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Before the

U.S. House of Representatives Committee on Energy & Commerce
Subcommittee on Health

On

“ARPA-H: The Next Frontier in Biomedical Research.”

February 8, 2022

Chairwoman Eshoo, Ranking Member Guthrie, and distinguished members of the Subcommittee on Health:

My name is Brian Miller and I practice hospital medicine at the Johns Hopkins Hospital. As an academic health policy analyst I serve as an Assistant Professor of Medicine and Business (Courtesy) at the Johns Hopkins University School of Medicine. My research focuses on how we can make use policy to create a more competitive and vibrant health sector for the benefit of patients. This perspective derives from my experience as a practicing physician, a family member of those who suffered from severe, terminal diseases; and my prior regulatory experience at the Federal Trade Commission, Federal Communications Commission, U.S. Food and Drug Administration, and the Centers for Medicare and Medicaid Services. Through my role as a university faculty member, I regularly engage with regulators, policymakers, and businesses in search of solutions to help create a better healthcare system for all. Today I am here in my personal capacity and the views expressed are my own and do not necessarily reflect those of Johns Hopkins Medicine or Johns Hopkins University.

In my testimony today, I will focus on:

1. The vast federal biomedical research enterprise and why innovation is important
2. The challenges with ARPA-H as proposed
3. A rising China and why ARPA-H is not enough
4. How we can have a strong response to China

1. Innovation and the Federal Biomedical Research Enterprise

Life sciences innovation is important to our country at many levels. As physician, I see and treat patients in the hospital. Each shift I am acutely aware that every drug I prescribe, every diagnostic test ordered, and every device that I or other physicians use has had a long “train of development.” I am thankful that we as a country are wealthy enough to choose to fund and deploy the tools that result from our country’s vast biomedical research enterprise.

Each of us as citizens has or will experience at some point in our lives these products directly ourselves or have them touch the lives of our family members. My late father passed away from glioblastoma multiforme, a rare brain cancer, immediately before I started medical school. His two and a half years struggling with the disease highlighted the benefits of therapeutic innovation – innovation gave him back time that otherwise would have been stolen from him. My mother passed away just last summer from dementia, a disease for which she had no treatment options and where friends and family slowly watch her mind recede. The isolation of the pandemic was broken in her final months by Operation Warp Speed, a public-private partnership launched by previous Administration that resulted in COVID-19 clinical preventive therapeutics. COVID-19 vaccines allowed her friends to visit her in the months preceding her passing, a small saving grace. The pain that individuals and their experience when confronted with a terminal disease for which there is no treatment available along with the benefits of biomedical innovation is well known to me as both a physician and family member.

As a wealthy country we have made a choice to spend a specific portion of our economic resources on healthcare delivery, with half of our annual healthcare expenditures dedicated to hospital and physician services.¹ While the healthcare delivery sector has suffered from the ills of consolidation and monopoly, the life sciences sector has remained vibrant with innovation in prescription and medical devices driving much of how medical care has changed. The treatment of myocardial infarction (MI) – commonly known as a heart attack – represents the benefits of biomedical innovation. Throughout the first half of the twentieth century, the standard of care was bedrest, avoidance of emotional stress, inhaled oxygen, and eventually blood thinners to prevent reinfarction along with nitroglycerine to relieve coronary spasm. Patients rarely resumed usual activity.² In the subsequent decades, both domestic and global medical innovation transformed the treatment of MI, with the development of reperfusion therapy through percutaneous coronary intervention and drug-eluting stents to open up blocked arteries, along with the addition of new

¹ Marin AB, Hartman M, Lassman D, et al. National Health Care Spending In 2019: Steady Growth For The Fourth Consecutive Year. *Health Affairs*. 2021;1:14-24. doi: 10.1377/hlthaff.2020.02022

² Braunwald E. (2012). The treatment of acute myocardial infarction: the Past, the Present, and the Future. *European heart journal. Acute cardiovascular care*, 1(1), 9–12. <https://doi.org/10.1177/2048872612438026>

therapeutics for secondary prevention such as statins for lipid management and beta-blockers and ace inhibitors for blood pressure control.³

Long a competitive global leader in pharmaceutical research and development and sales,^{4,5} American leadership in pharmaceutical product innovation – and medical device innovation too – is a complex multi-factor product of both bench and translational research investment in the private sector and governments shaped by U.S. Food & Drug Administration regulatory policy and payment policy, the latter highlighted by the controversy^{6,7,8} over the debate regarding administrative pricing and potential innovation losses centered around the recently proposed Build Back Better legislation.⁹

A subject of far less debate is the federal government’s reach into biomedical innovation. The government’s existing reach is vast,¹⁰ covering over ten agencies and over \$70 billion in annual funding (see Appendix).

2. Challenges with ARPA-H as Proposed

Policymakers seeking to promote biomedical research and innovation face many challenges with the proposed ARPA-H structure. Firstly, a strategic plan for the proposed organization’s research priorities remains elusive, with proposed legislation noting that ARPA-H director should provide one – including a list of research priorities – either 180 days¹¹ or one year¹² after the agency is established. In the face of over \$70 billion in annual, pre-existing federal biomedical research expenditures and after conducting ten listening sessions¹³ with over 5,100 stakeholders,¹⁴ the administration should make public a list of specific, initial scientific and medical research priorities so that policymakers, federal agency leaders, experts, and the public can understand identified research gaps and evaluate if existing programs can fill this gap.

³ Smith, S. C., Jr, Benjamin, E. J., Bonow, R. O., Braun, L. T., Creager, M. A., Franklin, B. A., Gibbons, R. J., Grundy, S. M., Hiratzka, L. F., Jones, D. W., Lloyd-Jones, D. M., Minissian, M., Mosca, L., Peterson, E. D., Sacco, R. L., Spertus, J., Stein, J. H., Taubert, K. A., & World Heart Federation and the Preventive Cardiovascular Nurses Association (2011). AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation*, 124(22), 2458–2473. <https://doi.org/10.1161/CIR.0b013e318235eb4d>

⁴ Grabowski, H. G. (1989). An Analysis of US International Competitiveness in Pharmaceuticals. *Managerial and Decision Economics*, 10, 27–33. <http://www.jstor.org/stable/2487208>

⁵ U.S. International Trade Commission. *Review of Global Competitiveness in the Pharmaceutical Industry, Staff Research Study #25*. 1999. Available from: <https://www.usitc.gov/publications/332/pub3172.pdf>

⁶ Durie, T., Philipson T. (2021). The Evidence Base on the Impact of Price Controls on Medical Innovation. Working Paper No. NO. 2021-108. Becker Friedman Institute for Economics at The University of Chicago. Available from: https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf

⁷ Holt, C., & Holtz-Eakin, D. (2022, January 13th, 2022). THE POTENTIAL IMPACTS OF THE BUILD BACK BETTER ACT’S DRUG POLICIES. Available from: <https://www.americanactionforum.org/insight/the-potential-impacts-of-the-build-back-better-acts-drug-policies/>

⁸ *Summary of Cost Estimate for H.R. 5376, the Build Back Better Act*. (2021). Washington, DC Retrieved from <https://www.cbo.gov/publication/57627>

⁹ BUILD BACK BETTER ACT, H.R. 5376, 117th Congress (2021).

¹⁰ Breakdown of Science Funding in 2021 Appropriations Request. *American Society for Microbiology* Retrieved from <https://asm.org/Articles/Policy/2020/Breakdown-of-Science-Funding-in-the-President-s-20> (Advocacy, 2020)

¹¹ Cures 2.0 Act, H.R. 6000, 117th Congress (2021)

¹² Advanced Research Project Agency–Health Act, H.R.5585, 117th Congress (2021)

¹³ Proposed Advanced Research Projects Agency for Health (APRA-H). (October 26, 2021). Retrieved from <https://www.nih.gov/arpa-h/events>

¹⁴ *ARPA-H Listening and Feedback Session Summary*. (2021). Washington DC Retrieved from <https://www.nih.gov/sites/default/files/research-training/initiatives/arpa-h/20211020-feedback-summary.pdf>

Culture is paramount, as noted in multiple planning documents.^{15,16} Former NIH Director Francis Collins, M.D., Ph.D., notes challenges with the peer review process that is key to the NIH Study Section grant review process:¹⁷

Another challenge is the peer review process. In theory, peer review, which is having other scientists external to the NIH evaluate and score the proposals, can help ensure that a proposal makes scientific sense and provides value. It is important to integrate peer review into many funding processes because when done appropriately peer review can provide the lens of the scientific community overall. However, when it comes to more unusual and innovative proposals, peer review can be fraught with land mines. The outcome of the review can depend heavily on which specific peers are assessing your application. Scientists can vary substantially in their willingness to entertain new ideas and take risks. Some peer reviewers may be stuck in particular ways of thinking. So if your proposal doesn't resonate with even one of the peer reviewers, it could sink like a pair of cinder block water skis.

Then there are the politics. Peer review can become a bit like the set of the movie Mean Girls, or perhaps more often Mean Boys. The scientific community is full of cliques and social clubs, especially among those who had the same advisors or are in the same narrow field or discipline. There's the risk of reviewers favoring applications from people whom they know and like. Those from more diverse backgrounds, who cross disciplines, or who don't have the "proper" connections may run into walls during peer review too. Ultimately traditional peer review may not always bring fresh new ideas and new people to the table.

As proposed, ARPA-H is to exist as an off-site arm of the NIH, with geographic distance, term limits for the director (5 years) and program managers (3-5 years), and direct oversight of grant administration¹⁸ as ameliorating tactics. While geographic distance and managerial independence have worked to empower some innovation-focused private-sector organizations such as Bell Labs and Xerox PARC, federal government-sponsored results have been more mixed.

DARPA represents a shining example of success having played a key role in the development on ARPANET (the predecessor to the internet), advances in microelectronics, and GPS receivers among other innovations;¹⁹ other federal examples raise significant questions. A more recent example, the CMS Innovation Center, was created in 2010 with a \$10 billion, ten-year budget. Conducting experiments in health finance, the Chief Actuary of CMS has only certified four of over fifty models for national scaling,²⁰ with only two – the Diabetes Prevention Program^{21,22} and components of the Pioneer ACO model – scaled.²³ Market impact has been limited: despite over 16.4 million beneficiaries

¹⁵ Lander, E., & Schwetz, T. (2021). *Advanced Research Projects Agency for Health (ARPA-H): A New Paradigm for Biomedical and Health Research*. Retrieved from https://www.acd.od.nih.gov/documents/presentations/06112021_ARPA-H.pdf See Slide 9 “Culture”

¹⁶ Lander, E., & Collins, F. (2021). *Advanced Research Project Agency for Health (ARPA-H): Concept Paper*. Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/06/ARPA-H-Concept-Paper.pdf>

¹⁷ Lee, B. (2021, July 6th, 2021). President Biden Proposes ARPA-H, New \$6.5 Billion Health Entity To Transform How Research Is Done. *Forbes*. Retrieved from <https://www.forbes.com/sites/brucelee/2021/07/06/president-biden-proposes-arpa-h-new-65-billion-health-entity-to-transform-how-research-is-done/?sh=4835aa254dab>

¹⁸ *ARPA-H Frequently Asked Questions*. (2021). Washington DC Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/09/092921-ARPA-H-FAQ.pdf>

See page 6, note that final programmatic decisions rest solely with the director, not the program managers.

¹⁹ *DARPA Accomplishments: Seminal Contributions to National Security*. October 2015. Retrieved from <https://www.darpa.mil/attachments/DARPAAccomplishmentsSeminalContributionsToNationalSecurity.pdf>

²⁰ Berwick DM, Gilfillan R. “Reinventing the Center for Medicare and Medicaid Innovation.” *JAMA* 325(13):1247-1248.

²¹ *Independent experts confirm that diabetes prevention model supported by the Affordable Care Act saves money and improves health*. (2016) Retrieved from <https://wayback.archive-it.org/3926/20170127185647/https://www.hhs.gov/about/news/2016/03/23/independent-experts-confirm-diabetes-prevention-model-supported-affordable-care-act-saves-money.html>

²² Medicare Diabetes Prevention Program Expansion. Centers for Medicare & Medicaid Services (2016). Available from: <https://www.cms.gov/newsroom/fact-sheets/medicare-diabetes-prevention-program-expansion>

²³ Berwick, DM., Gilfillan, R. (2021) Reinventing the Center for Medicaid and Medicare Innovation. *JAMA*. 2021;325(13):1247–1248. doi:10.1001/jama.2021.3203

estimated to meet eligibility criteria for the Diabetes Prevention Program,²⁴ by 2019 only 200 beneficiaries had enrolled.²⁵

Structural concerns must be addressed. If created as an independent agency, ARPA-H would either have to contract for or directly duplicate many core functions that existing research infrastructure at other federal research enterprises already operate; including program management, policy and planning, financial management, facilities management, and Congressional relations. Further, as proposed, an off-site campus site would be located several miles from the NIH main campus in one of the most expensive real estate markets in the country as opposed to lower cost locales.²⁶

Finally, leadership concerns should be carefully considered. Current legislation proposes that the ARPA-H director be a Presidential appointee.²⁷ However, other core public health agencies such as the NIH have Senate-confirmed heads, with recent legislation proposing that the CDC director be transitioned from a Presidential appointment to a Senate-confirmed position given the agency's sustained struggle across administrations during the pandemic.²⁸ If ARPA-H as proposed fills such a large public health need, Congressional input should be sought in selecting its leader.

3. A Rising China: Why ARPA-H Is Not Enough

A product of political strategy, regulatory reform, and talent recruitment, China's biomedical research investment and the growth of its life sciences industry has far exceeded that of many countries and represents a rising threat to American innovation. Chinese regulatory reform began in earnest in 201 as China's National Medical Products Administration (NMPA) implemented flexible pathways such as accelerated regulatory approval in 2016, with 774 applications received by the end of 2018, followed by the introduction of conditional approval in 2018 for drugs fulfilling unmet needs.²⁹

The corresponding market capitalization of Chinese biopharmaceutical companies has expanded, growing over one-hundred fold, or from \$3 billion in 2016 to \$380 billion in July 2021 and 23 IPOs in 2020, including seven of the ten largest global biopharma IPOs.³⁰ By 2020, over 272 China-based life sciences companies submitted applications for new molecular entities, with recent growth driven by the success of China-based companies as opposed to multinational pharmaceutical companies operating in China,³¹ and many Chinese companies focused on building platform technologies.

²⁴ Meyer H. (2021). Medicare Diabetes Prevention: Enrollment Short Of Projections. *Health Affairs (Project Hope)*, 40(11), 1682–1687. <https://doi.org/10.1377/hlthaff.2021.01292>

²⁵ Tahir, D. (2019). Medicare diabetes prevention program helps a few hundred instead of hundreds of thousands. *Politico*. Retrieved from <https://www.politico.com/news/2019/10/22/medicare-diabetes-hhs-055006>

²⁶ Guzior, B. (2018). Cities with the most affordable office space. *Bizwomen*. Retrieved from <https://www.bizjournals.com/bizwomen/news/latest-news/2018/05/cities-with-the-most-affordable-office-space.html?page=all>

²⁷ Cures 2.0 Act, H.R. 6000, 117th Congress (2021)

²⁸ Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act (PREVENT Pandemics Act) - Discussion Draft 117th Congress. (2022) Retrieved from <https://www.help.senate.gov/imo/media/doc/PREVENT%20Pandemics%20discussion%20draft%20sxs%20final.pdf>

²⁹ Le Deu, F., Tang, S., & Zhou, G. (2019). *Biopharma in China: Insights into a market at a crossroads*. Retrieved from <https://www.mckinsey.com/~media/mckinsey/industries/life%20sciences/our%20insights/biopharma%20in%20china%20insights%20into%20a%20market%20at%20a%20crossroads/biopharma-in-china-insights-into-a-market-vf.pdf?shouldIndex=false>

³⁰ Han, K., Le Deu, F., Zhang, F., & Zhou, J. (2021). *The dawn of China biopharma innovation*. (Page 2) Retrieved from <https://www.mckinsey.com/~media/mckinsey/industries/life%20sciences/our%20insights/the%20dawn%20of%20china%20biopharma%20innovation/the-rise-of-biopharma-innovation-in-china-vf.pdf?shouldIndex=false>

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³¹ Han, K., Le Deu, F., Zhang, F., & Zhou, J. (2021). *The dawn of China biopharma innovation*. (Page 5) Retrieved from <https://www.mckinsey.com/~media/mckinsey/industries/life%20sciences/our%20insights/the%20dawn%20of>

At a societal level, Chinese investment – public and private – in research and development simultaneously is reaching new heights, with China previously targeting a 2.5% of GDP spend on R&D, with public and private science and technology expenditures reaching \$322 billion in 2019.³² Researchers at the Baker Institute examined gross scientific and technical R&D expenditures, educational attainment, patent, and employment trends over the prior decade. They found that Chinese researchers are already exceeding their American counterparts in number and in patents granted, while Chinese gross domestic expenditures on overall R&D are expected to exceed those of the US (see Appendix for Figure). This growth is not accidental, and our trillion dollar “bioeconomy” faces significant global political risk.³³ China’s stated goals of its fourteenth five-year plan emphasize growing links between China’s academic researchers and industry and significant increases in basic science R&D as a share of GDP,³⁴ albeit challenges remain.³⁵

Chinese public and private investment growth and focus has coincided with the growth of the “Thousand Talents” program. Launched in 2008 and the subject of a recent U.S. Senate staff report,³⁶ the Thousand Talents program recruited researchers with salaries, research funding, and infrastructure.³⁷ While the scope within the US remains a source of debate, the program has reached prominent researchers³⁸ such as Charles Lieber, Ph.D., the former Chair of Harvard University’s Chemistry Department.^{39,40}

4. We Need A Strong Response to China

It is within this global context that consideration of domestic biomedical research funding is examined. There is no doubt that the role of the NIH is critical to innovation, with its extramural grant program serving as the agency’s crown jewel. Exploration of the origins of FDA-approved new molecular entities (NMEs) demonstrate this, with one study estimating that all drugs from a 2010 - 2016 were associated with an NIH-funded study at preceding drug targets, representing 20% of NIH funding during that very same period.⁴¹ Other studies found that 6.7% of new drugs

[%20china%20biopharma%20innovation/the-rise-of-biopharma-innovation-in-china-vf.pdf?shouldIndex=false](#) See Page 5

³² Normile, D. (2020). China again boosts R&D spending by more than 10%. *ScienceInsider* doi:doi:10.1126/science.abe5456

³³ Cumbers, J. (2020). China’s Plan To Beat The U.S. In The Trillion-Dollar Global Bioeconomy. *Forbes*. Retrieved from <https://www.forbes.com/sites/johncumbers/2020/02/03/china-now-out-invests-america-in-the-global-bioeconomy-by-30/?sh=1132a0fa7440>

³⁴ Mallapaty S. (2021). China’s five-year plan focuses on scientific self-reliance. *Nature*, 591(7850), 353–354. <https://doi.org/10.1038/d41586-021-00638-3>

³⁵ Bai, A., Wu, C., & Yang, K. (2021). Evolution and Features of China’s Central Government Funding System for Basic Research. *Frontiers in research metrics and analytics*, 6, 751497. <https://doi.org/10.3389/frma.2021.751497>

³⁶ *Threats to the U.S. Research Enterprise: China’s Talent Recruitment Plans* United States. Congress. Senate. Committee on Homeland Security and Governmental Affairs Retrieved from <https://www.hsgac.senate.gov/imo/media/doc/2019-11-18%20PSI%20Staff%20Report%20-%20China's%20Talent%20Recruitment%20Plans.pdf>

³⁷ Jia, H. (2018). WHAT IS CHINA’S THOUSAND TALENTS PLAN? *NATUREJOBS Career Guide: China* Retrieved from <https://media.nature.com/original/magazine-assets/d41586-018-00538-z/d41586-018-00538-z.pdf>

³⁸ Barry, E., & Kolata, G. (2020). China’s Lavish Funds Lured U.S. Scientists. What Did It Get in Return. *The New York Times* Retrieved from <https://www.nytimes.com/2020/02/06/us/chinas-lavish-funds-lured-us-scientists-what-did-it-get-in-return.html>

³⁹ Department of Chemistry and Chemical Biology: Charles Lieber. Retrieved from <https://chemistry.harvard.edu/people/charles-lieber>
Accessed February 4, 2022

⁴⁰ Harvard University Professor Convicted of Making False Statements and Tax Offenses. (2021). *U.S. Department of Justice* [Press release]. Retrieved from: <https://www.justice.gov/usao-ma/pr/harvard-university-professor-convicted-making-false-statements-and-tax-offenses>

⁴¹ Galkina Cleary, E., Beierlein, J. M., Khanuja, N. S., McNamee, L. M., & Ledley, F. D. (2018). Contribution of NIH funding to new drug approvals 2010-2016. *Proceedings of the National Academy of Sciences of the United States of America*, 115(10), 2329–2334. <https://doi.org/10.1073/pnas.1715368115>

originated in academia or government facilities,⁴² while still other work found that anywhere from 9.3 to 21.2% of new drugs or new indications originated in public-sector research institutions.⁴³ While opinions as the magnitude of the role vary, most policy experts agree that the NIH plays a critical role in funding bench research that serves as the subsequent basis for the private sector's impressive translational research enterprise.

The rise of China and an increasingly competitive global platform for the life sciences industry necessitate that we think bigger. Instead of creating ARPA-H as an independent agency or as an NIH institute, we should instead look to how we can apply the principles and concerns elaborated towards the entire NIH extramural grant program. Taxpayer funds should invest in projects where the “risk is too high, the cost is too large, the time frame is too long, the focus is too applied for academia, there is a need for complex coordination among multiple parties, and the near-term market opportunity is too small to justify the commercial benefit.”^{44,45} That is, taxpayer dollars should seek high-risk, high-reward opportunities as opposed to incremental innovation, while at the same time avoid areas of overlap⁴⁶ already targeted by the nearly \$36 billion life sciences investment put forward annually by the domestic venture capital community.⁴⁷

In pursuit of high-risk, high-reward opportunities for taxpayer funds, the ARPA-H proposal notes how DARPA is run by program managers who decide to fund applications or not,^{48,49} as opposed to a peer-review score-based system favored by the NIH study section. Applying a program manager model or adopting the FDA's “professional staff reviewer” model⁵⁰ could promote more rapid decision-making, increase flexibility, and allow for greater discretion and positive “idea risk” in project selection.

In this vein, policymakers may seek to increase funding for researchers to engage in revolutionary research. Luckily, direct research funding may be increased without additional expense to taxpayers. Most NIH grant proposals cover two types of costs: direct and indirect costs. Direct costs⁵¹ include expenses such as salaries, travel, equipment and supplies, or items linked directly to a project. In contrast, indirect costs or facilities and administrative costs,⁵² cover expenses such as buildings, maintenance, and administration. Initially only covering direct costs, indirect costs were

⁴² DiMasi, J. A., Hansen, R. W., & Grabowski, H. G. (2003). The price of innovation: new estimates of drug development costs. *Journal of health economics*, 22(2), 151–185. [https://doi.org/10.1016/S0167-6296\(02\)00126-1](https://doi.org/10.1016/S0167-6296(02)00126-1)

⁴³ Stevens, A. J., Jensen, J. J., Wyller, K., Kilgore, P. C., Chatterjee, S., & Rohrbaugh, M. L. (2011). The role of public-sector research in the discovery of drugs and vaccines. *The New England journal of medicine*, 364(6), 535–541. <https://doi.org/10.1056/NEJMsa1008268>

⁴⁴ *ARPA-H Frequently Asked Questions*. (2021). (Page 1). Washington DC Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/09/092921-ARPA-H-FAQ.pdf> See page 1

⁴⁵ Lander, E., & Collins, F. (2021). *Advanced Research Project Agency for Health (ARPA-H): Concept Paper*. Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/06/ARPA-H-Concept-Paper.pdf>

⁴⁶ *ARPA-H Listening and Feedback Session Summary*. (2021). Washington DC Retrieved from <https://www.nih.gov/sites/default/files/research-training/initiatives/arpa-h/20211020-feedback-summary.pdf>

⁴⁷ Miller, D. (2021). Record Year for U.S. Venture Capital Industry Despite Pandemic and Economic Downturn [Press release]. Retrieved from <https://nvca.org/pressreleases/record-year-for-u-s-venture-capital-industry-despite-pandemic-and-economic-downturn/>

⁴⁸ Collins, F. S., Schwetz, T. A., Tabak, L. A., & Lander, E. S. (2021). ARPA-H: Accelerating biomedical breakthroughs. *Science (New York, N.Y.)*, 373(6551), 165–167. <https://doi.org/10.1126/science.abj8547>

⁴⁹ *ARPA-H Listening and Feedback Session Summary*. (2021). (Pages 4-6) Washington DC Retrieved from <https://www.nih.gov/sites/default/files/research-training/initiatives/arpa-h/20211020-feedback-summary.pdf> See pages 4-6

⁵⁰ Miller, B., & Richardville, K. (2019). The NIH needs to become leaner and more innovative. Here's how to do that. *Stat News*. Retrieved from <https://www.statnews.com/2019/01/22/making-nih-leaner-more-innovative/>

⁵¹ NIH Grants Policy Statement (2021). Retrieved from https://grants.nih.gov/grants/policy/nihgps/html5/section_7/7.3_direct_costs_and_facilities_and_administrative_cost_s.htm

⁵² NIH Grants Policy Statement (2021). Retrieved from https://grants.nih.gov/grants/policy/nihgps/html5/section_1/1.2_definition_of_terms.htm#indirect_costs

later included with the rate raised to 8% in the 1940s.⁵³ The history of indirect cost rates⁵⁴ is complex, with a cap of 26% implemented in 1994. However, institutions in some circumstances may also negotiate with the government a specific indirect rate for the institution. A 2015 Government Accountability Office (GAO) study noted challenges with the indirect cost rate-setting process, with three offices – the HHS Cost Allocation Service, the NIH Division of Financial Advisory Services, and the Department of Defense Office of Naval Research – involved in negotiating indirect cost rates for NIH-funded grants.⁵⁵ With indirect grant rates now averaging 52%, over the preceding decade both Republican and Democratic administrations have proposed reforms.⁵⁶

Process reforms could provide significantly increased funding and allow policymakers to help transform the NIH's \$31 billion extramural grant program,⁵⁷ specifically:

1. *Improve accountability*
 - a. Require organizations to specify and make public where indirect dollars flow for all extramural grants using the principles of activity-based costing (i.e. transparency in flow of funds)
 - b. Support HHS OIG oversight of grant-making to ensure appropriate use of funds and protect against problematic project selection.^{58,59}
2. *Decreasing investigator administrative burdens* by simplifying grant application processes and eliminating unnecessary steps such as laudatory references letters,⁶⁰ noting that the grant submission guidance itself is now 153 pages in length⁶¹
3. *Increase available direct research funding* by capping and/or tiering indirect rates
 - a. Caps: mirroring other governmental⁶² or private foundation^{63,64} best practices
 - b. Tiering: create a three tier indirect cost rate policy inversely tied to the institution's rolling three-year average of NIH funding to combat concerns regarding the lack of diversity of funded institutions and investigators^{65,66} and correct the current system which favors wealthy institutions
 - c. Providing transparency of achievements to program managers, in addition to creating innovation-driven metrics of success and failure, both short and long-term

⁵³ Allen, E. (1980). Early Years of NIH Research Grants. Retrieved from <https://history.nih.gov/display/history/Publications?preview=/1016824/8883687/AllenGrantsHistory.pdf#Publications-InstitutionalHistories>

⁵⁴ Rockey, S. (2015). All About Indirect Costs. Retrieved from <https://nexus.od.nih.gov/all/2015/09/11/all-about-indirect-costs/>

⁵⁵ *NIH BIOMEDICAL RESEARCH: Agencies Involved in the Indirect Cost Rate-Setting Process Need to Improve Controls*. Government Accountability Office (2016). Retrieved from <https://www.gao.gov/assets/gao-16-616.pdf>

⁵⁶ NIH plan to reduce overhead payments draws fire. ScienceInsider 2017. doi: 10.1126/science.aan6926

⁵⁷ Lauer, M. (2021). *FY 2020 By the Numbers: Extramural Investments in Research*. Retrieved from <https://nexus.od.nih.gov/all/2021/04/21/fy-2020-by-the-numbers-extramural-investments-in-research/>

⁵⁸ Ohio State study: Even healthy cats act sick when their routine is disrupted. (2011). Retrieved from <https://news.osu.edu/ohio-state-study-even-healthy-cats-act-sick-when-their-routine-is-disrupted/>

⁵⁹ Stella, J., Croney, C., & Buffington, T. (2013). Effects of stressors on the behavior and physiology of domestic cats. *Applied animal behaviour science*, 143(2-4), 157–163. <https://doi.org/10.1016/j.applanim.2012.10.014>

⁶⁰ NIH Grant Application: Reference Letter. Retrieved from <https://grants.nih.gov/grants/how-to-apply-application-guide/submission-process/reference-letters.htm>

⁶¹ Research Instructions for NIH and other PHS Agencies (2018). Retrieved from <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/research-forms-e.pdf>

⁶² Schiermeier Q. (2013). European deal cuts red tape. *Nature*, 499(7456), 18–19. <https://doi.org/10.1038/499018a>

⁶³ Indirect Cost Policy – Bill and Melinda Gates Foundation. (2017). Retrieved from https://docs.gatesfoundation.org/documents/indirect_cost_policy.pdf. The Gates Foundation allows up to a 15% IDC rate for non-government organizations and for-profit organizations, or a 10% rate for universities.

⁶⁴ Indirect Cost Policy – MacArthur Foundation. Retrieved from <https://www.macfound.org/about/our-policies/indirect-cost-policy/>. The MacArthur Foundation assigns a 29% IDC rate.

⁶⁵ Miller, B., & Richardville, K. (2019). The NIH needs to become leaner and more innovative. Here's how to do that. *Stat News*. Retrieved from <https://www.statnews.com/2019/01/22/making-nih-leaner-more-innovative/>

⁶⁶ Pohlhaus, J. R., Jiang, H., Wagner, R. M., Schaffer, W. T., & Pinn, V. W. (2011). Sex differences in application, success, and funding rates for NIH extramural programs. *Academic medicine : journal of the Association of American Medical Colleges*, 86(6), 759–767. <https://doi.org/10.1097/ACM.0b013e31821836ff>

In particular, increasing direct research funding – and decreasing indirect rates in order to do so – could free up over \$2 billion in direct research funds, offering hope for a new generation of researchers, who on average achieve their first R01 grant award now at age 42⁶⁷ in a hypercompetitive marketplace with the number of awardees remaining flat while the number of grant applicants has increased 50%.⁶⁸ Initially, Congress could support researchers through consolidating the authority for institutional indirect rate negotiations for NIH grants in a single office at the NIH, reducing administrative burdens, and implementing rigorous, public transparency requirements for indirect costs. Subsequent reforms focused around the indirect cost rate themselves would need to carefully consider institutional concerns, with ameliorating mechanisms such as a five-year phase-in for new indirect rates to help avoid supply shocks.

4. Conclusions: Supercharging Innovation

One of the great joys of policy regarding biomedical research funding is that it is uniquely bipartisan: everyone is trying to get to the same place, just with different ideas of how best to get there. Biomedical research ultimately powers innovations that are meaningful to us as patients, clinicians, and society as a whole. Both public and private sectors play a key role. The private sector drives translational research, with the pharmaceutical industry alone investing \$89 billion (2019)⁶⁹ while life sciences venture capital poured \$36 billion into the market (2020),⁷⁰ both individually exceeding the size of the NIH’s extramural grant program.

As a country we invest over \$70 billion annually in biomedical research across innumerable agencies. While structural, leadership, and strategic challenges remain, the rationale underlying the proposal for ARPA-H highlights many valid concerns present in our nation’s federal biomedical research infrastructure. Coupled with the rise of China and a state-sponsored life sciences industry, it is clear that ARPA-H as proposed is not enough for the U.S. to remain the leader in global biomedical innovation.

In order to ensure the continued success of the American life sciences industry, we must think bigger. Reforming the NIH’s \$31 billion extramural grant program to transform it along the principles of ARPA-H presents an opportunity to ensure sustainable innovation and growth for the benefit of all Americans. Specific changes providing benefits to taxpayers and relief to researchers include improved transparency, decreased administrative burdens for researchers, and increased direct research funding through modification of indirect costs along with other operational changes. Finally, in addition to sound research funding policy, policymakers must address downstream regulatory barriers to life sciences innovation, such as challenges that the Medicaid Drug Rebate Program presents to valued-based contracting⁷¹ and the need for a new FDA regulatory pathway to provide a less burdensome path to market for software-driven medical devices.

⁶⁷ Rockey, S. (2012) Our Commitment to Supporting the Next Generation. Retrieved from <https://nexus.od.nih.gov/all/2012/02/03/our-commitment-to-supporting-the-next-generation/>

⁶⁸ Lauer, M. (2016) How Many Researchers? Retrieved from <https://nexus.od.nih.gov/all/2016/05/31/how-many-researchers/>

⁶⁹ *Research and Development in the Pharmaceutical Industry*. (2021). Congressional Budget Office. Retrieved from <https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf>

⁷⁰ Miller, D. (2021). Record Year for U.S. Venture Capital Industry Despite Pandemic and Economic Downturn [Press release]. Retrieved from <https://nvca.org/pressreleases/record-year-for-u-s-venture-capital-industry-despite-pandemic-and-economic-downturn/>

⁷¹ Miller, B. J., & Zima, S. C. (2020). Exceptions for Exceptional Cures—Modernizing the Medicaid Drug Rebate Program. *JAMA Health Forum*, 1(8), e201058-e201058. doi:10.1001/jamahealthforum.2020.1058

Appendix

Federal Biomedical and Scientific Research Expenditures*

- a. NIH extramural grant program - \$38.3B (out of total \$42.9B)
 - i. \$31.2B is in the enacted budget and \$6.1 billion is in CAREST Act Funding
 - ii. Existing high-risk NIH programs
 - 1. Common Fund - \$0.648B in 2021
 - a. Includes the Director's High-Risk, High-Reward Research Program – \$0.197B
 - i. Early Independence Award - \$21.5M
 - ii. Transformative Research Award - \$38.7M
 - iii. Pioneer Award - \$50.5M
 - iv. New Innovator Award - \$62.4M
 - 2. NCATS - \$0.855B
 - b. BARDA - \$0.597B in 2021
 - c. HHS: Public Health and Social Services Emergency Fund - \$0.209B in 2021
 - d. DoD Basic and Applied Research, Development, Test, and Evaluation Activities – \$8.1B
 - i. DARPA - \$3.50B
 - ii. Armed Forces Research Institute. - \$0.035B
 - e. CDC - \$7.9B
 - f. VA Office of Research and Development - \$0.815B
 - g. USDA – \$1.4B
 - h. Dept of Energy - \$2.4B
 - i. NSF - \$9.1B
 - j. NOAA - \$4.1B
 - k. USGS - \$0.237B
 - l. EPA - \$0.73B
 - m. NASA = \$0.079B
- Sum total annual dollars spent: \$74B (2021)*

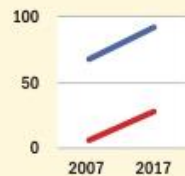
*2021 unless otherwise specified. This incomplete list does not include the efforts of other agencies the lack clear budgetary data for research expenditures such as the FDA, the intelligence agencies, and other entities.

China's Rise in Research and Engineering

1. Gross Domestic Expenditure on R&D, in billions of current \$USD PPP, 2007 - 2017



2. National Expenditures, in Basic Research, in billions of current \$USD PPP, 2007 - 2017



3. Patents Granted, Direct and PCT National Phase Entries, in thousands, 2008 - 2018



4. S&E Articles in All Fields, in thousands, 2008 - 2018



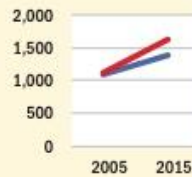
5. S&E First University Degrees (Bachelor's), in thousands, 2005 - 2015



6. S&E Doctorates, in thousands, 2005 - 2015



7. Researchers, in thousands, 2005 - 2015



— China — United States

Source: Figure 3 from “The Perils of Complacency: America at a Tipping Point in Science & Engineering.” Report Brief, Rice University’s Baker Institute for Public Policy, 2020.