources, is an important priority of policymakers.

There is very little transparency on drug prices in general and across different purchasers, manufacturer profit margins by product, manufacturing costs, and the effect of COVID-19 and related supply chain turbulence on supply chain costs.

Greater transparency in this area would greatly help federal agencies and researchers better analyze the relationship of profit margins to shortages, including identification of price levels that are both affordable and support a healthy supply of medicines. The proposed *Stop Drug Shortages Act* should therefore include provisions that increase the transparency of drug manufacturers' internal costs, including costs of manufacture (known as cost of goods sold, COGS) and profit margins.

[21] ibid

Sec. 202 requests that the Comptroller General of the United States submit to Congress "a report on the role of … Federal laws and programs that artificially keep the costs of generic drugs low." We welcome research into this important topic. However, as policymakers consider mechanisms that would raise prices of some medicines, **we emphasize the importance of carefully targeting these measures, and the context of relatively common extraordinary price increases that cost-containment measures were designed to address.** A 2016 report by the GAO found that from the first quarter of 2010 through the second quarter of 2015, "more than 300 of the 1,441 established generic drugs analyzed had at least one extraordinary price increase of 100 percent or more", and furthermore, that "extraordinary price increases generally persisted for at least 1 year and most had no downward movement after the extraordinary price increase."[22]

2. Congress should consider other more targeted policy instruments to address the root causes of shortages.

2.1. Federal agencies such as CMS and the FDA should have more transparent oversight of the supply chain.

Currently, the FDA does not receive adequate data on supply chain issues, relying on voluntary compliance from manufacturers, as they do not have mandatory reporting requirements to provide detailed information.[23] The FDA gathers some information from

[22] Government Accountability Office. (2016). *Generic Drugs Under Medicare: Part D Generic Drug Prices Declined Overall, but Some Had Extraordinary Price Increases.* [online] Available at: https://www.gao.gov/products/gao-16-706.
[23] Gupta, R., Dhruva, S.S., Fox, E.R. and Ross, J.S. (2017). The FDA Unapproved Drugs Initiative: An Observational Study of the Consequences for Drug Prices and Shortages in the United States. *Journal of Managed Care & Specialty Pharmacy*, 23(10), pp.1066–1076. doi:https://doi.org/10.18553/jmcp.2017.23.10.1066.

manufacturers on anticipated disruptions, but this data is limited and do not adequately assess supply chain vulnerabilities.[24]

2.1.1. Sec. 501. Noncompliance letters relating to volume reporting

There is a wide range of options available in generating necessary data to adequately monitor and regulate against shortages. At the lowest end of added administrative burden, the FDA should simply request that manufacturers give longer notice for discontinuation of products for commercial reasons (i.e. 18 months as enforced in other jurisdictions) and report annual manufacturing volumes as they have requested as part of their budget request for Fiscal Year 2024.[25] Such requirements would demand data already collected by firms and pose little to no threat in terms of commercial secrecy or advantage. A more intensive and likely more effective approach would be for firms to report data on production capacity, and for the FDA and actors like CMS to evaluate this data to identify and predict mismatches between supply and demand and proactively notify relevant departments to encourage firm entry, supply expansion, and shortage aversion. GAO should look at state of oversight after such provisions were passed as part of the legislation to evaluate their effectiveness.

[24] Office of the Assistant Secretary for Planning and Evaluation (ASPE). (2023). *Impact of Drug Shortages on Consumer Costs.*
[25] U.S. Food and Drug Administration. (2023). *Coronavirus Aid, Relief, and Economic Security Act (CARES Act) Drug Shortage Mitigation Efforts.* [online] Available at: https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts

2.2. Case-by-case review of exemptions from inflationary rebates (e.g. as the result of unavoidable supply chain challenges from natural disasters) is a more targeted and appropriate approach than exempting wider classes of drugs from these rebates.

CMS should handle reimbursement on a case-by-case basis, as CMS currently has statutory authority to increase or decrease rebates.[26] Assessing rebate reductions on a case-by-case basis would be necessary and would also compel sponsors to provide manufacturer supply chain data as there is an economic incentive to provide proprietary data. Greater reductions could occur when there is a clear supply chain shock that is external to company control, such as hurricanes and other catastrophic weather events. This would still require data to determine which manufacturers are experiencing supply chain issues.

2.3. CMS and FDA could consider lowering the burden of generic drug user fees under the Generic Drug User Fee Act (GDUFA) to incentivize new generic manufacturers to enter the market.[27]

New legislation should include a GDUFA waiver process that lowers fees for manufacturers with an approved ANDA, particularly for those drugs that FDA has designated as "essential" in return for firms routinely submitting comprehensive data and notifications on their drug(s). FDA in their legislative proposals as part of their Fiscal Year 2024 budget request has outlined several of these data elements that could be required from manufacturers including on manufacturing volume, original manufacturers of active

[26] Wosińska, M. (2023). *Drug shortages and IRA inflation rebates: Considerations for CMS*. [online] Brookings. Available at: https://www.brookings.edu/articles/drug-shortages-and-rebates/.
[27] Dong, K., Boehm, G. and Zheng, Q. (2017). Economic Impacts of the Generic Drug User Fee Act Fee Structure. *Value in Health*, 20(6), pp.792–798. doi:https://doi.org/10.1016/j.jval.2016.05.003.

pharmaceutical ingredients, and other supply chain information.[28] User fees, many of which are annual, would be lowered only if manufacturers remain consistent and standardized in their survey reporting. The benefits of this model would be direct and flow to manufacturers.[29] Conditioning the reduction in fees on providing reliable information would also prevent potential gaming by manufacturers as the additional requirements on fees would prevent companies from engaging in short-term gains from quick market entry and exit. To address the potential shortfall from having a reduction in total user fees as a result of such conditioned waivers, this legislation should also appropriate supplemental Congressional funding specific to the activities that the FDA leverages fees for.

2.4. CMS could consider writing contracts with a "failure to supply" penalty clause.

These contracts could impose financial penalties on manufacturers that fail to provide essential medicines. However, this could have certain drawbacks and would have to be paired with other legislation that ensures the availability of alternative supply chains, as generic manufacturers could be pressured to exit the market if facing overwhelming cost pressures or insurmountable quality issues. Additionally, penalties could lead to hoarding from buyers and suppliers and subsequently, price stimulation due to artificially constrained supply.

2.5 DHHS should establish a single point of responsibility for drug shortages to work across federal agencies more effectively.

[28] U.S. Food and Drug Administration. (n.d.). *Summary of FY 2024 Legislative Proposals*. [online] Available at: https://www.fda.gov/media/166049/download

[29] Mattingly, T.J. and Conti, R.M. (2022). Ensuring a high-quality and resilient supply chain of essential medications means paying more. *Journal of Managed Care & Specialty Pharmacy*, 28(5), pp.573–576. doi:https://doi.org/10.18553/jmcp.2022.28.5.573.

Previously, then FDA Commissioner Scott Gottlieb established the Agency Drug Shortages Task Force, which included representatives from FDA, CMS, the Office of the Assistant Secretary for Preparedness and Response, Department of Veterans Affairs and Department of Defense. It is unclear whether this Task Force has continued their work. Considering the recent rise in drug shortages and the need for a coordinated response across multiple agencies, DHHS should re-establish such a group.

The Task Force should focus on the list of priority drugs that has been formulated by FDA in response to an August 2020 Executive Order 13944.[30] The drugs identified by the FDA are those "that are most needed for patients in U.S. acute care medical facilities," as well as FDA-regulated products that meet the definition of a "medical countermeasure" and may be needed to respond to "future pandemics epidemics, and chemical, and biological, and radiological/nuclear threats."[31]

2.6. Congress should target pricing interventions to incentivize manufacturers to strengthen the resilience of their supply chains.

With the appropriate data, FDA and CMS could rate generic manufacturers by the resilience of their supply chain. This rating could then be incorporated by payers to adjust reimbursement for generic drugs appropriately, in a similar way as value-based modifiers adjust payments to providers based on the quality of medical services provided.

[30] U.S. Food and Drug Administration. (2020). *Criteria For Identifying Human Drug and Biologic Essential Medicines, Medical Countermeasures, and Critical Inputs for the List Described in Section 3(c) of the Executive Order (EO) 13944.* [online] Available at: https://www.fda.gov/media/143407/download?attachment.
[31] U.S. Food and Drug Administration. (2020). *Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs.* [online] Available at: https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs

Given the various economic and regulatory drivers contributing to drug shortages, it is clear there is no single silver bullet for effectively addressing this longstanding problem. Currently, CMS's Innovation Center (CMMI) has no demonstration projects focused on drug shortages.[32] However, any of the aforementioned recommendations targeted towards CMS such as requiring manufacturers to provide data around supply chain quality and resiliency, rating manufacturers on supply chain quality and resiliency parameters, and adjusting reimbursement or rebate for essential products or at risk of shortage could be piloted by CMMI. CMMI should be given flexibility to pilot varied approaches without restriction from Congress and provide public evaluations of such approaches toward informing more long-term implementation to effectively address drug shortages.

Congress could also take legislative action through piloting proposed pay-for-performance models that encourage a healthy supply chain via hospital purchasing rather than manufacturer incentives.[33] This could be implemented by CMS as a value-based mechanism that rewards hospitals for building a stockpile of essential medicines and selecting vendors that are less likely to experience supply chain disruptions. For outpatient drugs dispensed by PBMs, pharmacies, and generic source programs, supply agreements between generic manufacturers and distributors could be attached to a similar pay-for-performance model, rewarding distributors who maintain a healthy flow of quality generics. CMS has statutory experience with value-based models, and in this case would rely on development of FDA's Quality Management Maturity program as described above.

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[32] CMS. (n.d.). *Innovation models: CMS Innovation Center*. [online] Available at: https://innovation.cms.gov/innovation-models#views=models&key=drug

[33] Wosinska, M. E., & Frank, R. G. (2023, June 3). *Federal Policies to Address Persistent Generic Drug Shortages*. Brookings Institution. Retrieved July 1, 2023, from https://www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf

This adjustment of reimbursement rates for generic drugs would create an economic incentive for manufacturers to improve and modernize their manufacturing systems, as manufacturers with demonstrated resilient supply chains would be able to sell their products at a higher price (since pharmacies and providers would be in turned reimbursed at a higher rate when dispensing generic products from highly rated manufacturers). Such a star rating system could be based on FDA's Center for Drug Evaluation and Research (CDER) QMM programs that assess the resiliency and robustness of drug supply chains. [34] This system would address the drug shortages problem by incentivizing pharmacies and providers to purchase products from companies with known resilient supply chains.

3. The proposed legislation includes many important first steps in improving the transparency of API markets. These measures should be further strengthened.

3.1. There is no systematically collected data on API manufacturing and markets.

The lack of systematically collected data on API manufacturing and markets makes analyzing essential questions for supply chain resilience difficult or impossible. Relevant data that should be collected by the FDA include: the number of suppliers for a given API, the location of such suppliers, and their annual manufacturing capacity.

Pharmaceutical supply chains are global. Most generics manufacturers use API purchased from a different company.[35] Solving shortages in the United States requires collaboration

[34] Maguire, J., Fisher, A., Harouaka, D., Rakala, N., Lundi, C., Yambot, M., Viehmann, A., Stiber, N., Gonzalez, K., Canida, L., Buhse, L., & Kopcha, M. (2023). Lessons from CDER's Quality Management Maturity Pilot Programs. *AAPS Journal*.

[35] Mallu UR, Nair AK, Sankar J, Bapatu HR, Kumar MP, Narla S, et al. Impact of API (active pharmaceutical ingredient) source selection on generic drug products. (2015). *Pharmaceutical Regulatory Affairs: Open Access*. [online] Available at: https://www.hilarispublisher.com/open-access/impact-of-api-activepharmaceutical-ingredient-sourceselection-on-generic-drug-products-2167-7689-1000136.pdf

with other regulatory authorities to map global supply, particularly for at risk products such as those with single-source API producers or those in frequent shortage. The backbone of any mapping and collaboration is a shared language; the FDA should work with other regulators and international actors like the World Health Organization (WHO) to standardize reporting standards and data indicators for shortages, which currently are not standardized even within FDA data.

3.2. Many generic medicines are at risk of shortage because API is manufactured in just one facility.

The only study tracing API of generic medicines found that approximately one-third of generic APIs produced for use in the United States market between 2020 and 2021 were manufactured by a single facility; an additional third was manufactured by two or three facilities.[36]

3.3. Existing powers in CARES should be expanded to further improve API transparency.

Through the Coronavirus Aid, Relief, and Economic Security (CARES) Act, the FDA currently has authority to have additional oversight of drug supply chains,[37] via identification, prevention, and visibility into supply chains, but data needs to be accessible in order to translate this authority into benefit.[38] CMS has the statutory ability to request mandatory

[36] Socal, M. P., Ahn, K., Greene, J. A., & Anderson, G. F. (2023). Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs*, 42(3), 407–415.
[37] U.S. Food and Drug Administration. (2023). *Notifying FDA of a Discontinuance or Interruption in Manufacturing of Finished Products or Active Pharmaceutical Ingredients Under Section 506C of the FD&C Act Guidance for Industry.* [online] Available at: https://www.fda.gov/media/166837/download
[38] U.S. Food and Drug Administration. (2023). *Coronavirus Aid, Relief, and Economic Security Act (CARES Act) Drug Shortage Mitigation Efforts.* [online] Available at: https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts

participation in surveys to identify drug, spending, distribution, and utilization information.[39] This authority should be expanded to request mandatory survey data on manufacturing and supply, as well as on current shortages. Additionally, FDA has also put forward legislative proposals in their Fiscal Year 2024 funding request to expand the notification requirements from manufacturers to include alerting the FDA of increases in demand, submission of the firm's quality management policies, and manufacturing quantities along with other reporting requirements.[40]

4. Sec. 506. New domestic facility inspection pilot program

The FDA evaluates all new applications for approval of generic medicines (ANDAs) to determine whether a facility inspection is necessary, based on a set of clinical and manufacturing criteria. As it stands, inspections are conducted after the submission of the ANDA.[41]

The proposed *Stop Drug Shortages Act* would create, by amending Sec 704A, a new "domestic facility inspection pilot program." Under this program, manufacturers planning the submission of ANDA for 'covered products' (in the meaning of the Bill) could request, up to a year before submission of an ANDA, for a pre-approval facility inspection by the FDA. The FDA would conduct a facility inspection within 90 days of determining the request to be valid.

[39] Park, E. (2023). New CMS Proposed Rule Could Help State Medicaid Programs Negotiate Greater Supplemental Rebates for Certain High-Cost Drugs. *Georgetown Center for Children and Families*. [online] Available at: https://ccf.georgetown.edu/2023/05/30/new-cms-proposed-rule-could-help-state-medicaid-programs-negotiate-greater-supplemental-rebates-for-certain-high-cost-drugs/
[40] U.S. Food and Drug Administration. (n.d.). *Summary of FY 2024 Legislative Proposals*. [online] Available at: https://www.fda.gov/media/166049/download
[41] U.S. Food and Drug Administration. (2017). *ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications (Pre-Submission Facility Correspondence) Guidance for Industry*. [online] Available at: https://www.fda.gov/media/105794/download; https://cacmap.fda.gov/media/162018/download

4.1. The faster review timeline created by this provision would create a significant incentive for manufacturers, which should be coupled with requirements ensuring supply chain resilience.

This new mechanism would likely accelerate the approval of 'covered' domestically manufactured generic medicines, that is, medicines deemed to be vulnerable to shortages. This represents a significant incentive for manufacturers, as shorter review timelines will lead to earlier profits.

We recommend using 'priority generic' designation to incentivize manufacturers to take steps that ensure supply chain resilience. The proposed legislation could add a requirement, as a condition of 'priority generic' designation, for the manufacturer to provide information on supply chains and for their manufacturing facilities to achieve a minimum level of quality and resilience. Only when these standards have been met would a generic drug be eligible for "priority review", which shortens the regulatory review period ahead of an approval decision. Federal agencies including CMS could also employ other conditional incentives, coupling coverage and reimbursement alongside requirements that manufacturers demonstrate robust and resilient supply chains, as well as provide detailed information to federal agencies on the status of their supply to allow for timely intervention should there be a risk of manufacturing delays or disruptions that could result in shortages.

4.2. New requirements on the FDA for faster review will likely require additional funding.

This mechanism will only be effective if it can be implemented by an adequately resourced FDA. This shorter timeline is likely to mean additional funding is needed, which we would encourage Congress to examine.

4.3. It is important to note that on-shoring of pharmaceutical manufacturing is important as a question of industrial policy, but in terms of health policy, domestic manufacture is not necessarily associated with higher quality.

Relocating manufacturing facilities domestically may not lead to higher quality. A recent study found that manufacturing facilities located within the U.S. had quality problems comparable to those located abroad.[42]

5. Sec. 502. Incentive for shelf-life extension studies

5.1. The proposed 1-month extension would apply only to new products, which are unlikely to make up a significant proportion of the drugs commonly affected by shortages.

Similar to points made above regarding the proposed exemption of shortage-affected products from inflation-linked rebates, the proposed 1 month extension would apply only to new products (new chemical entities or first generic market entrants). These types of products are unlikely to make up a significant proportion of the drugs commonly affected by shortages, as 97% of drugs currently affected by shortages are established generics.[43] Given

[42] Socal, M. P., Ahn, K., Greene, J. A., & Anderson, G. F. (2023). Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs*, 42(3), 407–415. https://doi.org/10.1377/hlthaff.2022.01120

[43] Of 1119 new drug shortages for 283 unique products reported by the FDA between January 2022 and June 2023, 97% were generics. See Center for Drug Evaluation and Research. (n.d.). *Current Drug Shortages*. [online] Available at: https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages

this, we would expect the 1 month extension to have little effect on drugs commonly affected by shortages.

5.2. The proposed granting of an additional 1 month of exclusivity for the conduct of shelf-life extension studies would add significant costs for CMS and likely overcompensate, at least by a factor of 60, the costs incurred by manufacturers in conducting relevant studies.

This section would create a new and additional period of exclusivity, lasting one month, awarded to both new chemical entities (i.e. generally, patented brand-name medicines) and the first generic to be approved by the FDA after patent expiry on the originator medicine. In general, this would extend the period of exclusivity from 5 years to 5 years and 1 month for NCEs and from 180 days to 210 days for the first generic market entrant.[44]

In this context, 'exclusivities' refer to a period in which the FDA cannot approve any competitor products. The exclusivity period therefore provides the proprietor with a time-limited monopoly in the US.

Extending the monopolies enjoyed by medicines manufacturers allows these manufacturers to charge higher prices for longer. The added cost to CMS would be significant. An analysis of the additional revenues generated for each medicine receiving 'pediatric exclusivity' (FD&C Act Section 505A, 21 U.S.C 355a), which lasts 6 months, found that median net benefit to the manufacturer was $134 million per therapeutic receiving this exclusivity (in a hypothetical model in which the exclusivity was only 3 month long, the median net benefit

[44] Section 505 of the FD&C Act (21 U.S.C. 355).

to the manufacturer was $64 million per therapeutic).[45] Scaling this estimate down to 1 month would suggest average additional costs to Americans of over $21 million paid in profits for each medicine receiving 1 month of additional exclusivity.

The Shelf-Life Extension Program, established in 1986, funded by US Department of defense and carried out by FDA, regularly conducts shelf-life extension studies on medicines deemed to be of military importance. It has been reported that studies under the Shelf Life Extension Program (SLEP) cost approximately $350,000 per year, for studies on multiple products.[46] These figures suggest that the estimated $21 million in additional profits gained through the proposed 1-month extension would overcompensate manufacturers' costs in conducting the studies by at least a factor of 60.[47]

5.3. There is a clear need for shelf-life extension studies to be mandated for all new drug approvals, and for a mechanism to ensure that shelf-life extension studies are undertaken for key generic medicines.

It would be reasonable and not overly burdensome on manufacturers (as outlined above regarding costs of shelf-life extension studies) to create a requirement for shelf-life studies on all new drugs, or at minimum drugs considered essential. The establishment of such a requirement would be similar to the requirement under the Pediatric Research Equity Act (Public Law 108-155) for pediatric studies to be conducted by the applicant for all new active

[45] Li, J.S., Eisenstein, E.L., Grabowski, H.G., Reid, E.D., Mangum, B., Schulman, K.A., Goldsmith, J.V., Murphy, M.D., Califf, R.M. and Benjamin, D.K. (2007). Economic Return of Clinical Trials Performed Under the Pediatric Exclusivity Program. *JAMA*, 297(5), p.480. doi:https://doi.org/10.1001/jama.297.5.480.
[46] Courtney, B., Easton, J., Inglesby, T.V. and SooHoo, C. (2009). Maximizing State and Local Medical Countermeasure Stockpile Investments through the Shelf-Life Extension Program. *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science*, 7(1), pp.101–107. doi:https://doi.org/10.1089/bsp.2009.0011.
[47] 21,000,000/350,000 (conservative as 350,000 is for multiple drugs)

ingredients or new dosage forms submitted in New Drug Applications and Biologics Licensing Applications.[48]

Regarding shelf-life extension studies for medicines that have been generic for many years (and are generally multisource), we support calls made by colleagues at the Duke Margolis Center for Health Policy that "[t]he joint DoD/FDA Shelf Life Extension Program (SLEP) should expand to proactively review the expiration dating of all essential medicines, along with those in the [Strategic National Stockpile], an entity under HHS that stores essential medicines and medical supplies for use in emergencies".[49]

Congress or CMS should analyze further the average costs of shelf-life extension studies. Based on the reports cited above, we expect that these costs will be found to be very small or even negligible compared to the average revenues for both new chemical entities (i.e. generally, originator products) and first generic market entrants.[50]

6. Leveraging and strengthening research and industrial capacity in the United States

6.1. Grant-making and organizations with significant research capacity like the National Institutes of Health (NIH) and Biomedical Advanced Research and Development Authority (BARDA) should invest in process manufacturing research.

[48] U.S. Food and Drug Administration. (2019). *How to Comply with the Pediatric Research Equity Act*. [online] Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/how-comply-pediatric-research-equity-act.
[49] Supporting Resilient Drug Supply Chains in the United States Challenges and Potential Solutions. (2021). [online] Duke-Margolis Center for Health Policy. Available at: https://healthpolicy.duke.edu/sites/default/files/2021-10/Supporting%20Resilient%20Drug%20Supply%20Chains%20in%20the%20United%20States.pdf.
[50] ibid

The United States expends enormous resources on biomedical research; this investment has been the foundation of every new drug approved by the FDA in recent years.[51] **Federal funding should also play a role in advancing innovation that improves the efficiency of manufacturing and the stability of medicine.** Investments should be made in research around process manufacturing, product stability, and other interventions that improve the shelf life of products. As one example of the application of such research, two recent studies demonstrated longer thermostability of insulin (a medicine with strict cold chain requirements) outside of refrigeration than previously known.[52] The FDA already extends allowed medication expiration dates in cases of emergency, where data is available that supports that any extension does not pose a risk to patients.[53] Generating evidence on product safety and stability is useful in averting wastage of products, extending supply, and in better understanding when it is safe to use products, particularly in emergencies and supply shortages. However, there is little incentive for manufacturers to conduct this research. As we have argued above, the costs of the proposed extension of exclusivity are not commensurate with the benefits. They also would not be relevant for medicines that are already off-patent, which are of greatest concern with regard to existing shortages. Instead, federal agencies with grantmaking authorities might consider supporting this research as it

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[51] Cleary, E.G., Jackson, M.J., Zhou, E.W. and Ledley, F.D., 2023, April. Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. In *JAMA Health Forum* (Vol. 4, No. 4, pp. e230511-e230511). American Medical Association.

[52] Zilker, M., Sörgel, F. and Holzgrabe, U. (2019). A systematic review of the stability of finished pharmaceutical products and drug substances beyond their labeled expiry dates. *Journal of Pharmaceutical and Biomedical Analysis*, 166, pp.222–235. doi:https://doi.org/10.1016/j.jpba.2019.01.016.

Kaufmann, B., Boulle, P., Berthou, F., Fournier, M., Beran, D., Ciglenecki, I., Townsend, M., Schmidt, G., Shah, M., Cristofani, S., Cavailler, P., Foti, M. and Scapozza, L. (2021). Heat-stability study of various insulin types in tropical temperature conditions: New insights towards improving diabetes care. *PLOS ONE*, 16(2), p.e0245372. doi:https://doi.org/10.1371/journal.pone.0245372.

Pendsey, S., James, S., Garrett, T.J., Nord, A.B., Pendsey, S., Malmodin, D., Karlsson, G., Maniam, J., Atkinson, M.A., Forsander, G. and Ogle, G.D. (2023). Insulin thermostability in a real-world setting. *The Lancet Diabetes & Endocrinology*. doi:https://doi.org/10.1016/s2213-8587(23)00028-1.

[53] USFDA. *Expiration Dating Extension*. [online] Available at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension

would provide other potential alternative approaches for ensuring adequate supply, especially during shortages and public health emergencies.

6.2. Public manufacturing should be considered for drugs in shortage.

There are several precedents for more direct Federal and State involvement in stepping in to ensure drug supply. **For medicines, vaccines, and other health products of high importance for public health and/or national security, Congress should support increasing public sector manufacturing capacity in the US.**

As outlined by the FDA, among others, relying on the private sector alone to manufacture certain products of high importance leaves the United States vulnerable to shortages, especially for products that may not have a dependable month-to-month demand, but may suddenly be needed in high volumes, such as medical countermeasures in a bioterrorism scenario.

Historically, the US has used public sector manufacture to ensure supply to such agents in certain cases, as in the example of anthrax vaccines manufactured federally from 1970 until 1995.[54] Such public sector manufacturing capacity would in many cases be additional to, rather than replacing, private sector manufacturers. This would support supply chain diversification, adding another dimension of protection against shocks to the supply chain.

[54] Institute of Medicine (US) Committee to Assess the Safety and Efficacy of the Anthrax Vaccine; Joellenbeck LM, Zwanziger LL, Durch JS, et al., editors. The Anthrax Vaccine: Is It Safe? Does It Work? Washington (DC): National Academies Press (US); 2002. 7, Anthrax Vaccine Manufacture. Available from: https://www.ncbi.nlm.nih.gov/books/NBK220526/

ASPR and DARPA are already exploring ways to develop public sector manufacturing capacity, including next-generation point-of-care manufacturing solutions.[55] We support these efforts and encourage Congress to explore expanding public sector manufacture to essential health products beyond the biowarfare context.

[55] USFDA. Drug Shortages: Root Causes and Potential Solutions. Retrieved September 12, 2023, from https://www.fda.gov/media/131130/download?attachment