Testimony of Brian J. Miller, M.D., M.B.A., M.P.H.

Assistant Professor of Medicine and Business (Courtesy)
The Johns Hopkins University School of Medicine
The Johns Hopkins Carey Business School

Nonresident Fellow
American Enterprise Institute

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On

"Stifling Innovation: Examining the Impacts of Regulatory Burdens on Small Businesses in Healthcare."

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Chairman Williams, Ranking Member Velázquez, and distinguished members of the U.S. House of Representatives Committee on Small Business:

My name is Brian Miller, and I practice hospital medicine at the Johns Hopkins Hospital. As an academic health policy analyst, I serve as an Assistant Professor of Medicine and Business (Courtesy) at the Johns Hopkins University School of Medicine and as a Nonresident Fellow at the American Enterprise Institute. My research focuses on how we can build a more competitive and vibrant health sector to make healthcare more flexible and personalized for patients. This perspective is based upon my prior regulatory experience at four federal regulatory agencies, including the U.S. Food & Drug Administration where I worked in policy and as a reviewer in the Center for Drug Evaluation and Research's Office of New Drugs. Through my current role as a faculty member, I regularly engage with regulators, policymakers, and businesses in search of solutions to help create a better healthcare system for all. Today I am here in my personal capacity, and the views expressed are my own and do not necessarily reflect those of the Johns Hopkins University, the American Enterprise Institute, or the Medicare Payment Advisory Commission.

In my testimony today, I will focus on:

1. Why Pharmaceutical Product Innovation Matters to Patients and Physicians
2. Historical Actions to Address FDA Barriers to Innovation
3. FDA Reform to Promote Pharmaceutical Product Innovation for Small Companies

1. Why Pharmaceutical Product Innovation Matters to Patients and Physicians

As one of the world's wealthiest countries, we spend over $4.5 trillion dollars[1] on healthcare services and related medical products to care for over 330 million Americans. While half of this is spent on physician services and hospitals, the latter a sector with flat or declining labor productivity growth,[2] life sciences innovation has a been a bright spot in the health sector's otherwise dark history with prescription drug spending representing an estimated 9% of national health expenditures.[3] With industry developing over 1,200 new drugs since 1950[4] and over 20,000 prescription drugs approved for marketing (including generics) and over 400 licensed biologic products,[5] patients and their physicians have options for a variety of diseases. Price competition from generics has resulted in increased affordability, with the U.S. Food & Drug Administration's (FDA) own economists demonstrating that entry of even a sixth generic competitor resulting in further price decrements.[6]

Yet, much work remains to be done. An estimated 10 million children suffer from rare diseases–or those affecting less than 200,000 children–and only 5% have treatments.[7] Chronic diseases such as insulin-dependent diabetes affect over 5 million Americans,[8] with the inconvenience and pain of checking one's blood sugar and injecting insulin multiples times per day for the rest of one's life. Complications range from limb amputations[9] and vision loss[10] resulting in significant functional impairment. Still other disease families such as heart failure, a disease managed primarily via

[1] NHE Fact Sheet. Centers for Medicare & Medicaid Services. https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/nhe-fact-sheet.
[2] Productivity. U.S. Bureau of Labor Statistics. https://www.bls.gov/productivity/highlights/hospitals-labor-productivity.htm
[3] NHE Fact Sheet. Centers for Medicare & Medicaid Services. https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/nhe-fact-sheet.
[4] Munos, B. Lessons from 60 years of pharmaceutical innovation. *Nat Rev Drug Discov* **8**, 959–968 (2009). https://doi.org/10.1038/nrd2961
[5] FDA at a Glance. U.S. Food & Drug Administration. October 2019. https://www.fda.gov/media/131874/download
[6] Conrad R, Lutter R. Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices. U.S. Food & Drug Administration. December 2019. https://www.fda.gov/media/133509/download?attachment
[7] Hwang TJ, Bourgeois FT, Franklin JM, Kesselheim AS. Impact Of The Priority Review Voucher Program On Drug Development For Rare Pediatric Diseases. *Health Affairs*. 2019/02/01 2019;38(2):313-319. doi:10.1377/hlthaff.2018.05330
[8] https://www.cdc.gov/diabetes/data/statistics-report/index.html
[9] Vogel TR, Petroski GF, Kruse RL. Impact of amputation level and comorbidities on functional status of nursing home residents after lower extremity amputation. *J Vasc Surg*. 2014;59(5):1323-30.e1. doi:10.1016/j.jvs.2013.11.076
[10] Brown MM, Brown GC, Sharma S, Landy J, Bakal J. Quality of life with visual acuity loss from diabetic retinopathy and age-related macular degeneration. *Arch Ophthalmol*. 2002;120(4):481-484. doi:10.1001/archopht.120.4.481

small molecule drugs, affects over 6 million Americans nearly half of whom have difficulty with basic activities such as climbing stairs.[11]

Cancer remains a longstanding policy and political focus as it affects all of us: in 2023, an estimated 1,958,310 Americans were newly diagnosed with cancer and an estimated 609,820 Americans died of cancer the same year.[12] Cancer as a disease family can be viewed through the lens of its organ, cellular, or even molecular origins. Some cancers such as melanoma are responsible for a large number of diagnoses and are frequently caught earlier, thus representing a lesser share of cancer deaths.[13] Others such as Merkel Cell Carcinoma are extremely rare,[14] discovered later, and result in significant mortality.[15]

Impacts are significant for society and individuals. The economic impact of diabetes is estimated at $412 billion,[16] while cancer deaths resulted in lost earnings of $94.4 billion[17]–a number from over a decade ago. The direct costs for those undergoing treatment are real, with a study of 1,037 patients undergoing treatment for acute myeloid leukemia having twice and five times the rate of short and long-term disability claims filed.[18] While statistical data provide an overarching claim, one cannot forget the individual cost: each patient is someone's spouse, children, friend, or co-worker. A new lease on life or restored functional status can transform someone's life–the release of etanercept (Enbrel) in 1998 marked a new chapter in my elderly grandmother's life as her Rheumatoid Arthritis came under control and she was able to bake her famous crescent roles again at Thanksgiving and work in her garden tending her roses. For some Americans, innovation is not just a new lease on life but better living through pharmaceuticals.

2. Historical Actions to Address FDA Barriers to Innovation

Barriers to pharmaceutical product innovation are very real, with the average drug taking 10-15 years to travel from bench to bedside and the average cost of development estimated at $2.6 billion,[19] innovators especially entrepreneurs and small companies face high barriers to innovation. With drugs traversing preclinical research, phase 1 (safety), phase 2 (efficacy and further evaluate safety), and phase 3 (efficacy and adverse events), each research stage acts as a scientific and clinical development gate, with 70% passing phase 1, 33% passing phase 2, 25-30% passing phase 3,[20] and fewer than 8% of experimental therapeutics making it through all three phases of development.

Recognizing the time, expense, and expected scientific and clinical failures in pharmaceutical product development, policymakers have worked through the prescription drug user fee acts in conjunction with agency actions to undertake key initial reforms at FDA to safely promote access to pharmaceutical product innovation, in addition to lowering barriers for small companies and entrepreneurs:

1. Priority Review: drugs that would offer significant improvements in safety or effectiveness–if so designated–are reviewed in 6 months instead of the standard 10 months.[21] A designation created under the original 1992

[11] Dunlay SM, Manemann SM, Chamberlain AM, et al. Activities of Daily Living and Outcomes in Heart Failure. *Circulation: Heart Failure*. 2015;8(2):261-267. doi:doi:10.1161/CIRCHEARTFAILURE.114.001542
[12] Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(1):17-48. doi:10.3322/caac.21763
[13] Cancer Stat Facts: Melanoma of Skin. National Cancer Institute. https://seer.cancer.gov/statfacts/html/melan.html
[14] Paulson KG, Park SY, Vandeven NA, et al. Merkel cell carcinoma: Current US incidence and projected increases based on changing demographics. *J Am Acad Dermatol*. 2018;78(3):457-463.e2. doi:10.1016/j.jaad.2017.10.028
[15] Fitzgerald TL, Dennis S, Kachare SD, Vohra NA, Wong JH, Zervos EE. Dramatic Increase in the Incidence and Mortality from Merkel Cell Carcinoma in the United States. *Am Surg*. 2015;81(8):802-806. doi:10.1177/000313481508100819
[16] Parker ED, Lin J, Mahoney T, et al. Economic Costs of Diabetes in the U.S. in 2022. *Diabetes Care*. 2024;47(1):26-43. doi:10.2337/dci23-0085
[17] Islami F, Miller KD, Siegel RL, et al. National and State Estimates of Lost Earnings From Cancer Deaths in the United States. *JAMA Oncol*. 2019;5(9):e191460. doi:10.1001/jamaoncol.2019.1460
[18] Pandya BJ, Young C, Packnett ER, et al. Work absenteeism, disability, and lost wages among patients with acute myeloid leukemia and their caregivers: a cohort study using US administrative claims and productivity data. *Expert Rev Pharmacoecon Outcomes Res*. 2024;24(4):521-532. doi:10.1080/14737167.2024.2311305
[19] *Research and development*. PhRMA Org. https://phrma.org/policy-issues/Research-and-Development-Policy-Framework
[20] Step 3: Clinical Research. U.S. Food & Drug Administration. https://www.fda.gov/patients/drug-development-process/step-3-clinical-research
[21] Priority Review. U.S. Food & Drug Administration. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review

Prescription Drug User Fee Act (PDUFA), priority review has been further expanded upon by a voucher program to incentivize entrepreneurs to develop products for areas such as rare pediatric disease,[22] a program set to expire this September.

2. Fast Track: drugs that are being development to treat a condition with no therapeutic options or that offer an advantage over current treatment qualify for this designation and product sponsors receive more frequent meetings with FDA, more frequent written communication with FDA, eligibility for rolling review, and eligibility for accelerated approval and priority review as salient.[23,24] A designation created as part of the 1997 FDA Modernization Act (FDAMA); of the 3,392 designations filed from 1998-2023, 2238 or 66% were approved.[25]

3. Breakthrough Therapy: Fast Track plus intensive guidance and organization commitment from senior managers.[26] A designation created as part of the 2012 FDA Safety and Innovation Act (FDASIA).[27]

4. Accelerated Approval: Permits earlier approval based upon a surrogate endpoint (e.g. laboratory, radiological measurement) for drugs that treat serious conditions and fulfill an unmet need. The sponsor is required to conduct confirmatory studies once the product is marketed to prove the clinical benefit, converting the accelerated into a traditional approval. Accelerated approval was created as part of PDUFA, in response to the HIV/AIDS epidemic of the 1980s.[28]

While some of these regulatory pathways have been the subject of academic controversy, research examining the accelerated approval pathway by its greatest critiques demonstrates that confirmatory trials are typically completed, albeit at times with a delay,[29,30] further emphasizing the need to increase the access to clinical trials (clinical trial recruitment is a frequent barrier). Still other research has critiqued[31] the FDA's use of surrogate endpoints/biomarkers,[32] failing to recognize that science-based regulatory policy involves tradeoffs between perfect and imperfect information for making regulatory decisions in a real-world setting. Erring on the side of restricting access results in death and debility for many, while permitting access with appropriate and robust oversight safely expands treatment options.

3. FDA Reform to Promote Pharmaceutical Product Innovation for Small Companies

Regulatory barriers are magnified for entrepreneurs and small companies who with limited financial capital, limited patent lives, and increasing payment policy uncertainty face unnecessary regulatory challenges at the FDA. Recent

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[22] Mease, C., Miller, K.L., Fermaglich, L.J. et al. Analysis of the first ten years of FDA's rare pediatric disease priority review voucher program: designations, diseases, and drug development. *Orphanet J Rare Dis* 19, 86 (2024). https://doi.org/10.1186/s13023-024-03097-x

[23] Fast Track. U.S. Food & Drug Administration. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track

[24] Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics. U.S. Food & Drug Administration. May 2014. https://www.fda.gov/media/86377/download?attachment

[25] CDER Fast Track Designation Requests Received Fiscal Year 1998 – Fiscal Year 2023. U.S. Food & Drug Administration. https://www.fda.gov/media/97830/download

[26] Break Through Therapy. U.S. Food & Drug Administration. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy

[27] Kepplinger EE. FDA's Expedited Approval Mechanisms for New Drug Products. *Biotechnol Law Rep*. 2015;34(1):15-37. doi:10.1089/blr.2015.9999

[28] Stengel K, Zalewski Z, West M, Gustafson K, Nell A. Understanding the History and Use of the Accelerated Approval Pathway. Avalere. January 4, 2022. https://avalere.com/insights/understanding-the-history-and-use-of-the-accelerated-approval-pathway

[29] Deshmukh AD, Kesselheim AS, Rome BN. Timing of Confirmatory Trials for Drugs Granted Accelerated Approval Based on Surrogate Measures From 2012 to 2021. *JAMA Health Forum*. 2023;4(3):e230217. doi:10.1001/jamahealthforum.2023.0217

[30] Delays in Confirmatory Trials for Drug Applications Granted FDA's Accelerated Approval Raise Concerns. U.S. Department of Health & Human Services. September 2022. https://oig.hhs.gov/oei/reports/OEI-01-21-00401.pdf

[31] Wallach JD, Yoon S, Doernberg H, et al. Associations Between Surrogate Markers and Clinical Outcomes for Nononcologic Chronic Disease Treatments. *JAMA*. Published online April 22, 2024. doi:10.1001/jama.2024.4175

[32] Table of Surrogate Endpoints That Were the Basis of Drug Approval or Licensure. U.S. Food & Drug Administration. https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure

FDA actions such as the recent the 528 page laboratory-developed test rule[33] have favored large companies that can bear the cost of regulation, bypassing small companies and entrepreneurs while favoring the precautionary principle instead of managing the complex interplay between continuum of risk and innovation. Instead, policymakers and regulators should promote dynamic competitive markets by doing the hard work of balancing risk and innovation. In this context, two primary policy levers present an opportunity to expand access to innovation, diversifying trials and moving them into the community setting: clinical trial reform and administrative simplification.

Clinical trial reform

While much of the recent focus about diversity in clinical trials has focused on equity,[34,35] practical science suggests that expanding access to clinical trials will improve the efficiency of evidence generation and clinical meaning of pharmaceutical product development. Ensuring that a broader range of Americans can access and are included in clinical trials will advance science, improve clinical practice, and expand access to novel therapeutics. Three policy levers within the FDA can expand access to clinical trials: 1) real world evidence to drive patient-reported outcomes, 2) flexibility in outcomes assessment, and 3) promoting positive creativity in trial design.

Patient reported outcomes using real-world evidence can lower barriers to and the costs of participating in and executing clinical trials. While the FDA has long had a framework for real world evidence[36] and guidance dating back to 2009 on patient-reported outcomes,[37] functionally what this means is focusing on outcomes meaningful to the end user. While lab tests and intermediate biomarkers are useful proxies and provide important interim and statistical insight into the efficacy of therapeutics, their collection may be burdensome to the patient involving transit to a study center, sample collection, and a delay in processing. High level patient-focused outcomes such as hospitalization matter, albeit in many conditions occur infrequently and thus require large study populations in order to detect statistically and clinically meaningful differences, massively raising costs thus favoring large companies and pushing product developers towards biomarkers.[38]

A shift towards patient reported outcomes does not have to be burdensome to patients or innovators. For example, in chronic obstructive pulmonary disease, breathlessness and loss of functional status are key indicators, with 46% of patients reporting moderate to severe shortness of breath[39] while functional capacity as measured by six-minute walk distance and muscle strength declined with time.[40] Other conditions such as Parkinson's disease result in impairments in strength and coordination, that can potentially be measured through simple functional tests.[41] While historically functional assessments occur in a clinical setting undertaken by a physician, many could be undertaken in the home setting, either by the patient themselves assisted by a family, or remotely with automated or live guidance from a trained layperson or skilled medical professional such as a study nurse. Examining pharmaceutical product development through this lens would both reduce the cost of development for small companies, lower barriers to trial participation for poor and minority beneficiaries, and improve the clinical meaningfulness of outcomes of clinical trials.

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[33] "Medical devices, Laboratory Developed Tests." May 6, 2024. https://www.federalregister.gov/documents/2024/05/06/2024-08935/medical-devices-laboratory-developed-tests

[34] Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups. National Academies of Sciences, Engineering, and Medicine. 2022. https://nap.nationalacademies.org/catalog/26479/improving-representation-in-clinical-trials-and-research-building-research-equity

[35] Schwartz Aaron L, Alsan M, Morris Alanna A, Halpern Scott D. Why Diverse Clinical Trial Participation Matters. *New England Journal of Medicine*. 2023/04/05 2023;388(14):1252-1254. doi:10.1056/NEJMp2215609

[36] Framework for FDA's Real-World Evidence Program. U.S. Food & Drug Administration. December 2018. https://www.fda.gov/media/120060/download?attachment

[37] Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. U.S. Food & Drug Administration. December 2009. https://www.fda.gov/media/77832/download

[38] Hinder M, Yi BA, Langenickel TH. Developing Drugs for Heart Failure With Reduced Ejection Fraction: What Have We Learned From Clinical Trials?. *Clin Pharmacol Ther*. 2018;103(5):802-814. doi:10.1002/cpt.1010

[39] Müllerová H, Lu C, Li H, Tabberer M. Prevalence and burden of breathlessness in patients with chronic obstructive pulmonary disease managed in primary care. *PLoS One*. 2014;9(1):e85540. Published 2014 Jan 10. doi:10.1371/journal.pone.0085540

[40] Kapella MC, Larson JL, Covey MK, Alex CG. Functional performance in chronic obstructive pulmonary disease declines with time. *Med Sci Sports Exerc*. 2011;43(2):218-224. doi:10.1249/MSS.0b013e3181eb6024

[41] Clael S, Brandão E, Caland L, et al. Association of Strength and Physical Functions in People with Parkinson's Disease. *Neurosci J*. 2018;2018:8507018. Published 2018 Dec 12. doi:10.1155/2018/8507018

Real world evidence and patient reported outcomes must be partnered with flexibility in assessment of outcomes. Clinical trials as executed today require patients to travel to study sites for assessment, interview, and exam by clinical staff throughout the duration of a clinical study. This incurs direct (e.g. transit cost) and indirect cost (e.g. lost wages, childcare) for study participants, limiting access to those without financial means or adequate family and social support. While the FDA has issued draft guidance for decentralized clinical trials,[42] the FDA and small companies together must make this policy a reality. For movement disorders, conducting exams at home with subsequent review of recorded standardized exams by a fellowship-trained movement disorders neurologist at a subsequent date would reduce the cost of trial execution for small companies, increase access to a broader patient population, and support a focus on meaningful outcomes. This type of thinking is rare in product development, as it requires close engagement and supportive partnership for creative small companies by FDA review divisions, with the FDA's 2017 review of valbenazine representing one such example.[43]

Finally, positive creativity in trial design is a must. Over a hundred years of clinical progress has demonstrated that we have a variety of ways in which researchers can answer the question of a drug's safety and effectiveness. While the FDA's standard of two adequate and well-controlled studies was historically seen as a high barrier to entry,[44] positive creativity in trial design such as enrichment,[45] adaptive designs,[46] master protocols,[47] and the transition of clinical trials into community settings[48] as part of routine clinical practice can expand access, increase the diversity of trials, and lower costs thus lowering the barriers to small companies and entrepreneurship in pharmaceutical product innovation. Other steps to use historical trial designs that are less frequently deployed such as a repurposing a study population after a washout period and crossover trials can allow product developers to "do more with less." While small companies can legally take these steps, a management top-heavy FDA with overburdened and inaccessible review staff drives companies to take well-trodden, risk averse paths in clinical development programs, raising costs and limiting patient populations studies.

Administrative simplification to both support and transform the role of the FDA reviewer

In order to realize the long held goal of clinical trial reform, the FDA needs to provide more customized counseling to entrepreneurial small pharmaceutical product developers. In order to do so, the FDA will need to refocus the efforts of staff. Consider the Center for Drug Evaluation and Research (CDER), the primary drug review center at FDA with 5,482 employees in 2022[49] that grew to 5,785 employees in Q1 2024.[50] Out of 12 offices reporting to the CDER Center Director, 2 are directly responsible for drug review: the Office of New Drugs (responsible for reviewing novel, branded products) and the Office of Generic Drugs.[51] As one can see below, some of the offices below could potentially be combined (e.g. Office of Executive Programs, the Office of Management, and the Office of Strategy Programs), eliminating management overhead and freeing up highly trained and technically-skilled staff to be deployed within the Office of New Drugs on other review and product development oversight tasks. Administrative simplification

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[42] Decentralized Clinical Trials for Drugs, Biological Products, and Devices: Guidance for Industry, Investigators, and Other Stakeholders. U.S. Food & Drug Administration. May 2023. https://www.fda.gov/media/167696/download

[43] Davis Michael C, Miller Brian J, Kalsi Jasmeet K, Birkner T, Mathis Mitchell V. Efficient Trial Design — FDA Approval of Valbenazine for Tardive Dyskinesia. *New England Journal of Medicine*. 376(26):2503-2506. doi:10.1056/NEJMp1704898

[44] Temple R. FDA's Clinical Investigator Course: Design of Clinical Trials. U.S. Food & Drug Administration. November 12, 2013. https://www.fda.gov/media/159878/download

[45] Temple R. Complexities in drug trials: enrichment, biomarkers and surrogates. Interview with Robert Temple. *Biomark Med*. 2008;2(2):109-112. doi:10.2217/17520363.2.2.109

[46] Temple R. Enrichment Strategies for Clinical Trials. U.S. Food & Drug Administration. March 25, 2013. https://www.fda.gov/files/drugs/published/Enrichment-Strategies-for-Clinical-Trials-%28PDF-—-933KB%29.pdf

[47] Woodcock J, LaVange Lisa M. Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. *New England Journal of Medicine*. 377(1):62-70. doi:10.1056/NEJMra1510062

[48] Woodcock J, Araojo R, Thompson T, Puckrein Gary A. Integrating Research into Community Practice — Toward Increased Diversity in Clinical Trials. *New England Journal of Medicine*. 2021/10/06 2021;385(15):1351-1353. doi:10.1056/NEJMp2107331

[49] Center for Drug Evaluation and Research & Center for Biologics Evaluation and Research Net Hiring Data. U.S. Food & Drug Administration. https://www.fda.gov/industry/prescription-drug-user-fee-amendments/center-drug-evaluation-and-research-center-biologics-evaluation-and-research-net-hiring-data

[50] Center for Drug Evaluation and Research & Center for Biologics Evaluation and Research Net Hiring Data (FY 2023-2027). U.S. Food & Drug Administration. https://www.fda.gov/industry/fda-user-fee-programs/center-drug-evaluation-and-research-center-biologics-evaluation-and-research-net-hiring-data-fy-2023

[51] Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research [Chart]. U.S. Food & Drug Administration. https://www.fda.gov/media/131211/download

would also reduce the number of direct reports, empowering the Center director to advocate and be a stronger lead for organizational change.

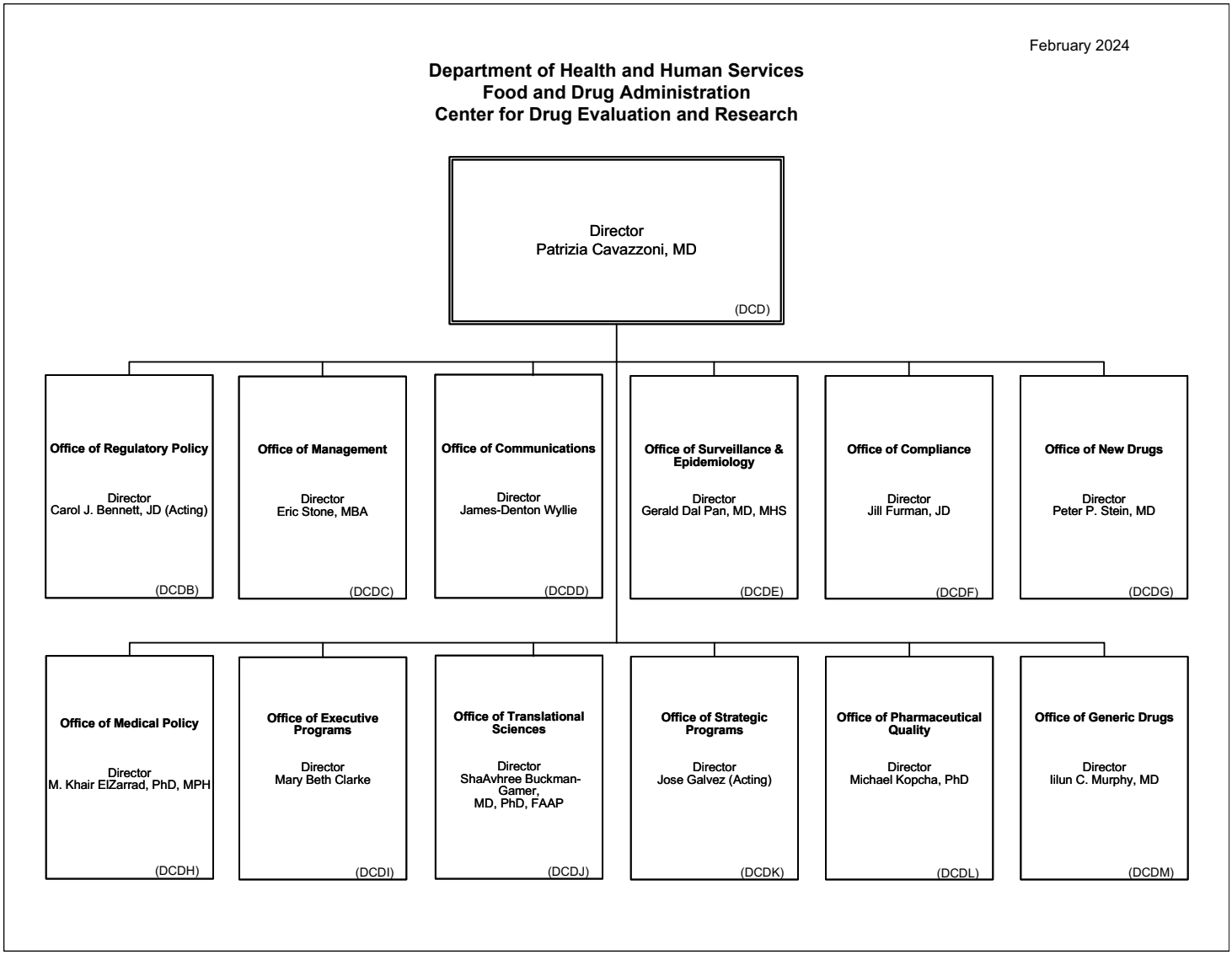

Figure 1: CDER Organizational Chart

Focusing on the Office of New Drugs (OND), administrative layers[52] should also be collapsed in order to reduce administrative overhead and free up staff for front-line product review activities. As a super office, OND has 9 large therapeutic area offices reporting in,[53] each of which are comprised of multiple therapeutic divisions. For example, OND has within it the Office of Rare Diseases, Pediatrics, Urology, and Reproductive Medicine (OPURM). Within OPRUM, one of multiple divisions is the Division of Pediatrics and Maternal Health (DPMH), which has a Division Director, Deputy Director, and then Team Leaders for each of the review teams comprised of medical officers (who are directly responsible for the review) and other technical leads.

[52] "Reorganization of the office of new drugs with corresponding changes to the office of translational sciences and the office of pharmaceutical quality." September 26, 2019. https://www.outsourcedpharma.com/doc/reorganization-office-new-drugs-corresponding-changes-translational-sciences-pharmaceutical-quality-0001

[53] Office of New Drugs. U.S. Food & Drug Administration. https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-new-drugs

As a consequence, OND, OPURM, and DPMH each have highly paid physician and scientific leaders who are primarily involved in management activities, as opposed to scientific review of novel pharmaceutical products. In addition to simplifying offices reporting to CDER, flattening the organizational structure within the Office of New Drugs would free up highly trained medical and scientific staff for primary review work. This would rebalance the workload for front-line clinical reviewers who are responsible for new drug application (NDA) reviews with statutory timelines and investigation new drug (IND) reviews where the sponsor can initiate the trial within 30 days,[54] all in addition to regular internal and external meetings.

The FDA can also increase efficiency of reviewers by using artificial intelligence (AI) to assist with basic analyses. Doing so would allow reviewers to operate at a higher level focusing on the intellectual framework and review strategy as opposed to pure computational work, empowering reviewers to better partner with small businesses to promote efficient and effective development programs. Promoting customized and efficient review would transform CDER and broadly make it more like its counterpart, the Center for Biologics Evaluation and Research (CBER), which regularly engages with small companies working in boutique product and rare disease areas.

Increasing the number of reviewers interfacing with industry by repurposing administrative and managerial staff will decrease the average workload of the clinical review while allowing the FDA to meet its statutorily-required review tasks. What does this mean operationally? For a small company that needs guidance on how to creatively design and execute trials, FDA reviewers will finally have the bandwidth to apply their knowledge and guide product developers to more efficiently and effectively assess safety and efficacy, deploying their "top of industry" view as partners in the regulatory review and product development process, improving safety and efficacy all for the long-term benefit of patients.

This redeployment will also make possible the potential transformation of the role of the FDA reviewer. Reviewers are typically highly trained physicians who depart clinical work and transition into a pure regulatory setting. While there are enormous benefits to seeing a wide range of development programs across a therapeutic area, clinical knowledge and pragmatism fades with time. By increasing the number of review staff without increasing the total FDA CDER head count, there is potential for the reviewer role to be transformed from a pure analytical desk job to that of a hybrid practitioner-reviewer–a role exemplified by some current and former FDA reviewers despite current barriers. By continuing to experience the realities and challenges of clinical practice including the problems that patient face, reviewers will better understand the limitations of the data they see, prioritize clinically meaningful outcomes, more fully grasp the need to decrease data collection burdens, and enthusiastically embrace patient-centered outcomes.

Overall, administrative simplification by eliminating managerial layers, providing clarity in lines of command, and expanding the reviewer pool without increasing headcount will empower CDER to serve as a counselor and regulator to small companies developing products, all to the benefit of patients.

4. Conclusion

Healthcare is one of the most complex and regulated industries in the U.S. Yet, stacked administrative regulation raises costs, reduces access, and favors large companies. As the nation's consummate product regulator, the FDA is responsible for ensuring that approved drugs are safe and effective. The current regulatory regime often presents significant barriers to small companies and entrepreneurs, while simultaneously restricting access to clinical trials and limiting diversity and medical progress. While 30 years of Congressional efforts have served to add appropriate flexibility to the FDA's product regulatory schema while preserving and even improving safety, executing on clinical trial reform for the first time in decades coupled with administrative simplification would reduce burdens on small businesses. This would result in expanded access to innovation by diversifying and reducing the cost of clinical trials while promoting their movement into the clinical setting.

[54] Investigational New Drug (IND) Application. U.S. Food & Drug Administration. https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application#Introduction