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CENTRALIZING PHARMACEUTICAL INNOVATION

SAPNA KUMAR*

The United States has a mostly decentralized system for promoting new medicine development. By offering patents and regulatory exclusivities, the government incentivizes pharmaceutical companies to invent and bring to market new medicines. Although this development model offers benefits for promoting innovation, it comes at a cost: Market-based incentives lead companies to prioritize research and development ("R&D") for medicines that offer a safe path to profitability, as opposed to those that offer the greatest social benefit. In particular, pharmaceutical companies are reluctant to invest in R&D for critically-needed antibiotics and infectious disease vaccines—both of which are difficult to develop and provide uncertain financial returns. This Article proposes that the government oversee the development of needed “infrastructure-adjacent medicines”—medicines that can help prevent future collapses of the public healthcare system and mitigate major economic harm. In addition to boosting internal R&D in such critical areas, the government could directly support innovation by exclusively licensing promising drug candidates from small- to mid-sized entities or by purchasing small biotechnology companies on the open market. When suitable private partners are not available, the government could oversee the final stages of development and retain control over the resulting intellectual property rights. This approach would allow private-sector pharmaceutical development to continue to flourish while filling a critical public health gap.

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This article is dedicated to Dmitry Kashtedt, may he rest in peace.
INTRODUCTION

I. DECENTRALIZATION IN U.S. PHARMACEUTICAL DEVELOPMENT

A. Decentralized Medicine Development Through Market Exclusivities
   1. Patents
      a. Patent Legislation Impacting New Medicine Development
      b. Patents and Decentralization
   2. FDA Regulatory Exclusivities

B. Decentralization of Agencies in Promoting R&D of New Medicines
   1. Early Research
   2. Regulatory Approval for New Medicines

C. Decentralization in New Medicine Development
   1. Early Research & Development
   2. Clinical Trials
   3. Public and Private Insurance Benefits

II. PRIORITIZING GOVERNMENT SUPPORT FOR NEEDED MEDICINES

A. Degree of Market Incentivization
   1. Strongly Market-Driven Medicines
   2. Partially Market-Driven Medicines
      a. Orphan Drugs
      b. Children’s Vaccines
      c. mRNA Vaccines for COVID-19
   3. Non-Market-Driven Medicines
      a. New Antibiotic Development
      b. Medicines for Infectious Diseases Posing Threat of Future Public Health Emergencies

B. Support for Healthcare Infrastructure
   1. An Overview of Infrastructure
   2. Infrastructure-Adjacent Medicines

III. CENTRALIZATION AS A PARALLEL TRACK TO INNOVATION

A. Past Government-Led New Medicine Development
B. Centralized Development of Infrastructure-Adjacent Medicines
   1. Choosing Targets for Centralization
      a. Reducing “Crowding Out” of the Private Sector
      b. Prioritization Based on High Threat Level and Low Commercial Viability
   2. Generating Early Research
INTRODUCTION

New medicine development has thrived in a decentralized, market-driven environment. Consider, for example, the research of scientist Katalin Karikó. As a non-tenure-track professor, she failed repeatedly to obtain government grants for her work on messenger RNA (mRNA), causing the University of Pennsylvania to demote her.1 Yet, Karikó’s groundbreaking work, which government decisionmakers were late to appreciate, would later lead to the development of mRNA vaccines and earn her and her collaborator the Nobel Prize.2 Under a fully centralized system of new medicine development, such a breakthrough would likely not have been possible.

By contrast, centralized government-led development is disfavored.3 Because no one individual possesses all relevant knowledge, a centralized decision-maker may struggle both to acquire needed information and to adapt a chosen approach to changing circumstances.4 With regard to new technologies, government-led research and development (“R&D”) can lead

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4. Id. at 519, 524; see also Tim Wu, Intellectual Property, Innovation, and Decentralized Decisions, 92 VA. L. REV. 123, 127 (2006) (arguing that although decentralization leads to greater waste, it results in greater innovation); CRAIG CALCATERA & WULF KAAL, DECENTRALIZATION: TECHNOLOGY’S IMPACT ON ORGANIZATIONAL AND SOCIETAL STRUCTURE, at XLI (2021) (discussing how centralization reduces waste but leads to ossification).
to dead ends or failures to foresee important advances. Furthermore, centralized hierarchies tend to be risk-averse, meaning that decision-makers may fail to invest in R&D that offers a low chance of success but a potentially large reward. The result is a system that, overall, generates fewer novel ideas compared to a decentralized, private-sector-driven approach.

It is therefore not surprising that the government relies primarily on decentralized new medicine development, offering patents and regulatory exclusivities as incentives. This means that market forces generally dictate what medicines pharmaceutical companies develop. Bringing a new medicine to market is expensive, time-consuming, and risky. The development process typically takes between ten and fifteen years at an average cost of roughly $1 billion, and the clinical trial failure rate is ninety percent. Pharmaceutical companies consequently invest in R&D based on expected development costs, anticipated revenue, and policies that impact supply and demand. This includes making R&D decisions based on how long a medicine must be taken, how much patients can afford to pay, and whether the market for the medicine will remain robust.

The trade-off to this system is the underdevelopment of socially valuable medicines that offer uncertain or limited financial returns. In particular, there are two categories of medicines that support critical healthcare infrastructure that pharmaceutical companies are reluctant to develop. First, pharmaceutical companies generally avoid developing medicines for infectious diseases that currently impact only low-income countries, but that pose a substantial risk of causing a future pandemic or

5. See Calcaterra & Kaal, supra note 4, at XLI (discussing how centralization can lead to blind spots with regard to new information); Michael Kremer, Patent Buyouts: A Mechanism for Encouraging Innovation, 113 Q.J. ECON. 1137, 1137–38 (1998) (noting that “the government may not know the costs and expected benefits of research, and may not even be able to conceive of some inventions”).

6. See Wu, supra note 4, at 130–31 (noting that unlike decentralized polyarchies, hierarchies reject too many good ideas, including projects that turn out to be profitable).

7. Id.


11. See infra Section I.C.

12. See infra Section II.A.3.
epidemic. Profitability is too uncertain because a future public health emergency may never arise or may occur only after the relevant patents have expired. Consequently, the expected financial return is not proportionate to the benefit society receives.

Second, few pharmaceutical companies are willing to develop new antibiotics, and those that do rely on heavy government subsidization. New antibiotics are not viewed as profitable for several reasons. For example, health care practitioners often reserve new antibiotics as a last line of defense, using them only when older medicines fail to reduce the risk of antimicrobial resistance (“AMR”). This lack of new development is problematic because AMR is accelerating, meaning that a steady pipeline of new antibiotics is needed to prevent future deaths.

This Article proposes that the U.S. government create a centralized path of development for medicines that would support critical healthcare infrastructure but that pharmaceutical companies will not develop with traditional forms of government support. Rather than relying exclusively on long-term public-private partnerships (“PPPs”), in which the government cedes its intellectual property (“IP”) rights to a private partner in exchange for the partner assuming the risk of failure, the burdens and benefits would stay with the government. This model would create an alternative path for developing critically needed medicines that current approaches fail to incentivize.

This Article is structured in five parts. Part I looks at the current model for incentivizing the development of new medicines. It discusses how the current system of market exclusivities promotes decentralized development

13. See Ana Santos Rutschman, IP Preparedness for Outbreak Diseases, 65 UCLA L. REV. 1200, 1209 (2018) (noting that private companies “engaging in costly and risky R&D” are more likely to focus resources towards developing drugs for diseases that will financially pay off).
14. See infra Section III.C.
15. See infra Section III.C.
16. See Cecilia Källberg et al., Introduction and Geographic Availability of New Antibiotics Approved Between 1999 and 2014, PLOS ONE, Oct. 16, 2018, at 2 (noting antibiotics are “high-risk projects, with limited market potential” leading many companies to not develop them); Michael Eisenstein, Championing Research into Neglected Diseases, 598 NATURE S20, S21 (2021) (discussing how antibiotic developers struggle with solvency); see also infra Section II.A.3.a.
17. See infra Section II.A.3.a (discussing barriers to new antibiotic development).
19. See infra Section II.A.3.a.
and discusses existing fragmentation among government agencies that work in this space. It then explains how decentralization shapes the types of medicines that companies develop. Part II looks at the varying degrees of market incentivization for medicines, classifying them as either strongly market-driven, partially market-driven, or non-market-driven. It then explains how certain medicines play a vital role in supporting healthcare infrastructure by preventing the health care system from collapsing and staving off excess deaths and disability.

Part III then proposes that centralization be used in parallel to the existing system. For non-market-driven medicines that support critical healthcare infrastructure, the government could both boost internal R&D and also acquire the rights to promising drug candidates. By licensing medicines from smaller biotechnology companies, or purchasing such companies outright, the government could reduce internal blind spots and help create a market for early R&D in high-priority areas. The government would continue to use long-term PPPs where they are cost-effective and do not lead to excessive delays or harm to the public. But in some circumstances, the government would sponsor its own clinical trials and seek market approval for its medicines. This approach would allow the government to retain ownership of relevant IP rights, meaning that the government could broadly license medicines that reduce the transmission of infectious diseases, while strictly controlling the use of its new antibiotics. This Article concludes that the proposed approach would allow private-sector development to continue to flourish while closing dangerous gaps.

I. DECENTRALIZATION IN U.S. PHARMACEUTICAL DEVELOPMENT

U.S. pharmaceutical development is largely decentralized, with the government relying on market exclusivities to incentivize new medicine development. The agencies that support new medicine R&D—including the National Institutes for Health (“NIH”), Biomedical Advanced Research Development Authority (“BARDA”), Department of Defense (“DoD”), and Food and Drug Administration (“FDA”)—furthermore act with little coordination. These factors, coupled with the regimented process of developing new medicines, skew pharmaceutical companies’ R&D priorities.

Section A considers how patent rights and regulatory exclusivities promote decentralized pharmaceutical development. Section B discusses the various U.S. agencies that play a role in new medicine R&D. Section C then examines how decentralization shapes the types of medicines that pharmaceutical companies develop.
A. Decentralized Medicine Development Through Market Exclusivities

The U.S. government uses market exclusivities to incentivize new medicine development. Patents from the U.S. Patent & Trademark Office ("PTO") and regulatory exclusivities from the FDA shield pharmaceutical companies from generic medicine competition and increase the profitability of new medicines.

1. Patents

Patents promote decentralization in new medicine development by not only allowing inventors to exclude others from practicing the invention, but also facilitating the transferring of inventions between small and large pharmaceutical companies. This allows for small companies to serve as the innovators in bringing drug candidates to clinical trials and for larger companies to take the financial risks of obtaining FDA approval and marketing the medicine.

a. Patent Legislation Impacting New Medicine Development

Ordinarily, a new invention would be a public good: It would be non-rivalrous because one person’s use of the invention does not reduce the amount available to others, and it would be non-excludable due to the difficulty of preventing others from using the invention. Absent patent protection, third parties could freely use inventions without paying royalties, making it difficult for the inventor to earn a profit commensurate with the invention’s social benefits. The Patent Act changes this default by creating a type of property right for inventions. Patents issued by the PTO allow inventors to exclude others from making, using, selling, and importing their medicines for a limited time. This allows an inventor to capture a portion

21. See infra Sections I.A.1–2.
22. See 35 U.S.C. § 154(a)(1) (noting that every patent grants a “right to exclude others” from activities including making, using, and selling the patented invention); id. § 261 (noting that “patents shall have the attributes of personal property” and “shall be assignable in law”).
24. Id. at 307–08.
25. Commentators vary on how analogous they view patents to real property, versus newer forms of property such as government benefits. See Cynthia M. Ho, Unveiling Competing Patent Perspectives, 46 HOUS. L. REV. 1047, 1057–58 (2009) (observing that some commentators view patents “as a privileged property right”).
26. 35 U.S.C. § 154(a)(2) (specifying the patent term); id. § 271(a) (specifying what constitutes patent infringement).
of the invention’s economic value, therefore reducing the gap between the inventor’s financial benefit and the invention’s societal benefit.\textsuperscript{27}

Government agencies fund a substantial amount of private research.\textsuperscript{28} Notwithstanding the government’s use of taxpayer funds, under the Bayh-Dole Act, researchers and companies may patent and commercialize resulting inventions.\textsuperscript{29} Although the government retains “march-in rights” that allow it to use such inventions without paying a royalty in certain circumstances,\textsuperscript{30} such rights are only theoretical, because the government has never exercised them before.\textsuperscript{31}

A patent’s term begins on the date of issuance, yet ends twenty years after the original patent application’s filing date.\textsuperscript{32} Because it can take years for the PTO to issue a patent, the effective term is always shorter than twenty years.\textsuperscript{33} Moreover, there is an additional obstacle for new medicines: Companies cannot market new medicines until they receive FDA approval, which can take several years.\textsuperscript{34} Consequently, without an adjustment to the patent term, medicines would receive a substantially shorter exclusivity period.\textsuperscript{35}

Although the Patent Act offers a patent term restoration process for medicines,\textsuperscript{36} this process does not return all the lost time. For example, there is a five-year maximum that is restored for time lost to the FDA approval process and a limit of fourteen years of protection after FDA approval.\textsuperscript{37} Consequently, pharmaceutical companies have an incentive to develop

\begin{itemize}
\item \textsuperscript{27} See Mandel, supra note 23, at 308 (noting that patent law “bring[s] the private benefits of invention more in line with their social value”).
\item \textsuperscript{28} See infra Section I.B.
\item \textsuperscript{29} Sapna Kumar, Compulsory Licensing of Patents During Pandemics, 54 CONN. L. REV. 57, 70–73 (2022).
\item \textsuperscript{30} 35 U.S.C. §§ 202(a), 202(c)(1), 203(a)(2).
\item \textsuperscript{31} Kumar, supra note 29, at 72–73. Note that in December of 2023, the government sought comments on a proposal to use march-in rights as a mechanism for controlling the prices of medicines that are derived from government-funded research. Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights, 88 Fed. Reg. 85593 (Dec. 8, 2023).
\item \textsuperscript{32} 35 U.S.C. § 154(a)(2).
\item \textsuperscript{33} Cynthia M. Ho, Inoculation Inventions: The Interplay of Infringement and Immunity in the Development of Biodefense Vaccines, 8 J. HEALTH CARE L. & POL’Y 111, 123 (2005).
\item \textsuperscript{34} Erika Lietzan, The History and Political Economy of the Hatch-Waxman Amendments, 49 SETON HALL L. REV. 53, 68 (2018).
\item \textsuperscript{35} See id. (discussing problems of shortened patent terms for new medicines prior to the passage of Hatch-Waxman).
\item \textsuperscript{36} 35 U.S.C. § 156.
\item \textsuperscript{37} See Erika Lietzan & Kristina M.L. Acri née Lybecker, Distorted Drug Patents, 95 WASH. L. REV. 1317, 1335–37 (discussing patent restoration restrictions).
\end{itemize}
medicines that can quickly clear clinical trials to maximize the monopoly period.  

b. Patents and Decentralization

Decentralization is a background principle for the patent system, with companies making decisions based on market forces, as opposed to government guidance. The reasoning behind this approach is that no single entity possesses all of the relevant information needed to make accurate assessments of what should be developed. Companies may possess better information regarding R&D costs than the government. They can direct attention to improving technologies that the market deems beneficial but that have escaped the notice of policymakers. Because patents are not awarded to unsuccessful inventions, companies must carefully consider which lines of research they pursue, balancing the cost of developing a new invention with the potential for a financial payoff.

Patents facilitate another form of decentralization by allowing ideas and inventions to be transferred at various stages of development. Researchers at universities and small- to mid-sized entities (“SMEs”) may initially advance an invention forward through early R&D, with a larger company later acquiring and assembling the necessary pieces of technology to create a commercially viable product. Through a combination of patents rights and contracts, the conception and development of inventions can be decoupled, as can the roles of early development and bringing a product to market.
This practice is widespread in pharmaceutical development. Medicines are generally protected by several patents, meaning the ability to assemble rights from various parties is critical. Academic researchers frequently identify promising new drug targets, while venture-capital-funded SMEs tend to be active in drug discovery, preclinical development, and early-stage clinical trials. Seventy percent of Phase III clinical trials are initiated by small biotechnology companies with less than $500 million in annual revenue, while only twenty percent are initiated by large companies. Because smaller companies generally cannot afford the cost of obtaining regulatory approval and lack relevant expertise to do so, they frequently sell promising drug candidates to large companies. This decentralization means that the R&D agenda of SMEs is intertwined with that of larger companies—the possibility of acquisition helps SMEs attract initial venture capital funding and shapes SMEs’ early research. As discussed in Part II, this can create problems if large pharmaceutical companies pull out of the market for a societally valuable type of medicine, such as antibiotics.

The patent system’s one-size-fits-all system also under-incentivizes groundbreaking pharmaceutical research. Those who invent needed novel medicines do not necessarily receive a financial reward that captures the full


48. Christoph H. Emmerich et al., Improving Target Assessment in Biomedical Research: The GOT-IT Recommendations, 20 NATURE REV. DRUG DISCOVERY 64, 64 (2021). Target validation is often the first step in developing a new medicine; the researcher must show a medicine effects a drug target in the body “linked to a disease process.” Id.

49. See CONG. BUDGET OFF., supra note 10, at 3–4 (discussing how small companies contribute to new medicine development); Shiva Khalafpour, Supporting Drug Product Innovation Through Small Biotech Companies, DRUG DISCOVERY & DEV. (Apr. 12, 2019), https://www.drugdiscoverytrends.com/supporting-drug-product-innovation-through-small-biotech-companies/ (noting small biotechnology companies rely on venture capital funding for early R&D, then license medicines to larger companies after they clear Phase I clinical trials).

50. CONG. BUDGET OFFICE, supra note 10, at 4.

51. Id.


53. See Gabriela Gracia et al., Incentives for Drug R&D: A Survey of Biotech Venture Capitalists’ Perspectives, HEALTH AFFS. FOREFRONT (July 20, 2022), https://www.healthaffairs.org/content/forefront/incentives-drug-r-d-survey-biotech-venture-capitalists-perspectives (discussing how venture capitalists invest in small companies “with the aim of being acquired by a large pharma company”).

54. See infra Section II.A.3.a.
benefit to society. Pharmaceutical companies consequently seek to develop incremental improvements, such as extended release formulations of existing medicines, which are cheaper and easier to develop. By making minor improvements to existing lucrative medicines, companies can receive additional patents that they then use to artificially extend their monopoly period—a process known as “evergreening.” Such improvements may offer little real benefit to patients and can sometimes be harmful.

2. FDA Regulatory Exclusivities

The FDA provides companies with regulatory exclusivities that incentivize new medicine development by shielding medicines from generic competition. FDA exclusivities serve a similar role to patents: They promote innovation through a grant of an exclusory right to the name-brand medicine producer. For example, if a pharmaceutical company creates a new small-molecule medicine, the FDA provides it with a five-year New Chemical Entity exclusivity, during which time a generic manufacturer cannot submit an Abbreviated New Drug Application for the same active ingredient to the FDA. Given that it takes one to two years for the FDA to approve such applications, new small-molecule drugs receive effectively a...

55. Kremer, supra note 5, at 1137 (noting how patents “create insufficient incentives for original research, since inventors cannot fully capture consumer surplus or spillovers of their ideas to other researchers”).


59. See Robin C. Feldman et al., Negative Innovation: When Patents Are Bad for Patients, 39 NATURE BIOTECH. 914, 914 (2021) (discussing how patents sometimes incentivize companies to bring harmful medicines to market).

60. See Eisenberg, The Role of the FDA in Innovation Policy, supra note 8, at 359, 361 (referring to FDA exclusivities as “pseudo-patents”).

61. Small-molecule drugs are drugs produced through chemical synthesis and are typically taken orally as pills or tablets. See Kumar, supra note 29, at 97–98.

62. When a pharmaceutical manufacturer wants to market and sell a new medicine, they must file a New Drug Application, which is required to contain various data to establish the medicine’s safety and effectiveness. New Drug Application (NDA), U.S. FOOD & DRUG ADMIN. (Jan. 21, 2022), https://www.fda.gov/drugs/types-applications/new-drug-application-nda. By contrast, if a manufacturer is seeking to market and sell a generic equivalent of an existing FDA-approved medicine, it can utilize the less onerous Abbreviated New Drug Application instead, which generally does not require preclinical and clinical data to establish safety and effectiveness. Abbreviated New Drug Application (ANDA), U.S. FOOD & DRUG ADMIN. (Dec. 16, 2022), https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-nda.

six-to-seven year period without generic competition. 64 The FDA awards a twelve-year exclusivity period to biologics, which includes vaccines. 65 If a company conducts new clinical trials to establish a new way of delivering an active ingredient in a medicine or to establish a different disease that the medicine can treat, it is eligible for a three-year new clinical investigation exclusivity. 66 During this time, the FDA can accept a generic application but cannot grant it until the exclusivity expires. 67

The government may also tailor exclusivities to advance specific policy goals. For example, the FDA offers a special exclusivity to pharmaceutical companies that develop “orphan drugs” to treat “orphan diseases”—diseases that either affect fewer than 200,000 people domestically or for which there is no reasonable expectation that sales would recover the costs of R&D. 68 This includes a seven-year marketing exclusivity, which allows the beneficiary to exclude generic competitors even if the orphan drug’s patents have expired. 69

B. Decentralization of Agencies in Promoting R&D of New Medicines

In the United States, a decentralized administrative approach supports new medicine development, with powers distributed among various federal agencies. The NIH, BARDA, and DoD all contribute to the development of new medicines, while the FDA regulates which medicines can be sold.

1. Early Research

The NIH is part of the U.S. Department of Health and Human Services (HHS) and has a budget of over $40 billion to support biomedical research. 70 More than eighty percent of the funds support research at universities and other external institutions, while roughly eleven percent of the funds support


65. Sandoz, Inc. v. Amgen, Inc., 582 U.S. 1, 7 (2017) (discussing how under 42 U.S.C. § 262, “the manufacturer of a new biologic enjoys a 12-year period when its biologic may be marketed without competition from biosimilars”). Biologics are large-molecule medicines derived from living organisms. They tend to be harder to produce compared to small-molecule medicines. Kumar, supra note 29 at 98–99. Biosimilars are biological products that are highly similar to an FDA-approved biologic. Sandoz, 582 U.S. at 5.

66. 21 C.F.R. § 314.108(b) (2022).


68. 21 U.S.C. § 360bb(a)(2). Orphan drug developers can also receive tax credits and fee waivers. Feldman, supra note 67, at 75 & n.108.

69. Feldman, supra note 67, at 75.

research at NIH laboratories. The NIH’s internal Intramural Research Program is the largest biomedical research institute in the world, with 1,200 principal investigators and more than 4,000 postdoctoral fellows. The NIH sometimes supports early clinical trials for medicines it helps develop; for example, the NIH helped fund R&D and Phase I clinical trials for three experimental HIV vaccines using mRNA technology.

BARDA was established in 2006 as an HHS subagency; it supports the development of medicines and tools needed to address public health emergencies—such as pandemics, bioterrorism, and emerging infectious disease threats. For example, in 2016, BARDA launched the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), a global non-profit partnership that provides early-stage funding to start-ups and biotechnology companies developing new antibiotics. Under Operation Warp Speed, BARDA funded companies that were developing vaccines and treatments for COVID-19.

The DoD also helps develop vaccines to protect against infectious diseases. Much of this work occurs through the U.S. Army’s Walter Reed Army Institute of Research (“Walter Reed”). For example, for meningococcal disease, Walter Reed conducted early R&D and ran Phase I through III clinical trials for vaccine candidates. In collaboration with the Thailand government, Walter Reed developed an HIV vaccine and ran a Phase III trial, though the efficacy was ultimately too low for the vaccine to be brought to market. Although there is overlap between the DoD and BARDA’s missions, they are not the same: The DoD focuses on immunizing

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71. Budget, supra note 70.
74. 42 U.S.C. § 247d-7e (establishing BARDA).
76. Id. at 9.
77. Id. at 9, 27–28.
78. See ANA SANTOS RUTSCHMAN, VACCINES AS TECHNOLOGY 51 (2022) (discussing the history of the U.S. military in developing new vaccines).
troops prior to exposure to infectious diseases and has expertise in logistics, while BARDA focuses on protecting civilians from bioterrorism events, nuclear disasters, and emerging infectious diseases.\textsuperscript{81}

2. Regulatory Approval for New Medicines

The FDA is part of HHS and is charged with “protecting the public health by ensuring the safety, efficacy, and security” of medicines.\textsuperscript{82} Before a pharmaceutical company can market a new medicine to consumers, it must be FDA approved.\textsuperscript{83} This typically involves a multi-stage process, including preclinical testing, the submission of an Investigational New Drug Application, Phase I through III trials, and the submission of a New Drug Application.\textsuperscript{84} The cost and time that it takes for a drug candidate to go through the FDA process can impact which R&D a pharmaceutical company undertakes and the type of medicines that it is willing to develop.\textsuperscript{85}

In addition to promoting safety, the FDA promotes innovation.\textsuperscript{86} Beyond offering regulatory exclusivities, it is attempting to streamline clinical trials, modernize the approval process, and reduce barriers to generic medicine development.\textsuperscript{87} Furthermore, the FDA rewards development for medicines treating certain tropical diseases by granting the pharmaceutical company a priority review voucher,\textsuperscript{88} which allows the holder to get priority review for a subsequent drug application that does not qualify for special

\textsuperscript{81} See id. at 10 (discussing the differing missions of BARDA and the DoD).


\textsuperscript{85} See infra Section I.C.

\textsuperscript{86} As Rebecca Eisenberg has noted, FDA approval “confers valuable exclusionary rights as a reward for investing in certain kinds of R&D, thereby adding to both the profits and costs of drug development.” Eisenberg, The Role of the FDA in Innovation Policy, supra note 8, at 348.


Rare pediatric disease medicine developers can also receive such a voucher.89

C. Decentralization in New Medicine Development

New medicine development is a multi-stage process that can take many years.91 Each phase of development impacts the decisions that private pharmaceutical companies make regarding the diseases to target and the types of medicines to develop.

1. Early Research & Development

The potential marketability of medicines shapes early R&D. Pharmaceutical companies seek to develop medicines with a lucrative and sustained market that will support high stock prices.92 Larger companies’ development decisions also have ripple effects on smaller companies. SMEs are the drivers of new pharmaceutical innovation, spending a greater percentage of their research budget on developing new medicines, many of which are sold to larger companies.93 If larger companies are not buying a particular class of medicines, then SMEs are less likely to invest in that area.94

Consequently, some socially beneficial areas attract little early R&D. Companies have developed few new classes of antibiotics in the past twenty years because such medicines are challenging to develop and yield little profit.95 There is similarly a chronic lack of funding for research involving infectious diseases that primarily affect poorer populations, particularly outside the “big three” of HIV/AIDS, malaria, and tuberculosis.96

89. Id.


92. Rutschman, supra note 13 at 1209 (noting that private companies “engaging in costly and risky R&D” are more likely to focus resources towards developing drugs for diseases that will financially pay off); Yaniv Heled, Ana Santos Rutschman & Liza Vertinsky, The Problem with Relying on Profit-Driven Models to Produce Pandemic Drugs, J.L. & BIOSCIENCES, Jan.–June 2020, at 1, 8 (arguing stock prices drive R&D decisions).

93. CONG. BUDGET OFF., supra note 10, at 3–4 (noting small companies concentrate on research and account for 70% of medicines in Phase III trials, while large companies often acquire small companies with promising medicines).

94. See infra Section II.A.3 (discussing antibiotic development).

95. See Källberg et al., supra note 16, at 2 (noting antibiotics are “high-risk projects, with limited market potential” leading many companies to not develop them); Eisenstein, supra note 16, at S21 (discussing how antibiotic developers struggle with solvency).

NIH funding also shapes early R&D. A study of FDA drug approvals in a ten-year period showed that nineteen percent of them “had origins in publicly supported research and development.” 97 Such funding, however, does not always correlate to present or future disease burden. Diseases that in the past received high amounts of funding may continue to do so, even if a disease has become more or less burdensome over time. 98

Early R&D funding may also depend on what population gets a disease. For example, sickle cell disease and cystic fibrosis are both inherited disorders that lead to hospitalizations, a reduced quality of life, and a substantial reduction in life span; sickle cell disease primarily impacts African-American women, while cystic fibrosis primarily impacts white women. 99 Although sickle cell disease is three times as common in the United States as cystic fibrosis, both diseases received equal federal funding from 2008 to 2018. 100 Women’s reproductive health is also underfunded. 101 Cancers that are associated with stigmatized behaviors or that involve “embarrassing” body parts receive less funding compared to non-stigmatized cancers. 102 For example, the National Cancer Institute awarded lung cancer

98. Jeromie M. Ballreich et al., Allocation of National Institutes of Health Funding by Disease Category in 2008 and 2019, JAMA NETWORK OPEN, Jan. 27, 2021, at 1, 9, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7841468/ (“[T]he distribution of NIH funding for 46 specific diseases in 2019 was remarkably similar to that observed in 2008 (and for 29 diseases in 1996), despite changes in burden of disease.”).
102. See Suneel D. Kamath et al., Comparison of Cancer Burden and Nonprofit Organization Funding Reveals Disparities in Funding Across Cancer Types, 17 J. NAT’L COMPREHENSIVE CANCER NETWORK 849, 852–53 (2019) (discussing how cancers receive less funding if they are associated with stigmatized behavior or embarrassing body parts).
research $225 million less than breast cancer in 2018, even though lung cancer kills substantially more Americans.\textsuperscript{103}

Early R&D is further impacted by the reliability and constancy of available funding. As legal scholar Ana Santos Rutschman noted, for infectious diseases with the potential to trigger epidemics and pandemics, funding varies based on whether an outbreak currently exists.\textsuperscript{104} Yet, temporary spikes in funding are not conducive to the multi-year R&D process for developing new medicines.\textsuperscript{105} For example, during the 2016 Zika virus outbreak, scientists resorted to crowdfunding research money after Congress stalled on authorizing funding and while the NIH waited for approval to reallocate unused Ebola funds.\textsuperscript{106}

2. Clinical Trials

In developing new medicines, pharmaceutical companies must consider the expense of conducting clinical trials.\textsuperscript{107} It costs an average of $48 million to run a “pivotal trial[]” that demonstrates the efficacy of a medicine to the FDA.\textsuperscript{108} However, several factors can make trials even more expensive. Each additional month required for a Phase III trial costs an average of $671,000.\textsuperscript{109} The more patients that are needed to establish efficacy and the more visits the patients must make to the study clinic, the more expensive the trial will be.\textsuperscript{110} If a company must replicate its results in a second trial, the cost goes up further.\textsuperscript{111}

The patent system disincentivizes the development of medicines that require longer clinical trials. As discussed earlier, the default patent term ends twenty years after the application’s filing date,\textsuperscript{112} incentivizing R&D for

\begin{itemize}
  \item \textsuperscript{103} Lung cancer received only $350 million in 2018 from the National Cancer Institute, while breast cancer received $575 million. Heather Grey, \textit{MNT Investigates: How Lung Cancer Stigma Holds Back Research and Treatment}, MED. NEWS TODAY (Apr. 1, 2021), https://www.medicalnewstoday.com/articles/lung-cancer-stigma-holds-back-treatment-research.
  \item \textsuperscript{104} Rutschman, \textit{supra} note 13, at 1207.
  \item \textsuperscript{105} Id.; see also Clare Wenham, \textit{The Oversecuritization of Global Health: Changing the Terms of Debate}, 95 INT’L AFFS. 1093, 1107 (2019) (discussing the risk of short-term reactive responses to global health security).
  \item \textsuperscript{107} Linda Martin et al., \textit{How Much Do Clinical Trials Cost?}, 16 NATURE REV. 381, 381 (2017).
  \item \textsuperscript{109} Martin et al., \textit{supra} note 107, at 381.
  \item \textsuperscript{110} Moore et al., \textit{supra} note 108.
  \item \textsuperscript{111} Id.
  \item \textsuperscript{112} 35 U.S.C. § 154(a)(2).
\end{itemize}
medicines that can be quickly approved, as opposed to those that can help people the most. Because late-stage diseases such as Stage IV cancer progress quickly, companies can more easily prove a positive response in clinical trials, leading to faster FDA approval. Likewise, treatments for hematologic cancers, such as leukemia and lymphoma, are easier to establish efficacy through blood cell counts. By contrast, a company must run a longer trial to show that a medicine prevents a disease, such as Alzheimer’s, or that it helps treat early stages of a disease like cancer, meaning companies are less likely to develop such medicines. Economists argue that this “patent distortion” cost the United States $89 billion for just cancer in 2003 alone.

3. Public and Private Insurance Benefits

The U.S. multi-payer health insurance system influences the type of medicines that pharmaceutical companies develop. Health insurance coverage is subject to heavy “churn,” with fifteen to twenty percent of individuals experiencing either disruption in coverage or a change in insurance plan. This creates a time-based fragmentation problem: The insurer may not have a financial incentive to pay for a costly preventative treatment or cure, even if it is cheaper when averaged out over the lifetime of the patient. As legal scholar Rachel Sachs observed, if an insurer delays paying for a costly drug, it will save money if the patient later switches insurance. This behavior incentivizes pharmaceutical companies to

115. Budish et al., supra note 113.
116. See Rachel E. Sachs, Pricing Insurance: Prescription Drug Insurance as Innovation Incentive, 30 HARV. J.L. & TECH. 153, 164 (2016) (discussing how patent term expiration “favors interventions whose effect can be measured using surrogate endpoints rather than true endpoints,” and, when true endpoints must be used, favors therapeutic interventions over preventative ones).
117. Budish et al., supra note 113, at 2048, 2081. Although the Hatch-Waxman Act created exclusivities to help offset part of the lost patent term, it has been insufficient at mitigating this effect. Id.
119. See id. (discussing how churn “reduces insurer incentives to invest in preventative care”); Sachs, supra note 70, at 69–76 (discussing how time-based fragmentation impacts insurers’ willingness to pay for one-time treatments and cures).
120. Sachs, supra note 70, at 73.
develop lower-cost maintenance medicines that insurers are more likely to cover.121

State Medicaid coverage of Hepatitis C cures illustrates this problem. Although these medicines are cost-effective over the life of the patient, they cost between $25,000 and $95,000, which can strain state budgets.122 A majority of state programs consequently limit access, such as by treating only sober individuals or only those who have liver damage.123 The rationale is if the patient later switches off of public insurance, then the state saves money.

Government purchasing of medicines through the Medicare and Medicaid programs also influences medicine development. Under a current proposal, medicines would be eligible for Medicare price negotiations after nine years for small-molecule drugs, and thirteen years for biologics.124 Some argue that this could push pharmaceutical companies to focus more on biologic development.125 Decisions the government makes with regard to which prescription medicines it will partially or fully cover further impacts private R&D decisions.126

Overall, the impact of decentralization through market-based exclusivities, regulatory fragmentation, and the new drug development process contributes to societally valuable medicines not getting developed. Part II further explores the problems that these gaps create.

II. PRIORITIZING GOVERNMENT SUPPORT FOR NEEDED MEDICINES

To better understand the gaps in new medicine development, it helps to consider where medicines fall along two different axes: the degree of market incentivization and the level of support they provide for healthcare infrastructure. This framework reveals the important role that certain classes of non-market-driven medicines play in safeguarding the public health

121. Id. at 76–77.
126. CONG. BUDGET OFF., supra note 10, at 2.
system in times of emergency, as well as in preventing excess death and disability.

Section A looks at the degree of market incentivization for medicines, classifying them as either strongly market-driven, partially market-driven, or non-market-driven. Section B then discusses what health care infrastructure is and how “infrastructure-adjacent” medicines play a critical role in supporting it. Section B further observes that infrastructure-adjacent medicines generate significant externalities, making it challenging for pharmaceutical companies to profit from them. Such externalities mean that companies are reluctant to develop two important groups of infrastructure-adjacent non-market-driven medicines—new antibiotics and infectious-disease vaccines for diseases posing a substantial risk of a future epidemic or pandemic.

A. Degree of Market Incentivization

Medicines vary based on how much the market incentivizes their development. Strongly market-driven medicines do not require public support because patents and regulatory exclusivities sufficiently compensate the developer.127 Partially market-driven medicines benefit from moderate subsidies, such as support for early R&D or clinical trials.128 Finally, non-market-driven medicines will not be developed absent heavy government subsidization.129

1. Strongly Market-Driven Medicines

Strongly market-driven medicines do not require public support. Pharmaceutical companies engage in such R&D because it is neither prohibitively expensive nor time-consuming. They fund such clinical trials because efficacy is not unduly difficult to establish. A robust long-term market exists for the final medicine, promising a significant payoff to the developer. In this regard, market-driven medicines tend to most closely resemble classic private goods: The government can entrust their development to the private sector.

Several types of medicines fall into this category. Medicines that must be taken indefinitely to manage chronic health conditions or to treat their symptoms can be highly profitable.130 Unlike with cures, maintenance medicines do not erode their own market and can therefore yield significant

127. See infra Section II.A.1.
128. See infra Section II.A.2.
129. See infra Section II.A.3.
long-term profits.131 Specialty disease medicines that can be sold at high prices, such as late-stage cancer treatments, are also achieving “blockbuster” status.132 Medicines that offer incremental innovation over the developer’s existing medicines are also strongly market-driven, because the developer can piggyback off its work from the original medicine.133

A good example of a strongly market-driven medicine is Pfizer’s cholesterol drug Lipitor, which generated $94.67 billion in U.S. sales between 1992 and 2017.134 Although it was not the first statin on the market, it became a blockbuster due to both heavy marketing and a study showing that it could reduce heart attacks.135 High cholesterol is a chronic condition that statins do not cure, meaning that patients must take them indefinitely to manage the condition,136 thereby ensuring a steady stream of revenue.

2. Partially Market-Driven Medicines

Other medicines are only partially market-driven. This group includes those with a limited market in high-income countries or that require somewhat slow, risky, or expensive R&D. Although market forces alone may not adequately incentivize such medicines,137 additional modest subsidies can make them viable for private development. The government may consequently offer additional regulatory exclusivities and/or “push funding”—funding that supports a company’s R&D costs.138 Less frequently, the government offers “pull funding,” by pre-purchasing medicines to artificially boost the medicine’s market.139 It may also pass legislation to indemnify pharmaceutical manufacturers in certain circumstances, as it has

131. Id.; see also Sachs, supra note 70, at 77 (discussing a leaked Goldman Sachs report questioning whether “curing patients [is] a sustainable business model”).
133. See Ho, supra note 57, at 312 (discussing how incremental innovation is cheaper if pharmaceutical companies can rely on earlier clinical data to obtain FDA approval).
135. Id.
137. Gifford, supra note 39, at 82.
138. See J. Cama et al., To Push or To Pull? In a Post-COVID World, Supporting and Incentivizing Antimicrobial Drug Development Must Become a Governmental Priority, 7 ACS INFECTIOUS DISEASES 2029, 2030–31 (2021) (discussing governments’ attempts to spur antimicrobial development through push funding).
139. Id. at 2031.
done for certain vaccines.\textsuperscript{140} The FDA may furthermore expedite the approval process to allow urgently needed medicines to be marketed, such as through emergency use authorizations.\textsuperscript{141}

A key attribute of partially market-driven medicines is that market exclusivities only partially incentivize their R&D, because anticipated sales alone are not sufficient to justify their development. Orphan drugs, childhood vaccines, and mRNA COVID-19 vaccines, each discussed below, provide good illustrations.

\textit{a. Orphan Drugs}

The FDA offers various exclusivities for medicines treating orphan diseases, including a seven-year marketing exclusivity.\textsuperscript{142} This has yielded medicines for previously untreatable rare diseases, albeit at an extremely high cost to patients. For example, in 2016, Biogen Inc.’s Spinraza became the first FDA-approved medicine to treat spinal muscular atrophy,\textsuperscript{143} with a one-year supply costing a staggering $750,000.\textsuperscript{144}

Orphan drug exclusivities illustrate the difficulty of tailoring incentives to the types of medicines that need it. Companies frequently seek orphan status for popular mass-market medicines by running studies to show that the existing medicine can treat a new rare disease.\textsuperscript{145} Sometimes companies will do this multiple times.\textsuperscript{146} For example, the FDA approved AbbVie’s Humira in 2002 to treat millions of Americans suffering from rheumatoid arthritis, designated it as an orphan drug for juvenile rheumatoid arthritis several years later, then provided it with orphan designation for four more diseases.\textsuperscript{147} This resulted in AbbVie gaining market exclusivity until 2023—notwithstanding

\begin{itemize}
\item \textsuperscript{142} See supra Section I.A.2.
\item \textsuperscript{146} Id.
\item \textsuperscript{147} Id.
\end{itemize}
the fact that Humira was already the best-selling medicine in the world.\textsuperscript{148} Indeed, a 2023 study showed that orphan drugs earn nearly as much as non-orphan medicines.\textsuperscript{149} Overall, an argument can be made that many medicines that benefit from orphan status do not require this much government support.\textsuperscript{150}

\textit{b. Children’s Vaccines}

The government supports childhood vaccine development in several ways. The federal Vaccines for Children program covers the cost of certain vaccines for poor children who otherwise would not be able to afford vaccination.\textsuperscript{151} Furthermore, the Centers for Disease Control and Prevention (“CDC”) publishes a schedule of recommended vaccines, which helps to increase vaccine demand.\textsuperscript{152} Finally, the government partially shields childhood vaccine manufacturers from liability under the National Childhood Vaccine Injury Act.\textsuperscript{153} This legislation established the National Vaccine Injury Compensation Program, which financially compensates parents who allege injuries to their children from properly formulated vaccines.\textsuperscript{154}

\textit{c. mRNA Vaccines for COVID-19}

Moderna and Pfizer’s mRNA COVID-19 vaccines provide another illustration of a partially market-driven medicine.\textsuperscript{155} In the early R&D stage, the government spent $900 million to support pre-clinical studies of

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\textsuperscript{149} See S. Sean Tu et al., \textit{Five-Year Sales for Newly Marketed Prescription Drugs with and Without Initial Orphan Drug Designation}, 329 JAMA 1607–08 (2023), https://jamanetwork.com/journals/jama/fullarticle/2804613 (noting that there was no significant difference between sales of orphan and non-orphan medicines).

\textsuperscript{150} Indeed, when Congress passed the Inflation Reduction Act authorizing Medicare to negotiate lower prices for certain medicines that exceed $200 million a year in spending, it carved out medicines that treat a single rare disease, but not those that treated multiple diseases. The reason for the “sole orphan exemption” was to keep top-selling medicines eligible for negotiations. Matthew Vogel et al., \textit{Cost of Exempting Sole Orphan Drugs from Medicare Negotiation}, 184 JAMA INTERNAL MED. 63, 64 (2023).

\textsuperscript{151} CONG. BUDGET OFF., supra note 10, at 22.

\textsuperscript{152} See id. (noting a study showed the CDC’s inclusion of the hepatitis B vaccine on the childhood vaccine schedule was associated with an increase in vaccine development).

\textsuperscript{153} 42 U.S.C. § 300aa-1 \textit{et seq.}

\textsuperscript{154} Falvey, \textit{supra} note 140.

\end{footnotesize}
candidate COVID-19 vaccines.\textsuperscript{156} It then spent $2.7 billion to cover human trials, particularly Phase III trials, for several large pharmaceutical companies.\textsuperscript{157} The U.S. government also used pull funding: In the summer of 2020, it ordered 100 million doses of Pfizer’s vaccine for $1.95 billion\textsuperscript{158} and 100 million doses of Moderna’s vaccine for $1.53 billion.\textsuperscript{159} This was in addition to pre-purchase agreements with Johnson & Johnson, Sanofi, and GlaxoSmithKline\textsuperscript{160} and purchases of additional vaccine doses after the vaccines received emergency FDA approval.\textsuperscript{161} This support reduced pharmaceutical companies’ risk, helped hasten development, and gave Americans expedited access to the new medicines.\textsuperscript{162}

The government also broadly shielded manufacturers from legal liability. The Public Readiness and Emergency Preparedness Act (“PREP”) provides COVID-19 vaccine manufacturers with broad immunity from “all claims for loss” under state and federal law.\textsuperscript{163} Unlike with the National Childhood Vaccine Injury Act, PREP excepts only death or serious physical injury caused by “willful misconduct,”\textsuperscript{164} meaning that it provides even greater shielding from liability.

There has been criticism of the U.S. government’s heavy subsidization of the Moderna and Pfizer mRNA vaccines and the terms of the agreements. Although financial support helped speed up R&D, the vaccines likely would have been developed absent government funding, raising the question of whether the public overpaid.\textsuperscript{165} Several scholars criticized the government’s failure to secure promises regarding vaccine availability and pricing.\textsuperscript{166} These

\begin{itemize}
\item 156. Id.
\item 157. Id.
\item 160. Id.
\item 161. Frank, supra note 155.
\item 162. See id.
\item 163. 42 U.S.C. § 247d-6d(a)(1).
\item 165. CONG. BUDGET OFF., supra note 10, at 10.
\end{itemize}
concerns came to pass when both Pfizer and Moderna began charging insurance companies $120 to $130 for booster vaccines in 2023, with the federal government picking up the cost for uninsured patients.167

3. Non-Market-Driven Medicines

There is a class of medicines that pharmaceutical companies will not develop, even with moderate subsidies, because of high development costs and low expected financial return. For example, although cures for chronic or life-threatening diseases are extremely valuable from a public health perspective,168 companies cannot earn a sufficient profit to justify R&D.169 Similarly, existing orphan drug incentives are insufficient to incentivize development of new medicines for ninety-five percent of rare diseases.170 The government can incentivize some non-market-driven medicine development with substantial subsidization, but this approach is far from foolproof.

a. New Antibiotic Development

Widespread antibiotic use has given rise to antimicrobial resistance (“AMR”), which occurs when microbial organisms stop responding to medicines designed to eliminate or reduce them.171 AMR poses a growing global threat to public health—in 2019, it was the leading global cause of death, with 1.27 million directly attributable deaths and 4.95 million partially-attributable deaths.172 The CDC estimates that more than 3 million Americans acquire AMR infections or antibiotic-use-related C. difficile and the event of pandemic or epidemic-driven drug scarcity; Sydney Lupkin, Pfizer’s Coronavirus Vaccine Supply Contract Excludes Many Taxpayer Protections, NPR (Nov. 24, 2020, 4:46 PM), https://www.npr.org/sections/health-shots/2020/11/24/938591815/pfizers-coronavirus-vaccine-supply-contract-excludes-many-taxpayer-protections (quoting Professor Robin Feldman as stating that the government “ignor[ed] long-term serious costs” in COVID-19 vaccine supply contracts).


169. See supra Section I.C.3.

170. See Gareth Willmer, The Building Blocks to Make Rare Disease Treatments More Common, HORIZON (Feb. 28, 2022), https://ec.europa.eu/research-and-innovation/en/horizon-magazine/building-blocks-make-rare-disease-treatments-more-common (noting “only 5% or fewer of rare diseases are estimated to have at least one approved treatment”).

171. Chandler, supra note 18.

that 50,000 people die from it yearly.\textsuperscript{173} The United Nations estimates that without new treatments, the annual global death toll will reach 10 million by 2050 and cause “catastrophic” economic damage.\textsuperscript{174}

Epidemics and pandemics contribute to the growing AMR problem. During the first year of the COVID-19 pandemic, more than 29,000 people in the United States died from AMR infections tied to healthcare settings.\textsuperscript{175} Of that group, forty percent of them contracted the infection while hospitalized.\textsuperscript{176} From March to October 2020, close to eighty percent of patients hospitalized with COVID-19 received an antibiotic, and antibiotic use surged again in Summer 2021 when the Delta variant was prevalent.\textsuperscript{177} It is possible doctors were using antibiotics due to a lack of suitable treatments.\textsuperscript{178} Future public health emergencies could cause similar problems.

Most large pharmaceutical companies have exited the antibiotic market.\textsuperscript{179} New antibiotics cost as much as $2.6 billion to develop,\textsuperscript{180} and ninety-five percent of all new antibiotic candidates fail.\textsuperscript{181} Gram-negative bacteria, which poses a major threat to sick patients in hospitals, is especially difficult to target because many promising compounds prove to be highly toxic.\textsuperscript{182} There is furthermore little profit to be made: Patients take antibiotics for only a short time period\textsuperscript{183} and hospitals frequently restrict the use of new antibiotics both to decrease the risk of AMR and to save money.\textsuperscript{184} As CARB-X Executive Director and legal scholar Kevin Outterson noted, “[i]n no other

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\textsuperscript{175} 2022 CDC SPECIAL REPORT, supra note 173, at 3.

\textsuperscript{176} Id.

\textsuperscript{177} Id. at 9.

\textsuperscript{178} Id. at 10.

\textsuperscript{179} Källberg et al., supra note 16.


\textsuperscript{181} Christine Årdal et al., Antimicrobial Development—Economic, Regulatory and Societal Challenges, 18 NATURE REV. MICROBIOLOGY 267, 267 (2020).


\textsuperscript{183} See Källberg et al., supra note 16, at 2 (noting that compared to chronic disease treatments, “antibiotics are relatively cheap products given for short-term treatments”); Jacobs, supra note 180 (noting hospitals are sometimes reluctant to use newer antibiotics).

\textsuperscript{184} Årdal et al., supra note 181, at 267–68.
drug class do we lock up the most innovative new products to keep sales as low as possible.”

Although there are scientific and regulatory hurdles to new antibiotic development, Outterson maintains that “[t]he most pressing problems” for new antibiotic R&D “are economic.” Investing in new antibiotic development means forgoing investing in other potential new medicines. It is difficult for a company to invest billions into developing a new antibiotic when it could direct resources towards a potential blockbuster.

Large pharmaceutical companies’ decision to not pursue new antibiotic R&D has directly impacted SMEs, which are the backbone of new medicine development. SMEs depend on licensing medicines to, or being acquired by, large companies. When large companies exited the market, venture capitalists stopped making antibiotic-focused investments, placing antibiotic-focused SMEs in precarious financial positions. The majority of SMEs that brought a new antibiotic to market have commercially failed. For example, after fifteen years and a $1 billion investment, Achaogen received FDA approval for Zemdri—a medicine that treats antibiotic-resistant urinary tract infections. After failing to raise needed funds for marketing and additional clinical studies, Achaogen was forced to file for bankruptcy in 2019; Zemdri was purchased for a mere $16 million by a generic medicine manufacturer. That same year, Melinta Therapeutics also filed for bankruptcy and was ultimately bought out, notwithstanding having several FDA-approved

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185. Id. at 268.
186. Id.; see also AYLIN SERTKAYA ET AL., E. RSCH. GRP., INC., ANALYTICAL FRAMEWORK FOR EXAMINING THE VALUE OF ANTIBACTERIAL PRODUCTS 1-1 (2014), https://aspe.hhs.gov/sites/default/files/migrated_legacy_files//44241/rpt_antibacterials.pdf (noting “insufficient return to capital invested” in antibacterial drug and vaccine development has led large companies to exit the market).
187. See SERTKAYA ET AL., supra note 186, at 3–4 (discussing the real opportunity cost of capital in pharmaceutical development).
188. See Årdal et al., supra note 181, at 268 (noting “antibiotic development projects compare poorly” to other drug classes).
189. See Christine Årdal et al., Insights into Early Stage of Antibiotic Development in Small- and Medium-Sized Enterprises: A Survey of Targets, Costs, and Durations, J. PHARM. POL’y & PRAC., Apr. 5, 2018, at 1, 2, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5885303/ (discussing SME’s important role in antibiotic R&D and observing that 87.5% of recently approved antibiotics were based on smaller firm R&D).
191. See Gracia et al., supra note 53 (discussing how venture capitalists “see few M&A opportunities for early-stage innovators in the antibiotics space,” leading them to “prioritize[e] other investments”).
192. THOMAS & WESSEL, supra note 190, at 29.
193. See Jacobs, supra note 180 (discussing the Achaogen bankruptcy).
treatments. These high-profile bankruptcies raise the question of whether the antibiotic business model is inherently broken. Consequently, there are few new antibiotic candidates in the development pipeline, particularly for Gram-negative bacteria. This is problematic given that existing antibiotics are not an “inexhaustible resource,” but instead, are depleted over time by evolving microorganisms. Although AMR can be slowed down through various means, new antibiotics must be developed before currently effective medicines fail. This is not possible unless there is a steady pipeline of new antibiotic candidates.

Various publicly-funded initiatives have been introduced in an attempt to incentivize private development. Several countries have boosted financial support for early-stage research that could lead to future medicines. For example, CARB-X is a global non-profit partnership that is funded by various governments and foundations; it provides grants to companies working on AMR treatments. BARDA also funds companies with promising antibiotic candidates, including a $120 million investment in several AstraZeneca candidates.

Perhaps the most promising initiative is to have governments pay for flat-rate antibiotic “subscriptions,” which delinks payment from sales volume. In June 2022, the United Kingdom launched a subscription pilot.

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195. Id.
199. See SERTKAYA ET AL., supra note 186 (discussing how diagnostic testing and infection prevention can be used to reduce AMR). See generally CHARLES CLIFT, CTR. ON GLOB. HEALTH SEC., REVIEW OF PROGRESS ON ANTIMICROBIAL RESISTANCE (2019), https://www.chathamhouse.org/sites/default/files/publications/research/2019-10-04-AMR.pdf (discussing progress that has been made on various initiatives to reduce AMR).
200. Källberg et al., supra note 16.
201. Id.
204. Jacobs, supra note 180.
program, paying a yearly fee to Shionogi and Pfizer based on the public benefit of the medicines. Such initiatives are useful at addressing market-entry failure by supporting pharmaceutical companies that have successfully brought an antibiotic to market. In the United States, there has been an effort to pass the PASTEUR Act, which would set up a delinked payment system for novel antibacterial medicines. Subscription models alone, however, are unlikely to be enough. Various attempts to estimate how high the government payment would need to be to incentivize new antibiotic R&D arrive at figures between $1 billion and $8.9 billion.

It is clear that a multi-prong solution is going to be required for incentivizing new antibiotic development. For some needed antibiotics, moderate or even heavy government subsidization may be the most cost-effective and timely way to incentivize development. But for others, more may be needed. Some groups, such as pharmaceutical industry group Biotechnology Innovation Organization (“BIO”), have called for government support for the entire pathway of private antibiotic development.

Other scholars, more radically, have called for the public sector to assume a greater role.

b. Medicines for Infectious Diseases Posing Threat of Future Public Health Emergencies

Emerging infectious diseases pose a growing threat to high-income countries. Outbreaks can wreak economic havoc—straining the healthcare system, shrinking the workforce, and paralyzing critical infrastructure, such as transportation. This is especially true in the United States, whose healthcare system lags behind other high-income countries. Increased

207. Id. at 370.
208. Id. at 369–70.
209. See id. at 370 (noting “pull incentives are not golden tickets for wealthy companies”).
211. THOMAS & WESSEL, supra note 190, at 29–31.
212. See Rebecca E. Glover et al., NIMble Innovation—A Networked Model for Public Antibiotic Trials, 2 LANCET MICROBE, at e637, e637 (2021) (proposing “a global public infrastructure of institutes” that oversee the development and production of antibiotics).
213. Rutschman, supra note 13, at 1206.
215. See ERIC C. SCHNEIDER ET AL., COMMONWEALTH FUND, MIRROR, MIRROR 2021—REFLECTING POORLY: HEALTH CARE IN THE U.S. COMPARED TO OTHER HIGH-INCOME
travel, a shift towards urbanization, and the growing global population all increase the risk of future epidemics and pandemics.\footnote{216} One study estimates a thirty-eight percent chance of experiencing a COVID-level pandemic in one’s lifetime and notes that the risk may double within a few decades.\footnote{217} Medicines that can prevent illness from infectious diseases may also reduce the need for antibiotics, thereby slowing AMR.\footnote{218} For this reason, it is critical for the government to have all necessary tools to promptly deal with outbreaks, including appropriate medicines.

Pharmaceutical companies, however, are reluctant to develop infectious disease medicines. If a company develops a medicine to treat a disease that presently poses little risk to U.S. consumers, its patent rights and FDA exclusivities may end before an epidemic or pandemic occurs.\footnote{219} Although there is a high societal benefit of being prepared for future public health emergencies, pharmaceutical companies cannot commensurately profit.\footnote{220} As scholars have observed, “[p]andemic preparedness requires ‘inefficiencies’ from an economic point of view,”\footnote{221} including developing medicines for a health emergency that may never come to pass. Not surprisingly, there is little private sector interest in such undertakings.\footnote{222}

In particular, R&D for vaccines protecting against emerging infectious diseases is viewed as risky. It is difficult to accurately predict which pathogens will give rise to outbreaks and to guess when an outbreak will occur.\footnote{223} Vaccines are complex to develop and many vaccine candidates fail during clinical trials.\footnote{224} Furthermore, as the COVID-19 pandemic illustrated, mutations can undermine an existing vaccine’s efficacy.\footnote{225}

Vaccines benefit not just the person who receives it, but also the general public by reducing infection and building herd immunity.\footnote{226} Notwithstanding
these substantial societal benefits, individuals (and their health insurers) generally bear the financial burden of vaccination. People may be reluctant to pay high prices for vaccines given that they can freeride off of existing herd immunity.227 This means that companies are unable to charge prices that truly reflect the value of infectious disease vaccines.228

To overcome these obstacles, the government heavily subsidizes infectious disease vaccine development. For example, by 2014, BARDA had spent more than $1 billion towards the development, clinical trials, and manufacturing of Bavarian Nordic’s Jynneos smallpox and mpox vaccine.229 Since then, BARDA has provided additional funding for an updated freez-dried version, which would have a longer shelf life.230 As discussed further in Part III, the government also undertakes the expensive early R&D of infectious disease vaccines in-house, then licenses the rights to large pharmaceutical companies via PPPs.231 To attract PPP partners, the government typically does not control the pricing of the resulting vaccines, notwithstanding the high level of taxpayer support that makes such development possible.232

B. Support for Healthcare Infrastructure

In economic terms, medicines are regarded as private goods: They are rivalrous because one person’s consumption of medicine reduces the amount left for everyone else, and they are excludable through patent rights and regulatory exclusivities.233 However, a subset of medicines play an important

228. See Qiwei Claire Xue & Lisa Larrimore Ouellette, Innovation Policy and the Market for Vaccines, 7 J.L. & BIOSCIENCES, Jan.–June 2020, at 1, 21 (discussing how positive externalities that private actors cannot capture “contribute to substantial distortions in vaccine innovation markets”).
231. See infra Section III.A.
232. See Heled et al., supra note 92, at 9 (discussing the government’s failure to secure fair pricing when funding medicine R&D).
role in supporting public healthcare infrastructure, benefitting more than just the people who take them. These infrastructure-adjacent medicines exhibit either positive or negative externalities that make it difficult for pharmaceutical companies to fully capture their value to society.  

1. An Overview of Infrastructure

There is no one accepted definition regarding what comprises infrastructure. Narrowly, infrastructure may be limited to tangible, government-provided projects that are the closest to pure public goods, such as transportation and utilities. However, even the most traditional types of infrastructure can share the attributes of private goods. For example, roads and bridges can be excludable through a toll system and can be privately developed. Consequently, many economists more broadly construe infrastructure to encompass the structures and facilities that serve the government while supporting social development and economic growth.

Investments in infrastructure generate significant positive externalities—benefits to the public that are not reflected in the consumer price of the good or service. This inability of private entities to capture the full value of infrastructure deters private investment. For example, suppose that a private company constructed a high-speed railway between Houston and Dallas. Although paying train customers would benefit from the project, so too would people who drive between the two cities that would now enjoy reduced road congestion, as well as people who live in the area and who benefit from reduced air pollution. The train operator would have no way to profit from these benefitting third parties. Because infrastructure providers cannot charge a price that reflects the full societal value of the good or service

234. See id. at 89 (noting “[u]nappropriated consumer surplus creates a potential drag on innovation”).


237. Bartlett, supra note 236.

238. See Tankersley & Smialek, supra note 235 (noting economists “largely agree” that infrastructure “extends to the building blocks of a modern, high-tech service economy”); VIRENDRA PROAG, INFRASTRUCTURE PLANNING AND MANAGEMENT: AN INTEGRATED APPROACH 2–3 (2021) (defining infrastructure “as the means and forces of production which are necessary for social development”); BRETT M. FRISCHMANN, INFRASTRUCTURE: THE SOCIAL VALUE OF SHARED RESOURCES 10 (2012) (discussing how infrastructure supports economic growth and leads to substantial social gains).

239. Bartlett, supra note 236.
that they provide, infrastructure is consistently underprovisioned by the private sector alone. By contrast, the government need not chase after market rewards. It is not limited to projects with big payoffs because it can fund projects through taxation or long-term debt.

For government infrastructure development, there is a spectrum of involvement for the private sector. At one end of the spectrum is a heavily government-directed approach in which the government owns and operates the infrastructure. The government may use short-term design-build contracts with private entities for the initial construction of the project or may hire a private firm to undertake repairs. Alternatively, the government may lean more heavily on the private sector through PPPs that bundle different project phases together—such as project design, construction, and long-term maintenance—and that transfer various risks to the private sector. The more functions that are transferred to the private sector, the more closely it resembles private development.

In addition to supporting traditional forms of infrastructure, the government plays a critical role in healthcare infrastructure development. This includes funding transportation-related infrastructure so that people can reach healthcare services, ensuring that local hospitals have sufficient resources to serve the community, and providing adequate power and water so hospitals can operate. The government is further involved by helping healthcare facilities develop contingency plans to operate during emergencies that strain capacity.

Although inadequate healthcare infrastructure is commonly associated with lower-income countries, unexpected emergencies can strain hospitals
even in affluent areas. For example, the Texas state government failed to mandate winterizing its power plants and has refused to connect its state electricity grid to the national grid. Consequently, when a severe winter storm struck in February 2021, Texas hospitals lost access to water and power—severely impacting their ability to provide healthcare at a time when it was most needed.

The United States also experienced a “stress-test” of healthcare infrastructure during the COVID-19 pandemic. Many regional hospital systems were overwhelmed with patients and unable to save the lives of people with normally treatable medical conditions. Some doctors described this as a collapse of the U.S. healthcare system. During this time, vaccines that decreased disease transmission and reduced the rate of hospitalization among the sick were vital to reestablishing critical U.S. healthcare infrastructure.

2. Infrastructure-Adjacent Medicines

The COVID-19 pandemic illustrated how healthcare infrastructure is dependent upon certain types of medicines that prevent hospitals from becoming overwhelmed with patients and that, more broadly, prevent or reduce resulting economic harm. One can think of “infrastructure-adjacent medicines” as medicines needed to prevent the catastrophic collapse of the public health system but that require heavy government oversight and investment to be developed. Such medicines have infrastructure-like aspects: They serve the government by safeguarding the public healthcare system while supporting social development and economic growth.

For most medicines, their effectiveness is independent of the number of people who take it. For example, if one person takes a new cholesterol medicine, it will be no more or less effective for that person than if one.

248. See Mandy Cai et al., How Texas’ Power Grid Failed in 2021 – And Who’s Responsible for Preventing a Repeat, TEX. TRIB. (Feb. 15, 2021, 5:00 AM), https://www.texastribune.org/2022/02/15/texas-power-grid-winter-storm-2021/.
249. See Karen Brooks Harper, “An Emergency on Top of a Pandemic”: Texas Hospital Workers Scramble as Winter Storm Hampered Operations, TEX. TRIB. (Feb. 18, 2021, 7:00 PM), https://www.texastribune.org/2021/02/18/texas-hospitals-power-outages-winter-storm/ (detailing the impact of multi-day power and water failures on Texas hospitals).
253. See Spencer, supra note 252.
million people take it. Similarly, the medicine’s efficacy in the future does not depend on the number of people taking it at present. Infrastructure-adjacent medicines, however, appear to share a unique characteristic: They exhibit either positive or negative externalities that are dependent upon the number of people who use them.

For some medicines, the more people who take them, the more effective the medicine becomes on aggregate. Consider a vaccine that protects against a highly infectious disease. Use of the vaccine creates a positive externality, because the more people who receive the vaccine, the less the disease spreads in the community, thereby benefitting the unvaccinated.254 If a large enough percentage of people receive the vaccine, the public good of herd immunity is established, benefitting the entire community.255

Although medicines that reduce the transmission of infectious diseases have substantial public benefits, such as preventing the healthcare system from collapsing, the market does not adequately reward them.256 Like the railroad operator in the example above, pharmaceutical companies cannot financially benefit from third-party beneficiaries. Moreover, infectious disease vaccines can also exhibit a negative externality: As the percentage of vaccinated people increases, the unvaccinated have less of an incentive to pay for a vaccine given that they already benefit from herd immunity.257 This contributes to vaccines’ lack of profitability.258

Other infrastructure-adjacent medicines become less useful to future patients the more that people use them. Overuse of malaria treatments by uninfected people allowed mosquitoes to develop resistance first to chloroquine and now to artemisinin, raising fears that remaining medicines could become ineffective in the future.259 Antibiotics become less effective as AMR grows, meaning that new antibiotics have to be used only as a last line of defense.260 Most large pharmaceutical companies have exited the

254. See SERTKAYA ET AL., supra note 186, at 4-1 (discussing how vaccination creates a positive externality by reducing the risk that non-vaccinated people will get sick).
256. Xue & Ouellette, supra note 228, at 21.
257. See Adida et al., supra note 227, at 425–26 (discussing the “negative network effects of vaccines”).
258. See Xue & Ouellette, supra note 228, at 21, 36 (discussing how positive externalities contribute to a lack of profitability for vaccines).
260. See supra Section II.A.3.
antibiotic market, yet new antibiotics are needed to support health care infrastructure by ensuring preparedness against future AMR.  

The government has traditionally relied on a toolbox of strategies for incentivizing the development of infrastructure-adjacent medicines, but gaps persist between the medicines society needs the most and those that are developed. If the government utilized heavy subsidies at each stage of new medicine development, companies might develop some of the needed medicines. However, this raises several questions. First, if the public massively subsidizes a private company’s new medicine development, why should those companies own the final IP rights with no safeguards for protecting public health? Second, given that most of the real innovation is occurring in smaller companies, does subsidizing large pharmaceutical companies trickle down to this group? And third, why should the government rely so heavily on the private sector to develop these medicines, even if it can lead to substantial delays in getting needed medicines? 

III. CENTRALIZATION AS A PARALLEL TRACK TO INNOVATION  

The government should consider playing a greater role in developing infrastructure-adjacent medicines that private companies are unwilling to develop. Although federal agencies already engage in the earlier stages of new medicine development, the government could expand such R&D and could additionally purchase rights to promising drug candidates from SMEs. When private partners are not readily available to run Phase III trials, rather than delay, the government could oversee the trials itself. By retaining the final IP rights, the government could ensure that any resulting medicines are distributed as broadly as needed. Such a model would not replace current approaches but would instead be used to fill gaps where current approaches have failed.

261. *See supra* Section II.A.3.  
263. *See supra* notes 138–141 and accompanying text; *see also* RUTSCHMAN, *supra* note 78, at 106–14 (discussing governmental non-IP incentives currently used and their limitations).  
265. *See* Heled et al., *supra* note 92, at 8 (noting the government is attempting to “evoke accountability for ensuring pandemic preparedness by shifting responsibility to the private sector, which is beholden to stockholders, not the public”).
Section A looks at past examples of government-led new medicine development, such as penicillin and a Zika vaccine. Section B proposes that the government spearhead the development of needed non-market-driven infrastructure-adjacent medicines. Section C discusses possible agencies to run such a program. It initially considers the Army for this role because of its expertise in internal new medicine development. However, Section C ultimately concludes that BARDA would be a better choice to maintain transparency and to prevent the project from being sidelined.

A. Past Government-Led New Medicine Development

There is precedent for the government taking an active role in the development of needed goods, including new medicines. For example, during World War II, the government oversaw the development of penicillin, which has led some scholars to call for greater public involvement in new antibiotic development. More recently, the government has engaged in initial R&D and early clinical trials for new medicines, and then entered into PPPs with large pharmaceutical companies for the final stages of development. The government offers private partners exclusive licenses on its patented technology to entice them to assume the risks and burdens of conducting late-stage clinical trials, obtain FDA approval, and market the resulting medicines. For medicines that have a low chance of profitability, this can be the only way for the government to secure a private partner.

The government’s attempt to develop a Zika virus vaccine, however, reveals the cost of the current approach. A series of Zika outbreaks led the U.S. Army to initiate R&D on a vaccine in 2016, and a promising vaccine candidate soon emerged. When the vaccine was ready for clinical trials, the government entered into an agreement with Sanofi to conduct Phase II


267. RUTSCHMAN, supra note 78, at 655.

268. Id.

269. Note that this approach is not limited to the government; non-profit organizations involved in R&D frequently exclusively license their IP rights to private entities. See Szymon Jaroslawski & Mondher Touni, Non-Profit Drug Research and Development: The Case Study of Genethon, 7 J. MICT. ACCESS & HEALTH POL’Y, Nov. 15, 2018, at 1, 2 (discussing the U.S. Cystic Fibrosis Foundation’s licensing of IP for ivacaftor, and Genethon’s use of exclusive licensing for two gene therapy products).

270. See RUTSCHMAN, supra note 78, at 654–655 (discussing the Army’s decision to work on a Zika vaccine).

271. See id. (noting Army research began in January 2016 and was ready for patenting four months later).
clinical trials and seek FDA approval. Sanofi received $43.2 million from BARDA in September 2016 and began trials.272

Controversy erupted when the government announced its plan to exclusively license its Zika patents to Sanofi with no price controls.273 This led to criticism from some public officials, given the substantial amount of public funding Sanofi had received.274 Although the government subsequently attempted to require reasonable pricing for the final vaccine,275 Sanofi countered that it was taking significant financial risks for a vaccine that might never become commercially viable276 and argued that it would “make significant milestone and royalty payments” if it succeeded.277 During this time, Zika’s spread was decreasing, leading BARDA to pause funding on vaccine development.278 Consequently, Sanofi pulled out of the agreement in September 2017, and no vaccine was ever approved.

There are three major problems with the government’s heavy reliance on PPPs for new medicine development, especially for infectious diseases. First, although § 207(a)(2) of the Patent Act authorizes federal agencies to grant exclusive or partially-exclusive licenses to federally-owned inventions,279 § 209(a)(1) specifies that such a license may be granted only if it is “a reasonable and necessary incentive” to obtain resources needed to bring the invention to market or to “otherwise promote the invention’s utilization by the public.”280 In other words, government licensing to a single company is supposed to be a last resort, not a default solution.281

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272. Id.
276. Sagonowsky, supra note 273.
281. RUTSCHMAN, supra note 78, at 657.
Second, to attract private partners, the government trades off affordability and accessibility to the public.\textsuperscript{282} For example, government scientists collaborated with Gilead Sciences to develop the COVID-19 treatment remdesivir,\textsuperscript{283} and the government provided $37.5 million towards remdesivir's R&D.\textsuperscript{284} Nevertheless, the United States experienced a massive remdesivir shortage in Summer 2020, which was exacerbated by Gilead Sciences' unwillingness to work with third-party manufacturers to produce medicines for high-income countries.\textsuperscript{285} Similarly, Moderna accepted $2.5 billion in public funds but refused to license out its mRNA vaccine technology to willing third-party manufacturers notwithstanding urging from the Biden administration.\textsuperscript{286} Although the government could push for affordability and accessibility in its contracts, that could make it even harder to attract private partners.

Third, the search for PPP partners willing to assume costs and risks of development can lead to delays in getting new medicines to people, leading to unnecessary deaths. This is particularly true for infectious disease vaccines, for which there exists a narrow window of time to conduct clinical trials before the outbreak subsides.\textsuperscript{287} For example, when the next Zika outbreak occurs, it will take time to find a new private partner, complete clinical trials, and get a vaccine to market.\textsuperscript{288}

This third problem is further illustrated by the vaccine for the Zaire Ebola virus. In 2005, a Canadian research team developed a vaccine that showed 100% efficacy in early animal trials for developing antibodies against nocite.

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\textsuperscript{282} See Margaret Chon, \textit{PPPs in Global IP, in METHODS AND PERSPECTIVES IN INTELLECTUAL PROPERTY} 269 (Graeme B. Dinwoodie ed., 2014) (noting how PPPs “attempt to accommodate both commercial and non-commercial interests” and questioning whether public interest motivations can be reconciled with private partners’ for-profit missions).


\textsuperscript{284} Kumar, \textit{supra} note 29, at 82.

\textsuperscript{285} Id. Gilead Sciences did license remdesivir to third-party manufacturers but limited those medicines to use in low-income countries. \textit{Id.} at 83.

\textsuperscript{286} See Kumar & Rutschman, \textit{supra} note 166 (describing Moderna’s refusal to transfer mRNA technology); Stephanie Nolen & Sheryl Gay Stolberg, \textit{Pressure Grows on U.S. Companies to Share Covid Vaccine Technology}, N.Y. TIMES (Nov. 9, 2021), https://www.nytimes.com/2021/09/22/us/politics/covid-vaccine-moderna-global.html.

\textsuperscript{287} See Natalie E. Dean et al., \textit{Creating a Framework for Conducting Randomized Clinical Trials During Disease Outbreaks}, 382 NEW ENG. J. MED. 1366, 1366–67 (2020) (discussing how clinical trials for infectious disease medicines may not be concluded before an outbreak subsides).

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Ebola and Marburg virus. A lack of government funding for clinical trials led the Canadian government to license its patents to NewLink Genetics in 2010 in exchange for $205,000. Although NewLink lacked vaccine development experience, no other pharmaceutical company was interested in partnering with Canada. But NewLink made no effort to conduct clinical trials or take any other steps towards development, even after a new Ebola outbreak occurred. Finally, in 2014, NewLink transferred its IP rights to Merck, earning $30 million upfront, $20 million after Merck commenced clinical trials, plus a promise of future royalties if the vaccine was eventually approved, notwithstanding the fact that NewLink did no work in getting the vaccine to market. The vaccine did not gain approval until 2019—a delay of more than a decade. Commentators suggest that NewLink entered into the PPP for the sole purpose of making a large profit through licensing.

Notwithstanding these problems, PPPs are still a valuable tool for new medicine development. Problems with NewLink could have potentially been avoided through better vetting of the company and by contractually obligating it to take steps towards approval or forfeit its license. In the future, the government could demand royalty payments in the event that a vaccine makes it to market. It could pay PPP partners more if they promise to utilize fair pricing for any resulting medicines and could require them to transfer technology to third-party manufacturers in the event of a shortage.

As the Zika and Ebola vaccine projects illustrate, however, relying solely on a traditional PPP model can substantially skew what kind of medicines get developed, given that private partners are drawn to projects that offer predictable payoffs. The more assurances the government demands, the more it will have to pay to attract partners. Moreover, the search for a suitable private partner may take years, and private partners may delay

290. Id.
291. Id.
292. RUTSCHMAN, supra note 78, at 84.
293. Id. at 85.
294. Id. at 54.
295. Id.
296. See Kumar & Rutschman, supra note 166 (calling for greater public safeguards in government contracts funding new medicine R&D); see also supra notes 273–278 and accompanying text (discussing Sanofi’s agreement with the government, which included royalty payments).
297. See Kumar & Rutschman, supra note 166.
298. See Christopher Jones & David Reinecke, Infrastructure and Democracy, 33 ISSUES SCI. & TECH. 24, 30 (2017) (discussing the limitations of PPPs).
clinical trials.\textsuperscript{299} It is therefore worth considering a different approach for ensuring government-developed medicines make it to market in a timely fashion.

\textit{B. Centralized Development of Infrastructure-Adjacent Medicines}

The government should assume greater oversight in developing needed medicines that the private sector will not produce—overseeing the entire R&D process and utilizing short-term private contracts where they are more cost-efficient. Although this proposal would require the government to spend more money at the outset, it would reduce clinical trial delays and bring medicines to market that would not have otherwise been developed. Such an effort would not replace current approaches such as subscription models, but it would supplement them for the most needed areas.

\textit{1. Choosing Targets for Centralization}

The government would first need to assess which medicines are the highest priority for a centralized approach. In doing this, it would need to ensure that it does not “crowd out” existing private-sector innovation. It could do this by focusing development efforts on medicines that the private sector is not interested in developing.

\textit{a. Reducing “Crowding Out” of the Private Sector}

“Crowding out” refers to an economic theory that public sector spending in a particular area will reduce or eliminate private spending, potentially leaving the public with an inferior good.\textsuperscript{300} Economic studies support a hypothesis that public spending in areas such as education and public broadcasting leads to reductions of private contributions for the same services.\textsuperscript{301} Theoretically, if the government centralizes development of some types of new medicines, it could impact the private sector. A company might be less likely to invest in R&D for a type of medicine that the government is trying to produce, given that a government-developed medicine could be sold at cost or at a loss, allowing it to out-compete any private counterpart. This could lead to a vicious cycle of the government having to shoulder a greater share of medicine development due to scaring off private investment.

\textsuperscript{299} See \textit{supra} notes 289–295 and accompanying text (discussing delays in the development of Canada’s Zaire Ebola vaccine).

\textsuperscript{300} See Lemos & Charles, \textit{supra} note 241, at 156–57 (discussing how public financing for public goods can sometimes substitute private investment).

Crowding out problems do not appear to have manifested with regard to a common PPP development model for infectious disease vaccines, in which the government conducted the early stages of new medicine development and then licensed the technology exclusively to a private partner. It is possible that the risk may be greater if one considers boosting government development of new antibiotics or having the government oversee late-stage clinical trials and marketing of drugs.

There are ways that the government could reduce this risk. First, when expanding internal R&D, the government could focus its efforts in areas in which large pharmaceutical companies are reluctant to invest. This would include vaccine development for many emerging pathogens that pose a threat of a future public health emergency, as well as some classes of antibiotics. The government would want to steer clear of classes of medicines that smaller companies are currently attempting to develop.

Second, if the government develops a drug candidate that successfully clears a Phase I trial, it could first attempt to attract a private partner who is willing to commit to a reasonable timeline for the final stages of development and willing to agree to reasonable pricing restrictions on the final medicine. If a private partner is not interested, however, then the government could retain ownership and promptly move forward with development—either on its own or via short-term private contracts with third-parties.

For areas in which there is currently some private pharmaceutical development, it may make more sense for the government to contractually ensure affordability and accessibility when it offers subsidies. For example, the government could utilize a dormant license in its initial R&D funding agreements, requiring the recipient company to license out patents and know-how to alleviate medicine shortages during pandemics and epidemics.

b. Prioritization Based on High Threat Level and Low Commercial Viability

A second consideration is how the government could determine which medicines to develop. As discussed earlier, a mismatch exists between government-funded R&D and what is most needed. It is therefore critical

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302. See Rutschman, supra note 78, at 58–59 (discussing why R&D into infectious disease vaccines is viewed as risky).
303. See Källberg et al., supra note 16 (discussing the many obstacles to developing new antibiotics, including the technical challenges of developing them, the difficulties of obtaining regulatory approval, and the unpredictable market).
305. See supra Section I.C.1.
that the government develop and utilize neutral metrics in choosing which diseases to prioritize for its internal R&D.

There are several sources of information that the government could consider as a starting point. For new antibiotic candidates, the WHO maintains a global priority pathogens list of twelve species of multidrug-resistant bacteria that pose a threat in hospitals and nursing homes, classified as “critical,” “high,” and “medium” priority. The list emphasizes the need for antibiotics targeting gram-negative bacteria that can lead to potentially lethal bloodstream infections and pneumonia. The CDC similarly issued a 2019 Antibiotic Resistance Threats Report that highlighted eighteen AMR bacteria and fungi categorized by level of urgency. For infectious diseases, WHO maintains R&D Blueprint targeting infectious diseases that pose a threat of a future epidemic or pandemic, which includes COVID-19, Ebola, and Zika. The National Institute of Allergy and Infectious Diseases (“NIAID”) also ranks pathogens in three categories based on the risk they pose to public health and national security.

Using these reports as starting points, the government should then assess the domestic high-priority needs that are attracting the least private investment. At the outset, the government could commission a report, working with scientists, doctors, NGOs, and private industry participants to discern which medicines are needed but not being developed. It could hold roundtables and invite public and private sector researchers to contribute. The government could then borrow from the Administrative Procedure Act’s notice-and-comment rulemaking process, seeking feedback from the broader scientific community regarding areas in which R&D is most needed.

Such a prioritization process would build on what the government is already doing. For example, under NIAID’s Pandemic Preparedness Plan, its researchers will identify and study “prototype pathogens,” which are “viruses


307. Id.


311. 5 U.S.C. § 553.
within viral families with the potential to cause significant human disease.\footnote{NIAID Pandemic Preparedness Plan Targets ‘Prototype’ and Priority Pathogens, NAT’L INSTS. OF HEALTH (Feb. 2, 2022), https://www.nih.gov/news-events/news-releases/niaid-pandemic-preparedness-plan-targets-prototype-priority-pathogens; NAT’L INST. ALLERGY & INFECTIOUS DISEASES, NIAID PANDEMIC PREPAREDNESS PLAN (2021), https://www.niaid.nih.gov/sites/default/files/pandemic-preparedness-plan.pdf.} NIAID researchers will build a framework that will permit for rapid R&D of medicines in the event of an outbreak of a virus in the same family as the prototype pathogen.\footnote{Id.} NIAID further plans to support basic and preclinical research for these areas. Likewise, under the proposed PASTEUR Act, which would establish a subscription model of antibiotic development, Congress would create a Critical Need Antimicrobials Advisory Group to develop a list of infectious diseases for which new antibiotics are needed, taking into account unmet medical need.\footnote{See PASTEUR Act of 2021, S. 2076, 117th Cong. (2021).}

The government would focus its efforts on areas that lack private-sector interest. It could determine this by examining historical data and the current pipeline for new medicines in target areas. It would then reallocate funds to these projects and away from more market-driven ones. Ideally, Congress would also authorize additional funds for the highest-priority R&D.

It is critical that the government be transparent about the prioritization process and allow for scientific input. Under Operation Warp Speed, Senate Democrats criticized the Trump administration’s opaque selection process for financially backing vaccine candidates.\footnote{Jon Cohen, Operation Warp Speed’s Opaque Choices of COVID-19 Vaccines Draw Senate Scrutiny, SCIENCE (July 2, 2020), https://www.science.org/content/article/operation-warp-speed-s-opaque-choices-covid-19-vaccines-draw-senate-scrutiny.} The agency that runs the new program should provide detailed notice to the public about proposed areas of medicine development. It could then utilize a public commenting period to seek feedback from the scientific community, utilizing both scientific roundtables and an open commenting period. This would allow the government to identify areas in which commercial development is inadequate and in which moderate to heavy public subsidization has not yielded results.

2. Generating Early Research

There are two promising paths to spurring early research for needed medicines. One possibility is for the government to expand internal basic research related to priority areas that are identified through the process discussed above.\footnote{See supra Section III.B.1.b.} For infectious disease research, the government currently plays a major role in early R&D, including its ongoing work on a pan-variant
The government could utilize an existing federally-funded R&D center to focus on neglected infectious diseases or expand Walter Reed’s research agenda.

With regard to antibiotic research, the DoD receives modest funding for evaluating antimicrobial candidates under the Federal Task Force on Combating Antibiotic-Resistant Bacteria (“CARB”)’s National Action Plan for CARB. In the 2020–2025 plan, the CARB Task Force set modest goals for increasing interagency cooperation to expand research and to have the DoD “identify one candidate therapeutic for bacterial infections in human medicine” for further R&D. Depending on its level of success, this research could be expanded for high-priority pathogens.

There are, however, disadvantages to relying solely on internal research for centralized medicine development. As medical researcher Mark Fishman noted, “[t]he discoveries that lead to the creation of a new medicine do not usually originate in an experiment that sets out to make a drug.” Highly transformational medicines can emerge from fundamental research studies seeking to understand biological or chemical processes, or from the convergence of disparate lines of evidence. Also, small biotechnology start-ups are widely regarded as drivers of innovation, free from the bureaucracy of larger organizations. Moreover, while various agencies have experience with infectious disease vaccine development, they lack recent experience in developing new antibiotics.

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317. See Ratto-Kim et al., supra note 80, at 7 (discussing the U.S. government’s role in developing an HIV vaccine); Jon Cohen, Making Broader Coronavirus Vaccines is a Struggle, 377 SCI. 566, 567 (2022) (discussing Walter Reed’s pan-coronavirus vaccine candidate).


319. See Letter from Peter Levine to Thad Cochran, Chairman, Senate Subcomm. on Def., Comm. on Appropriations (June 6, 2016), https://www.health.mil/Reference-Center/Reports/2016/06/06/Combating-Antibiotic-Resistance (discussing progress on meeting CARB Task Force goals).


323. See CONG. BUDGET OFF., supra note 10, at 4 (discussing how small companies account for 70% of medicines in Phase III trials); Robin Robinson, Small Pharma Driving Big Pharma Innovation, PHARMAVOICE (Jan. 1, 2020), https://www.pharmavoice.com/news/2020-01-pharma-innovation/612330/ (observing that sixty-three percent of new prescription medicines originated from small companies, and that small companies are less hindered by bureaucracy).
To bridge this gap, the government could follow the practice of large pharmaceutical companies by acquiring promising drug candidates from SMEs. As discussed earlier, SMEs that develop new antibiotics struggle to profit because larger companies are not interested in acquiring their medicines. If the government exclusively licensed promising drug candidates from SMEs or purchased such companies outright, it could help incentivize private research in critical areas. Venture capitalists would presumably be more likely to fund biotechnology start-ups knowing that a government sale was a potential option, in addition to private buyers.

The government could also pre-negotiate purchases with researchers in government funding agreements for non-commercially viable areas of medical research. For example, the government could fund researchers to develop new antibiotics in high-priority areas, with the government retaining a right of purchase if the researcher is successful. The ability to make money through a government sale might help incentivize researchers to undertake what is normally a non-lucrative line of research.

A major benefit of this approach is that it cuts out the middleman—large pharmaceutical companies. Current approaches for incentivizing new antibiotic development skew towards subsidizing large pharmaceutical companies through pre-purchase agreements and subscriptions. Infectious disease vaccine research similarly involves government agencies finding large pharmaceutical company partners that are willing to enter into PPPs. These incentives do not directly help SMEs that seek to be acquired, leaving a potential gap.

Such an approach can help offset blind spots. Take, for example, mRNA vaccine technology. Although the NIH failed to fund Karikó’s early research, BARDA later recognized its potential and financially supported Moderna’s early clinical trials. It did so notwithstanding the fact that Moderna had

324. See Gracia et al., supra note 53.
326. See Glover, supra note 212, at e640 (noting for antibiotic development that “pretrial patent buyouts for promising compounds developed by industry” could potentially “create an attractive offloading point for small-sized and medium-sized enterprises struggling to attract venture capital”).
327. See supra notes 202–210 and accompanying text.
328. See RUTSCHMAN, supra note 78, at 655 (discussing the development of a Zika vaccine).
never brought a drug candidate to a Phase III trial before, helping to transform Moderna from a little-known startup into a biotechnology giant. Even if the government lacks the creativity to conduct its own early R&D in certain areas, it can close the gap by learning to recognize promising infrastructure-adjacent drug candidates and acquire them before their development stalls.

To put it another way, the value of large pharmaceutical companies is not solely in their innovativeness, but also in their ability to take significant financial risks in new medicine development. If the government could shoulder the risk for classes of needed medicines that larger companies will not develop, it could spur high-value private research that would otherwise be delayed or not occur at all.

3. Clinical Trials, Regulatory Approval, and Commercialization

The government should sponsor more clinical trials for the research that it undertakes, as well as for promising new uses of existing off-patent medicines. Government sponsorship already occurs for some Phase III trials, such as the NIH’s trial for the use of creatine in treating Parkinson’s Disease and Walter Reed’s trial for its internally-developed HIV vaccine candidate. The government has also made forward progress in centralizing Phase II and III trials for high-priority medicines through its Accelerating COVID-19 Therapeutic Interventions and Vaccines initiative (“ACTIV”).

Although the government would cover the financial costs of a trial as the sponsor, it could contract out responsibilities to a Contract Research Organization (“CRO”)—a third-party organization that can legally assume responsibility for part or all of the clinical trial. CROs are permitted to design and run clinical trials, evaluate data, and prepare regulatory materials to submit to the FDA. According to industry market research groups, the

330. Id.
331. A lesser alternative to acquisition might be for the government to provide financial support to an SME in exchange for an ownership stake in the company. This approach could have been used during the early stages of the COVID-19 pandemic when the government pumped billions of dollars into small private companies like Moderna.
333. See Ratto-Kim et al., supra note 80, at 7–8 (discussing the military’s role in developing an HIV vaccine).
334. See Asher Mullard, From Pandemic Preparedness to Public-Private Partnerships, 21 NATURE 486 (2022) (interviewing incoming Foundation for the NIH CEO Julie Gerberding regarding ACTIV). ACTIV is “a partnership between the NIH, industry and nonprofit organizations to run coordinated clinical trials of vaccines, antivirals, antibodies and other classes of drugs,” to result in more effective clinical trials. Id. at 486–87.
336. Id.
CRO market has been rapidly expanding due to demand from SMEs. Unlike with traditional PPPs, contracts with CROs would be short-term, allowing the government to retain control over any resulting medicine. To reduce costs, the government could seek out partners. U.S. agencies already work with non-governmental organizations (“NGOs”) for preclinical trials, such as the Trudeau Institute and the Texas Biomedical Research Institute’s Southwest National Primate Research Center. Non-profit biotechnology groups such as France-based Genethon have also been playing a growing role in sponsoring human clinical trials. Other NGOs, such as the Bill and Melinda Gates Foundation, provide funding for clinical trials for vaccines and treatments for infectious diseases. The government could also seek out partners among other countries, given that problems like AMR are global.

Once the government obtains FDA approval for a new medicine, it would need to produce and commercialize it. The government lacks experience in this area, relying instead on PPPs and agreements with foreign governments. Such a strategy is understandable, given that large

337. See Report Summary: Clinical Trials Outsourcing Market Share, Size, Trends, Industry Analysis Report, By End-Use (Pharmaceutical & Biotechnology Companies, Academic Institutes, Others); By Therapeutics Area; By Workflow; By Region; Segment Forecast, 2022 – 2030, POLARIS MKT. RSCH. (Sept. 2022), https://www.polarismarketresearch.com/industry-analysis/clinical-trials-outsourcing-market (reporting a $38.11 billion valuation of the 2021 global clinical trial market, with a compound annual growth rate (CAGR) of 6.7% predicted between 2022 and 2023, and noting SMEs are driving that growth); Catherine Eckford, Clinical Research Organisation Market Anticipated to Reach $140bn by 2033, EUR. PHARM. REV. (July 5, 2023), (citing a report from Future Market Insights predicting the CRO market to reach $139.56 billion by 2033, with an 8.4% CAGR between 2023 and 2033).


342. ’It’s Good to Have This Many Simultaneous Paths to a Vaccine’: U.S. Army Medical R&D, YAHOO!FINANCE (June 8, 2020), https://finance.yahoo.com/video/good-many-simultaneous-paths-
pharmaceutical companies spend a higher percentage of their budget on sales and marketing than they do on R&D, giving them substantial edge. But at the same time, the government would have different goals from the private sector—it would be seeking to facilitate the creation and accessibility of needed medicines and would not need to maximize profit. It could furthermore utilize short-term manufacturing contracts with private partners.

Government-led pharmaceutical production is already occurring in California with generic drugs. In March 2023, California entered into a $50 million ten-year contract with Civica to have it produce state-branded insulin and make it available to state residents for ten percent of the typical cost. The state is investing an additional $50 million towards building an insulin-manufacturing facility and is planning to manufacture its own naloxone in the future.

By retaining the IP rights, the government could control production and distribution of its medicines. In the event of an epidemic or pandemic, the government could work with multiple generic manufacturers to quickly scale production of its own vaccines and treatments, utilizing the Defense Production Act to facilitate this. This would help reduce the type of medicine shortages that were seen during the COVID-19 pandemic, when pharmaceutical companies with publicly-financed medicines refused to license out their proprietary technology to available manufacturers.

Government control over pricing for its medicines would also have benefits. The government could price infectious disease medicine cheaply to ensure widespread global adoption. For lower-income countries, the government could license the medicines at cost to local pharmaceutical manufacturers. While companies sometimes will voluntarily do this, such

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345. Id.

346. See Kumar, supra note 29, at 61 n.14 (discussing how the Defense Production Act was utilized during the COVID pandemic).

347. Id. at 85–86.

348. See Chris Dall, Agreement Aims to Improve Access to New Antibiotics in Low-Resource Countries, UNIV. MINNESOTA: CTR. INFECTIOUS DISEASE RSC. & POL’Y (Sept. 12, 2023), https://www.cidrap.umn.edu/antimicrobial-stewardship/agreement-aims-improve-access-new-
a practice does not appear to be widespread.\textsuperscript{349} By being able to ensure the swift adoption of infectious disease medicines, the United States would benefit by reducing the risk of the disease spreading or mutating past existing defenses. The government could also recoup some of its R&D costs through licensing agreements with higher-income countries.

\textit{C. Choosing an Agency to Oversee the Centralized Development of Medicines}

The government agency that runs a new medicine development program would need to oversee several tasks. It would first need to solicit feedback from scientists and choose priority areas for centralized development. For infectious disease treatments, the agency would assess the risk that various diseases pose and evaluate vaccine platforms that could be useful against future novel pathogens. The agency would then coordinate with the Army and NIH’s internal research divisions, as well as assess and acquire outside research from small biotechnology companies. Finally, it would sponsor clinical trials, seek FDA approval for new medicines, and license medicines to third-party manufacturers and foreign governments for production and distribution.

One possibility would be for the Army to take on this function, given its extensive experience in new medicine R&D, including sponsoring clinical trials. There has been growing awareness that infectious diseases threaten national security, leading the Army to promote “health security” by preventing and responding to public health emergencies.\textsuperscript{350}

The militarization of public health, however, comes with risks. The DoD leadership that would ultimately be responsible for any health-related program would likely have little healthcare experience. This problem was seen during Operation Warp Speed: BARDA scientists were removed from leadership positions in favor of military officials,\textsuperscript{351} and a four-star Army

\textsuperscript{349} Seemingly “voluntary” price drops and licensing agreements can sometimes be the result of companies fearing future compulsory licensing. See Kumar, supra note 29, at 69, 89 (discussing Bayer’s Cipro and AbbVie’s Kaletra).


general served as Chief Operating Officer. The military officials were chosen to lead due to their experience in complex logistics, but many lacked any healthcare-related experience. Furthermore, placing public health operations into the military would sacrifice transparency, which could undermine trust in any resulting medicines and contribute to the erosion of funding for supporting public healthcare systems. There is also a risk that if a military conflict arises, health-related funds could be diverted to national defense and any public health projects could be sidelined.

The demilitarization of public health has been a focus of the Biden administration, which elevated the Assistant Secretary for Preparedness and Response to a new operating division—the Administration for Strategic Preparedness and Response—and tasked it with overseeing healthcare logistics, including vaccine distribution during public health emergencies. The Biden administration furthermore transferred management of COVID-19 vaccine development from the military to HHS. Admittedly, the Government Accountability Office has identified some gaps in HHS’s current workforce and skillset, but the hope is that with time and resources, HHS can acquire more skilled personnel.

Because of potential issues with military-led new medicine development, an HHS subagency would perhaps be a better choice, with BARDA being the most obvious candidate.


355. See MOODIE ET AL., supra note 350, at 17–18 (discussing the risks of depending on the military for health responses).

356. See id. at 15 (noting that “by framing health crises as security threats, resources that should go to strengthening public health systems may be diverted to other policy priorities”).


359. Id.

360. Another possibility is the Advanced Research Projects Agency for Health (“ARPA-H”), which is a subagency of the NIH that was established to support high-impact medical research. See
Congresswoman Rosa DeLauro observed early in the COVID-19 pandemic, BARDA alone has “the mission and capability to develop, manufacture and facilitate distribution of medical countermeasures during a public health emergency.”361 BARDA supported various COVID-19 vaccine candidates by funding R&D, increasing manufacturing capacity, and entering into advanced purchase agreements.362 It also has experience working across multiple agencies. For example, during the Zika outbreak, BARDA coordinated with Walter Reed, the NIH, and the FDA for vaccine development and testing.363

Before BARDA can take the lead, the government must address several issues. HHS has a decade-long history of misappropriating BARDA’s funding for unrelated expenses, siphoning funds meant for pandemic preparedness for unrelated expenses such as removing furniture and covering non-BARDA salaries.364 The practice was so widespread that it acquired the nickname “Bank of BARDA.”365 The government would need to root out corruption and ensure that funds for medicine development are used for their intended purpose. BARDA would also need to hire people capable of making decisions regarding what technology to acquire from the private sector and develop the skill set to license government-owned inventions to pharmaceutical manufacturers and foreign governments.

The process of centralizing some medicine development into HHS will, undoubtably, take time. But such learning curves are not unique to the public sector. For example, Moderna was founded in 2010 but did not bring a drug candidate to a Phase III trial until it developed the COVID-19 mRNA vaccine in 2020, which later became Moderna’s first FDA-approved medicine.366 Given the persistent gaps in new medicine development, coupled with the public health benefits that would be gained through a government program,

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361. Letter from Murray and DeLauro to Azar, supra note 351.
365. Id.
366. Kuznia et al., supra note 329.
it is worth the upfront cost of investing in public sector medicine development.

CONCLUSION

The pharmaceutical industry is largely regarded as the success story for decentralized innovation. Driven by market-based incentives, companies decide which medicines to develop based on the expected time and cost of R&D, coupled with the expected return on their investment. Highly innovative medicines, such as mRNA vaccines, have resulted from this largely decentralized process.

Yet, many critically needed medicines that support healthcare infrastructure will never be developed through a purely decentralized approach. Companies value a safe path to profitability over developing what is most badly needed by society. Consequently, the private sector is generally unwilling to invest in R&D for infrastructure-adjacent medicines that can help mitigate public health crises, such as infectious disease vaccines and new antibiotics. Some of this gap can be cost-effectively addressed through middle-ground approaches, such as push and pull incentives. But other gaps have proven to be far more persistent.

To prepare for future public health emergencies, it is critical that the government oversee the development of high-priority infrastructure-adjacent medicines that private companies will not develop. The government should expand internal R&D for needed infrastructure-adjacent medicines and acquire promising drug candidates from willing SMEs. When the government has a drug candidate that successfully clears early clinical trials, if it cannot quickly find a private partner willing to promptly run late-stage clinical trials and willing to provide pricing assurances for any resulting medicine, then the government should oversee such trials itself.

This approach would yield several important benefits. It would provide a development path for medicines that the private sector will not generally develop, even with subsidization, such as vaccines for infectious diseases that could give rise to future pandemics. By licensing promising drug candidates from SMEs, or purchasing such companies outright, the government would be directly supporting the backbone of new medicine development. This approach would also speed up the development of infectious disease vaccines, in which time is of the essence for running clinical trials.

By retaining ownership over the resulting IP rights, the government could control the production and distribution of the resulting medicines. For medicines that prevent or treat infectious diseases, the government could price them based on what people in various countries could afford, to reduce the risk of further spread and decrease the likelihood of new variants developing. It could furthermore recoup some of its investment by entering
into licensing agreements with high- and middle-income governments. Government IP ownership would furthermore prevent delays in scaling up manufacturing during public health crises, such as what the United States experienced during the COVID-19 pandemic.

The downside of centralized medicine development is the upfront costs. The government would have to invest more money in R&D, including the cost of sponsoring expensive clinical trials. It would also bear the financial risk of failure. But such an investment would pay off in the future, protecting the economy against public health emergencies and reducing excess deaths and disability from infectious diseases and multidrug-resistant bacteria. As AMR increases and pandemics grow in frequency, it is imperative that the U.S. government take action now and not wait for the next public health catastrophe to unfold.