NIH IN THE 21st CENTURY:

ENSURING TRANSPARENCY AND AMERICAN BIOMEDICAL LEADERSHIP

Senate Committee on
Health, Education, Labor & Pensions
Senator Bill Cassidy, M.D. , Ranking Member

Introduction

The National Institutes of Health (NIH) funds more biomedical research than any other public institution in the world, making the agency a key driver of the United States' strategic advantage in science and technology. NIH consists of 27 institutes and centers (ICs) and has a budget of more than $49 billion. Yet NIH's authorization of appropriations lapsed at the end of fiscal year (FY) 2020, and Congress' last large-scale review of the agency's activities and authorities occurred nearly a decade ago, culminating in the enactment of the 21st Century Cures Act.

As Ranking Member of the Senate Health, Education, Labor, and Pensions (HELP) Committee, I issued a request for information (RFI) from stakeholders in September 2023 seeking feedback on NIH's current activities and statutory framework. Respondents to the RFI ranged from academic institutions; relevant professional societies, think tanks, and trade associations; patient advocates; and individual researchers sharing their observations from careers working within the NIH ecosystem. Respondents identified multiple opportunities for legislative action that would build upon past congressional efforts to strengthen NIH and the U.S. biomedical research enterprise. In this white paper, I put forward a selection of proposals to invite discussion of policies that may be appropriate for legislative action. I look forward to working with my colleagues in Congress and all interested stakeholders to ensure that NIH is well prepared to seize scientific opportunities to advance the health and wellbeing of Americans in the decades to come.

Brief Legislative History

NIH began in 1887 with the creation of the Laboratory of Hygiene as part of the Marine Hospital Service, the predecessor to the modern Public Health Service. Over the next 40 years, Congress repeatedly charged the Marine Hospital Service via the Hygiene Laboratory with researching specific infectious diseases and other conditions.[1] In 1930, Congress passed legislation sponsored by then-Louisiana Senator Joseph E. Ransdell to rename the Hygiene Laboratory the National Institute of Health and created research fellowships within the Institute.[2] The National Institute of Health began building its current Bethesda, Maryland headquarters through a series of land donations and congressional appropriations later that decade.[3]

In 1944, Congress enacted the Public Health Service Act, which revised the previous patchwork of federal public health laws into a more cohesive framework to support biomedical research, disease control, and patient care. The Public Health Service Act reorganized the National Cancer Institute into the National Institute of Health, provided authorities that eventually led to the establishment of the NIH Clinical Center, and created other divisions to support NIH's biomedical research mission.[4] Between the 1940s and 1970s, Congress enacted multiple laws to establish new ICs within NIH, make "institutes" plural in the agency's name, expand its authorities to support biomedical research capacity, and prioritize certain areas of research.[5]

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1 *Chronology of Events*, NATIONAL INSTITUTES OF HEALTH, https://www.nih.gov/about-nih/what-we-do/nih-almanac/chronology-events (last updated Oct. 5, 2023) (during this period, Congress changed the name from the Laboratory of Hygiene to the Hygiene Laboratory).

2 *WWI and the Ransdell Act of 1930,* NATIONAL INSTITUTES OF HEALTH, https://history.nih.gov/display/history/WWI+and+the+Ransdell+Act+of+1930 (last visited Apr. 29, 2024).

3 *Id.*

4 *Id.*

5 NATIONAL INSTITUTES OF HEALTH, supra note 1.

In the 1980s, Congress focused on incentivizing the commercialization of federally funded research through laws such as the Bayh-Dole Act, the Small Business Innovation Development Act, and the Stevenson-Wydler Act.[6] While not limited to NIH, these laws profoundly reshaped NIH's intramural and extramural research operations and emphasized the importance of translational science. In the 1990s, Congress authorized the Foundation for NIH, which supports intramural scientists and helps broker NIH's public-private partnerships, and passed the NIH Revitalization Act, which established multiple new components of NIH and the Department-level Office of Research Integrity, allowed NIH to support extramural construction activities, established the Institutional Development Award (IDeA) program, and created scholarship and loan repayment programs.[7]

Over the past two decades, Congress has enacted multiple laws to continue improving NIH operations. In 2000, Congress passed the Public Health Improvement Act, which supported biomedical research capacity, and the Children's Health Act, which established the NIH Pediatric Research Initiative. Congress enacted the NIH Reform Act in 2007, which addressed NIH's structure, operations, and public transparency.[8] Specifically, the NIH Reform Act created the Common Fund to support crosscutting NIH research initiatives of strategic and scientific importance and the Council of Councils to advise the Director on administering the Common Fund and carrying out other crosscutting NIH research initiatives. The law also consolidated authorizations of appropriations for individual NIH programs into a single authorization level for the agency, created the Scientific Management Review Board to advise on NIH's structure and organization, and directed NIH to establish an electronic system for reporting and categorizing NIH-funded research.[9] The current system is known as the Research Portfolio Online Reporting Tools (RePORT). As part of the Food and Drug Administration Amendments Act of 2007, Congress directed NIH to expand the information included about ongoing studies on clinicaltrials.gov and required certain trials to be registered with and report results on the website. The 21st Century Cures Act (commonly referred to as "Cures"), enacted in 2016, built on the NIH Reform Act by emphasizing the importance of strategic planning, streamlining administrative requirements, providing additional authorities to the NIH Director, and establishing a process for the periodic review of each IC Director's performance.[10] The 21st Century Cures Act also included policies to encourage more high-quality research, support the next generation of scientists, and facilitate the participation in research of pregnant and postpartum women, children, and other underrepresented populations. The law also provided one-time funding for certain large-scale research initiatives. Despite these bipartisan legislative successes and consistent, annual investment in NIH, opportunities remain to improve NIH's operations to better support the U.S. biomedical research enterprise.

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6 *Id.*

7 *Id.*

8 *Id.*

9 Judith A. Johnson & Kavya Sekar, The National Institutes of Health (NIH): *Background and Congressional Issues,* CONGRESSIONAL RESEARCH SERVICE 5 (Apr. 19, 2019), https://www.crs.gov/reports/pdf/R41705/R41705.pdf.

10 Amanda K. Sarata, *The 21st Century Cures Act (Division A of P.L. 114-255)*, CONGRESSIONAL RESEARCH SERVICE (Dec. 23, 2016), https://www.crs.gov/reports/pdf/R44720/R44720.pdf.

Maximizing the Effectiveness of Current NIH Funding

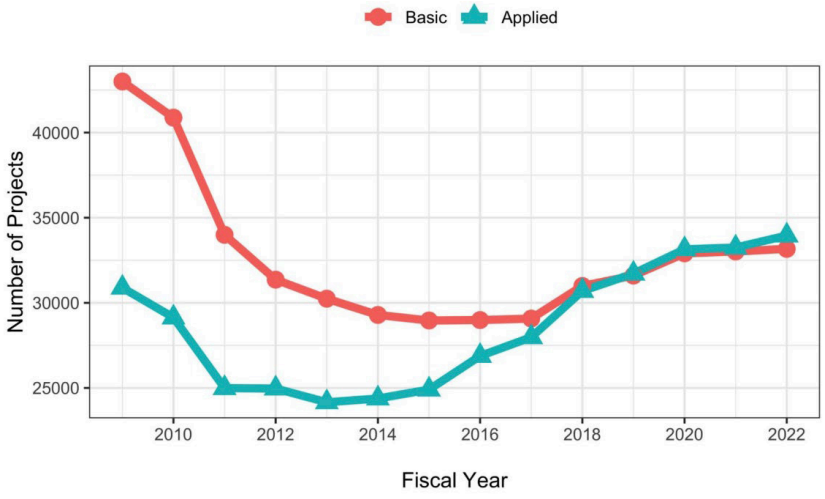
Balancing NIH's Portfolio

Each year, NIH dedicates 80 percent of its budget to extramural research activities and an additional 11 percent to its intramural research program.[11] NIH annually supports approximately 50,000 new or ongoing extramural projects, over 30,000 of which (60 percent) are R01-equivalent grants.[12] R01-equivalent grants support specific, often investigator-initiated research activities for a limited duration of three to five years.

A recent analysis from NIH's Office of Extramural Research found that applied projects represent a growing portion of NIH's extramural portfolio. In FY22, over 45 percent of R01 grants and 50 percent of all awards were for applied projects, compared to approximately 38 percent and 42 percent, respectively, in FY09.[13] Figure 1 is taken from this Office of Extramural Research analysis and demonstrates this shift toward applied research in terms of overall number of projects.

This shift toward applied research is consistent with recent government-wide trends because applied research often has a more immediate, tangible impact on Americans' daily lives (evident in developments like the creation of the Advanced Research Projects Agency for Health and the National Science Foundation's (NSF) new Directorate for Technology, Innovation, and Partnerships).[15] However, many respondents expressed concern that NIH's increasing focus on translational and clinical research will come at the expense of investigator-initiated, basic science, the historic heart of NIH's business model. The U.S. Government plays a unique role in supporting basic discovery, which enables long-term biomedical innovation. One RFI respondent noted that the Office of Management and Budget (OMB) has historically directed NIH to dedicate at least 55

Figure 1. NIH Extramural Research Portfolio, FY 2009-2022



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11 Francis S. Collins, *NIH-Wide Strategic Plan for Fiscal Years 2021–2025*, NATIONAL INSTITUTES OF HEALTH 1 (July 30, 2021), https://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2021-2025-508.pdf.

12 *Id.*; *see also* NIH Data Book, *R01-Equivalent Grants,* NATIONAL INSTITUTES OF HEALTH, https://report.nih.gov/nihdatabook/category/3 (last visited Apr. 29, 2024).

13 Mike Lauer, *Trends in NIH-Supported Basic, Translational, and Clinical Research: FYs 2009-2022*, NATIONAL INSTITUTES OF HEALTH OFFICE OF EXTRAMURAL RESEARCH (Oct. 31, 2023), https://nexus.od.nih.gov/all/2023/10/31/trends-in-nih-supported-basic-translational-and-clinical-research-fys-2009-2022/.

14 *Id.*

15 *Technology, Innovation and Partnerships,* U.S. NATIONAL SCIENCE FOUNDATION, https://new.nsf.gov/tip/latest (last visited Apr. 29, 2024).

percent of its portfolio to basic research in recognition of this unique role, and some previous NIH directors have sought to exceed that recommended level. Waning federal focus on basic research could lead to a decline in treatments and cures eventually developed through private funding. Unlike certain areas of clinical research, the private sector would not be equipped to fill gaps in support for basic research.

Another challenge within NIH's research portfolio is balancing the need to direct research toward specific topics of significant public health interest (referred to as "targeted research") with investigator-initiated research. In FY23, targeted research comprised 12 percent of all new research project grants made by NIH, a total of 20 percent of all new research project grant funding awarded.[16] This targeted funding ties back to more than 60 discrete funding levels specified by Congress in the FY23 annual appropriations report language.[17] On the one hand, direction from Congress and NIH senior leadership can be beneficial to focus the research community on high-impact areas of research and ensure NIH is appropriately prioritizing work to address diseases of significant unmet need. For example, Box 1 briefly describes NIH's underinvestment in nutrition and obesity research, an area of public health importance. However, too much direction can warp the portfolio as a whole, dissuading investigators from pursuing other research topics that could have broad benefit and to create a naturally diversified portfolio.[18] Further analysis of NIH's internal data could help the research community, policymakers, and stakeholders better understand how to appropriately balance these competing interests.

Box 1. Nutrition and Obesity Research

Obesity is correlated with multiple leading causes of death in the U.S. and contributes more than $147 billion annually in medical costs. However, one analysis found that NIH dedicated a mere $1.9 billion to nutrition research in FY19, and only 1.3 percent of all NIH-funded research projects addressed the role of diet and nutrition in the prevention and treatment of disease. This compares to over $3.8 billion spent in the same year on cardiovascular disease and $16.9 billion on Type 2 diabetes research.

At the same time, NIH attempted to shut down its intramural metabolic research unit, one of a handful of facilities around the country capable of conducting complex clinical research to evaluate the metabolic effects of diet. This historic devaluing of the importance of nutrition science likely resulted in missed opportunities to improve the rigor of nutrition research and indicates a misalignment between NIH spending and public health impact.

Reducing Redundancy and Finding Efficiencies

Reducing redundancy could improve the balance of NIH's portfolio by making more resources available within NIH's existing budget. Under statute, the NIH director is responsible for classifying and publicly reporting NIH-funded research projects and conducting priority-setting

16 NIH Data Book, *Research Project Grants*, NATIONAL INSTITUTES OF HEALTH, https://report.nih.gov/nihdatabook/category/4 (last visited Apr. 29, 2024).

17 *National Institutes of Health (NIH) Funding: FY1996-FY2024,* CONGRESSIONAL RESEARCH SERVICE 13-17 (May 17, 2023), https://crsreports.congress.gov/product/pdf/R/R43341.

18 Box 1 Citations; NIH RePORTER, NATIONAL INSTITUTES OF HEALTH, https://reporter.nih.gov/search/4iuRVEmSKUG9nSmDJCJB4A/projects/charts (last visited Apr. 29, 2024); Sheila Fleischhacker et al., *Strengthening national nutrition research: rationale and options for a new coordinated federal research effort and authority,* AMERICAN SOCIETY FOR NUTRITION (Jul. 20, 2020), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7454258/; Catherine Boudreau & Helena Bottemiller Evich, How Washington keeps America sick and fat, POLITICO (Nov. 4, 2019), https://www.politico.com/news/agenda/2019/11/04/why-we-dont-know-what-to-eat-060299; *Obesity Basics*, CENTERS FOR DISEASE CONTROL AND PREVENTION, https://www.cdc.gov/obesity/basics/index.html (last updated June 3, 2022).

reviews for the agency.[19] However, it is unclear what steps current and former directors have taken to formally conduct these reviews and whether analysis of NIH's internal and public-facing data contributes to the reviews. These reviews and corresponding analyses should provide a unique opportunity for the NIH director to identify areas of research duplication and potential collaboration between ICs.

In addition to duplication within IC research portfolios, NIH should also consider potentially redundant research infrastructure. For example, each IC supports its own clinical trial networks that may have overlap in their capabilities and purposes. During the planning process for NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) initiative, an NIH working group assessed the capabilities of 60 clinical trial networks to identify the most appropriate sites through which to carry out ACTIV trials.[20] NIH should build on this assessment to explore integrating its existing trial networks into a more cohesive, enterprise-wide clinical trials capability. As part of this process, NIH should consider how best to reach patients who may be prospective research participants. For example, the National Cancer Institute's Community Oncology Research Program (NCORP) is a community-based model for trial design that brings clinical trials directly to patients through their local hospitals and doctors' offices. The Council of Councils recently approved a proposal from NIH Director Bertagnolli to establish an NIH-wide primary care clinical trial network over a five-year period.[21] Community-based clinical trial networks that more centrally involve non-degree granting institutions could improve the accessibility of clinical trials for patients across the country. However, any new network must account for and build upon existing capabilities without exacerbating existing duplication within NIH's portfolio.

Learning from Scientific Successes and Failures

Other untapped resources include data NIH and its extramural partners possess on applications for funding and the outcomes of funded projects. NIH currently publishes data on which projects and researchers receive funding (commonly referred to as the "success rate").[22] However, more granular data about how specific proposals fare through the peer review process and are ultimately selected or rejected for funding are not available. Several respondents to my RFI stated that access to this data would enable researchers to conduct metascience research on the scientific process. NIH's Office of Portfolio Analysis has supported some metascience initiatives by aggregating information related to citations of published papers and contributing to the development of best practices in the field.[23] Piloting a process for the secure sharing of NIH application and review data with trusted researchers would help identify or validate trends within NIH processes and recommend process improvements.

Researchers also often lack insight when experiments produce null or inconclusive results (collectively referred to as "negative results") because these findings are typically not published in academic journals. Yet, negative results can themselves advance lines of scientific inquiry, such as questioning or ultimately refuting a

19 Public Health Service Act § 42 U.S.C. § 282(b); 42 U.S.C. § 282(b)(3).
20 *Clinical Trial Capacity Working Group*, NATIONAL INSTITUTES OF HEALTH, https://www.nih.gov/research-training/medical-research-initiatives/activ/clinical-trial-capacity-working-group (last updated Dec. 23, 2020).
21 Council of Councils Meeting, *Agenda*, NATIONAL INSTITUTES OF HEALTH, https://dpcpsi.nih.gov/council/april-5-2024-agenda (last updated Apr. 5, 2024).
22 *NIH Success Rates*, NATIONAL INSTITUTES OF HEALTH, https://report.nih.gov/funding/nih-budget-and-spending-data-past-fiscal-years/success-rates (last visited Apr. 29, 2024).
23 George M. Santangelo, *Office of Portfolio Analysis Strategic Plan FYs 2021-2025*, NATIONAL INSTITUTES OF HEALTH OFFICE OF PORTFOLIO ANALYSIS 19 (Aug. 27, 2023), https://dpcpsi.nih.gov/sites/default/files/OD-OPA-FY2021-2025-SP-Public-508_11_1_2021.pdf#page=19.

hypothesis, pointing investigators in more fruitful directions, or identifying flaws in a methodology. While some peer-reviewed journals do accept negative results for publication, the direct expenses and opportunity costs to the researcher associated with preparing an article, along with any perceived reputational costs associated with an unsuccessful experiment, may serve as a disincentive to publish these results. NIH should consider strategies to encourage the voluntary sharing of negative results, such as the establishment of a negative results repository within the National Library of Medicine.

Sustaining the United States' Competitive Advantage in Biomedical Research

According to some estimates, every dollar NIH spends on research generates $2.46 in economic activity.[24] FY23 investments provided support for over 400,000 jobs and generated nearly $93 billion.[25] However, China's aggressive investment in biomedical research, such as through the Thousand Talents program and Made in China 2025, threatens the US' long-term competitive advantage. Winning the biomedical research arms race requires a critical review of NIH's current policies and practices to better support the domestic biomedical research enterprise.

Incentivizing Innovation

Respondents to my RFI noted that NIH's extramural research programs tend to reward incremental science, rather than high-risk, but potentially transformational studies and identified the current approach to peer review as a driver of incrementalism. Peer review is foundational to the NIH model, and peer reviewers provide an invaluable service to the research enterprise by volunteering their time and expertise. However, some respondents noted that the heavy involvement of subject matter experts—rather than "generalists" who are not as embedded in a particular area of research—can bias study sections toward the approaches and methodologies favored by such experts. Respondents also noted that this phenomenon leads peer review committees to focus heavily on the mechanics of the proposed methodology and likelihood of success, rather than the overall scientific vision and potential impact of the proposal. The structure of funding applications lend themselves to such a discussion during peer review: R01 applications consist of a one-page statement of objectives and a 12-page research strategy, which includes discussion of proposed methodology and preliminary results.[26] As a result, respondents noted that researchers face significant pressure to demonstrate proof of concept through robust preliminary data prior to applying for funding. Respondents also noted inconsistencies between peer reviewers, review cycles, and situations when peer reviewers turn over mid-review. In some cases, researchers might even tailor their application to target specific study sections that may be more receptive to their proposal. To address these myriad challenges, NIH should pilot and evaluate multiple approaches to changing the application and peer review process, including staffing committees with more generalists, streamlining application discussion of methodology and preliminary results, regularly reviewing the focus and members of study sections to promote alignment with current science, and improving training of peer reviewers to make reviews more consistent.

NIH's Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs

24 *NIH's Role in Sustaining the U.S. Economy,* UNITED FOR MEDICAL RESEARCH 1 (Mar. 2024), https://www.unitedformedicalresearch.org/wp-content/uploads/2024/03/UMR-NIHs-Role-in-Sustaining-the-US-Economy-2024-Update.pdf.
25 *Id.*
26 *Write Your Research Plan*, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, https://www.niaid.nih.gov/grants-contracts/write-research-plan#:~:text=The%20Research%20Strategy's%20page%20limit (last updated July 26, 2017).

also demonstrate room for administrative improvement to better achieve program goals. Respondents specifically cited as barriers NIH's longer window to make awards compared to other Federal departments that operate their own SBIR and STTR programs. For example, the Department of Defense takes three months, on average, to notify successful applicants of an award, compared to NIH's six and a half months.[27] NIH also uses similar program management and peer review structures for its SBIR and STTR programs to those described above for other extramural research. A recent National Academies of Sciences, Engineering, and Medicine review recommended that Congress and NIH explore piloting ways to make NIH SBIR and STTR programs more timely and responsive to the needs of small businesses.[28] The John S. McCain National Defense Authorization Act for Fiscal Year 2019 directed the Department of Defense to establish a similar pilot program to speed up its SBIR and STTR review and awards process.[29] Some respondents to my RFI recommended NIH take a more venture capital-style approach to its administration of the program by exempting from, or dramatically reworking, the peer review process for SBIR and STTR to speed application review timeframes and hiring individuals with venture capital or other business expertise to serve as program officers. NIH's successful Rapid Acceleration of Diagnostics (RADx) program during the COVID-19 pandemic provides one model for how NIH could quickly and effectively assess the promise and feasibility of SBIR and STTR proposals.

Program officers also play a key role in NIH's extramural research prioritization and funding decisions. As staff scientists responsible for managing grant portfolios, program officers advise prospective applicants on the relevance of their proposed projects, develop requests for proposals and targeted research opportunities, and provide expertise to the agency.[30] NIH program officers are typically permanent employees of the agency who develop specific areas of interest and expertise over time. Respondents pointed out that other agencies, such as the NSF, employ temporary program officers through "rotator" programs.[31] Similarly, advanced research projects agencies across the federal government limit the term of their program managers to only a few years. These time-limited appointments enable more individuals to work within the agency, inject the agency with fresh ideas and up-to-date scientific knowledge, and take their understanding of the agency and its priorities back to their research positions following the conclusion of their rotation. NIH should pilot a rotator approach to fill program officer positions and related key roles.

Fundamental to the success of NIH's model is collaboration: with researchers and their institutions, small businesses, and larger biopharmaceutical firms via formal public-private partnerships. Without robust partnerships, NIH would not have the same degree of impact on the advancement of science and economic activity. As Congress and NIH explore strategies to strengthen and improve these partnerships, policymakers must avoid the temptation of policies, such as the abuse of march-in rights, that would ultimately have a chilling effect on collaboration. In addition to undercutting the goals of the Bayh-Dole Act, the use of march-in rights to address drug prices would explicitly violate congressional intent, according to the bipartisan authors of the law, former Senators Birch Bayh (D-IN) and Bob Dole (R-KS).[32]

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27 *Assessment of the SBIR and STTR Programs at the National Institutes of Health*, NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE 78 (Feb. 9 2022), https://www.ncbi.nlm.nih.gov/books/NBK577834/.

28 *Id*. at ix.

29 15 U.S.C. § 638 as amended by P.L. 115-232 § 854(b).

30 *Program Officers SOP*, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, https://www.niaid.nih.gov/research/program-officers (last updated June 9, 2020).

31 *Rotator Programs*, U.S. NATIONAL SCIENCE FOUNDATION, https://new.nsf.gov/careers/rotator-programs (last visited Apr. 29, 2024).

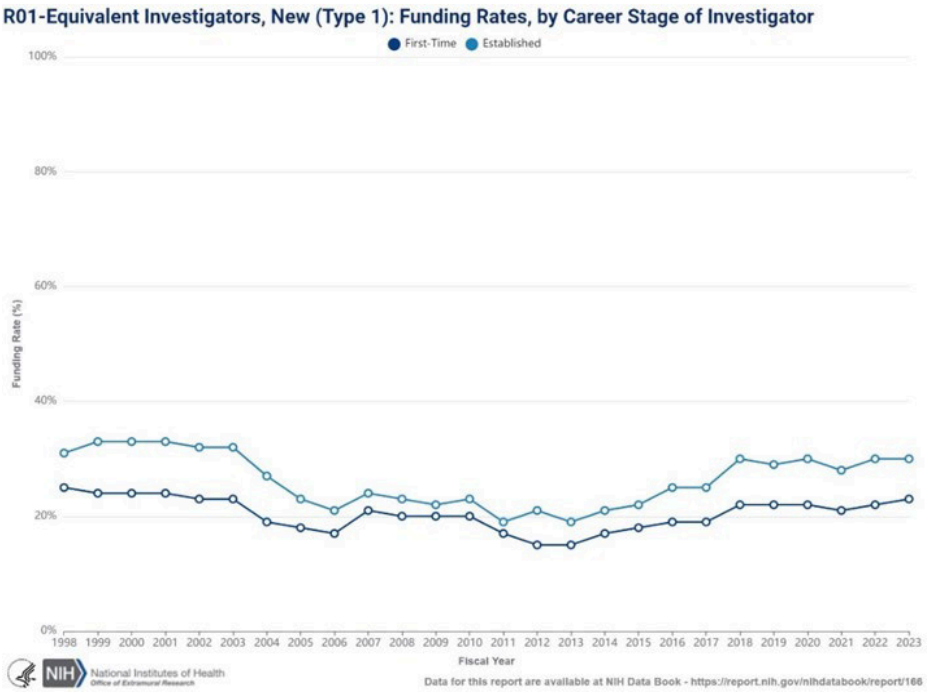
32 Robert Dole & Birch Bayh, *Our Law Helps Patients Get New Drugs Sooner*, THE WASHINGTON POST (Apr. 10, 2002), https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-

Supporting the Biomedical Research Workforce

A core component of the modern scientific research and development enterprise is investment in the scientific workforce to enable future discoveries.[33] Along with other Federal research agencies, NIH invests heavily in fellowships and training programs and promoting STEM education. However, the realities of extramural research funding have resulted in a system that works well for certain institutions and investigators, at times to the detriment of others.

Respondents cited institutions' use of "soft money"—reliance upon NIH funding to reimburse themselves, in part or in whole, for researchers' salaries. One respondent referred to this practice as a rarely discussed but glaring conflict of interest: if researchers are dependent upon successfully securing NIH grants in order to retain their jobs, they are likely to avoid taking risks in the projects they propose for NIH funding. This practice also has a disproportionately negative effect on early-stage investigators, who typically have lower success rates than established investigators (see Figure 2).

Other respondents pointed to the use of clinical margins to cover research costs. In some cases, this could give physician-scientists more ability to remain in research compared to basic scientists who do not have these types of alternative funding sources. However, it could also create a perverse incentive for physician-scientists to dedicate most of their time to clinical care, rather than research activities. These points mirror findings from the NIH Advisory Committee to the Director (ACD) Next Generation Researchers Initiative Working Group.[34] Other respondents highlighted that postdoctoral researchers are increasingly choosing careers in industry or nonacademic research institutions over academia. A 2014 National Academies study attributed this trend to



8da3-d9698552fa24/.

33 Vannevar Bush, Science the Endless Frontier: A Report to the President, OFFICE OF SCIENTIFIC RESEARCH AND DEVELOPMENT (July 1945), *https://www.nsf.gov/od/lpa/nsf50/vbush1945.htm#ch4*.

34 NIH Advisory Committee to the Director (ACD) Next Generation Researchers Initiative Working Group Report, NATIONAL INSTITUTES OF HEALTH 21 (Dec. 2018), https://acd.od.nih.gov/documents/presentations/12132018NextGen_report.pdf.

more clearly defined roles, higher salaries, and more clear career development opportunities.[35] NIH's funding model relies heavily on academic research institutions and the complementary role that academic researchers play relative to government intramural or industry-conducted science. Respondents noted that established academic investigators also are expected to cover training costs through research grants but are often not incentivized to dedicate time to mentoring trainees.

Taken together, these observations demonstrate severe structural problems in how government and academia together finance biomedical researchers. Some respondents recommended increasing the amount of a single NIH grant that can be used for salaries. On the other hand, the Next Generation Researchers Initiative Working Group previously explored lowering this amount to reduce institutions' reliance on NIH funding for salaries.[36] Congress and NIH should explore this problem in further detail and identify policy options that ensure NIH and institutions each provide appropriate degrees of support for federally funded academic researchers.

Box 2. Next Generation Researcher Initiative

The 21st Century Cures Act (P.L. 114-255) established a Next Generation Researchers Initiative within the Office of the NIH director. Senators Susan Collins (R-ME) and Tammy Baldwin (D-WI) championed this policy. In response to the directive, then-director Dr. Francis Collins commissioned a working group of the Advisory Committee to the Director, which led to the development of 30 recommendations, including recommended definitional changes, monitoring progress under the Initiative, updating relevant data (including a 2007 report on how much NIH funding goes toward extramural salaries), providing professional development opportunities for trainees listed on NIH funding applications, and reducing programmatic bias that benefits established investigators. NIH has updated its policies in response to these and related recommendations. For example, NIH announced that, beginning in 2025, a new peer review scoring rubric will go into effect that is intended to reduce reputational bias. These changes benefit both early-stage investigators and those who are established but from less well-resourced institutions.

Reimagining the Intramural Program

NIH's Intramural Research Program is the world's largest biomedical and behavioral research institution, consisting of over 1200 principal investigators, 1800 clinicians and scientists, and 5000 trainees.[37] Respondents noted that the intramural program in many cases performs research that is similar to, or functionally the same as, projects funded under the extramural program. While the intramural program does currently possess unique capabilities, such as the NIH Clinical Center, this observation raises questions about how to distinguish the intramural program's role and reduce potential duplication between the two portfolios.

Respondents suggested reorganizing the intramural program into interdisciplinary, inter-IC programs, similar to NIH's Porter Neuroscience Research Center, in which over 800 scientists from across NIH work together on research that cuts across the expertise of individual ICs.[38] This reorganization would enable the intramural

35 *The Postdoctoral Experience Revisited*, NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE (2014), https://nap.nationalacademies.org/catalog/18982/the-postdoctoral-experience-revisited.
36 NATIONAL INSTITUTES OF Health, *supra note* 30, at 20-21.
37 Collins, *supra note* 11, at 12.
38 *The John Edward Porter Neuroscience Research Center*, NATIONAL INSTITUTES OF HEALTH, https://www.nih.gov/about-nih/john-edward-porter-neuroscience-research-center (last reviewed July 21, 2015).

program to more easily tackle complex problems that cannot be easily addressed through extramural projects, for reasons such as their capital-intensive nature or anticipated time horizon. One respondent recommended looking to the National Aeronautics and Space Administration's (NASA) practice of using "decadal surveys," through which the National Academies convenes scientists to identify "the most compelling science questions."[39] These surveys guide NASA's strategic investments over the successive decade. The use of this model should not preclude the reallocation of resources to address unforeseen needs over the next ten years. For example, NIH would need to be able to adapt to the emergence of a new pathogen of pandemic potential or disruptive technology. Yet, a decadal survey could help create buy-in across the scientific community and the general public on NIH's strategic priorities and ensure its intramural portfolio addresses areas of true unmet need. NIH's existing five-year strategic planning process could be adapted to account for a decadal survey, with interim updates.

This reimagined intramural program could also benefit from a mix of staffing approaches. Principal investigator-led permanent laboratories may still play a necessary role under this new model. At the same time, a rotator model could bring in academic researchers for a defined period of time to work on interdisciplinary projects to advance the priorities established in the decadal survey.

Restoring Public Trust in Science

NIH-funded research provides significant opportunities to improve the health and wellbeing of all Americans. However, public sentiment toward scientific institutions has degraded in recent years, exacerbated by a perceived lack of transparency and concerns about political biases during the COVID-19 pandemic response. In order for the potential of future NIH research to be fully realized, the agency must make restoring public trust in the scientific process and scientific institutions a priority.

Ensuring Transparency into NIH Operations

Rebuilding public trust in NIH will require improving meaningful transparency and public discourse about NIH operations. While NIH is a highly visible agency, members of Congress have expressed concern about a lack of engagement with congressional oversight requests related to the COVID-19 pandemic response. Similarly, respondents noted instances of the agency deprioritizing statutory requirements, such as the lack of engagement of the Science Management Review Board (SMRB). Established under the NIH Reform Act, the SMRB is tasked with reviewing NIH's structure and making recommendations every seven years. However, NIH has not convened the SMRB since 2015, and one of its only recommendations prior to that time—the consolidation of two ICs with similar research focuses—was disregarded by agency leadership. As an initial step to improving transparency into NIH operations, Congress should reconstitute the SMRB and incorporate the perspectives of individuals from outside the scientific community to inform SMRB recommendations to the director.

Transparency and evaluation are hallmarks of the scientific process. Many of the policies proposed in this white paper could have significant effects, both intended and unintended, on the U.S. biomedical research enterprise, and should therefore be piloted on a voluntary basis. Respondents also noted that NIH is still heavily reliant on paper-based processes and human review, despite having significant technological capabilities. Respondents suggested applying a more scientific approach to how NIH runs its programs, such as using machine learning

39 Decadal Survey, *Biological and Physical Sciences Research in Space*, THE NATIONAL AERONAUTICS AND SPACE ADMINISTRATION, https://science.nasa.gov/biological-physical/resources/decadal-surveys/ (last visited Apr. 29, 2024).

to better predict which proposals will yield the most transformative science. NIH should establish an initiative to use scientific tools to evaluate the impact of NIH operations and policies closer to real time. NIH should publicize the results of these evaluations to inform policy recommendations. While NIH does engage in these types of analyses for specific issues, a more formal initiative would help NIH measure the value and tradeoffs of piloted policy reforms and identify other interventions.

Promoting Research Integrity

Research misconduct is another major issue facing NIH. Recent high-profile cases of research misconduct, specifically within Alzheimer's research, and the potential applications of artificial intelligence to data fabrication and falsification raise questions about how NIH can protect the integrity of its research investments. HHS' Office of Research Integrity (ORI) is responsible for developing research misconduct policies and conducting investigations on behalf of NIH and other HHS public health agencies. Last fall, ORI proposed updates to its research misconduct regulations for the first time since 2005. The office has a small footprint relative to the volume of NIH-funded research and does not have independent investigative authorities. A recent editorial in Science noted that NSF's Office of the Inspector General (OIG) tends to identify more instances of research misconduct than ORI, despite NIH having a significantly larger extramural research portfolio.[40] Given these factors, ORI's ability to proactively identify or prevent research misconduct within the NIH-funded research portfolio is likely limited.

Within NIH's authorities, the agency recently issued a data sharing policy that will enable researchers to more easily validate or refute claims.[41] New technologies could also play a role in helping to quickly identify inconsistencies in research claims. For example, the Defense Advanced Research Projects Agency (DARPA) previously carried out the Systematizing Confidence in Open Research and Evidence (SCORE) program, which demonstrated the feasibility of using algorithms to validate claims.[42] Congress and NIH should identify opportunities to leverage these types of technologies, coupled with data sharing policies, to restore public confidence in research claims. Congress should also review the statutory authorities of HHS' ORI to identify any areas that could be strengthened, clarified, or updated to reflect current research misconduct challenges. This review should also take into consideration the complementary role of the Department of Health and Human Services' (HHS) OIG.

Adhering to Grants Management Processes

In order for NIH to rebuild public trust, the public must first have confidence that NIH is appropriately overseeing its research portfolio. Over the past year, HHS-OIG has issued three reports describing deficiencies in NIH's oversight of award and subaward recipient compliance with grant requirements.[43] Box 3 describes

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40 Ivan Oransky & Barbara Redman, *Rooting out scientific misconduct*, 383 SCIENCE 131 (2024), https://www.science.org/doi/10.1126/science.adn9352.

41 *Data Management & Sharing Policy Overview*, NATIONAL INSTITUTES OF HEALTH SCIENTIFIC DATA SHARING, https://sharing.nih.gov/data-management-and-sharing-policy/about-data-management-and-sharing-policies/data-management-and-sharing-policy-overview#after (last visited Apr. 29, 2024).

42 *Systematizing Confidence in Open Research and Evidence (SCORE)*, DEFENSE ADVANCED RESEARCH PROJECTS AGENCY, https://www.darpa.mil/program/systematizing-confidence-in-open-research-and-evidence (last visited Apr. 29, 2024).

43 Christi A. Grimm, *The National Institutes of Health and Ecohealth Alliance Did Not Effectively Monitor Awards and Subawards, Resulting in Missed Opportunities to Oversee Research and Other Deficiencies*, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES OFFICE OF INSPECTOR GENERAL (Jan. 2023), https://oig.hhs.gov/oas/reports/region5/52100025.pdf; Amy J. Frontz, *The National Institutes of Health Did Not receive 81 of 109 Required Audit Reports For Foreign Grant Recipients,* U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES OFFICE OF INSPECTOR GENERAL (Dec. 2023), https://oig.hhs.gov/documents/audit/7901/A-05-21-00019-Complete%20Report.pdf.

OIG's findings in detail.

Collectively, OIG's findings demonstrate systematic deficiencies in how NIH conducts post-award monitoring. These findings are echoed by RFI respondents: one respondent noted that, while many researchers do comply with award terms and conditions, such as the requirement for submission of annual progress reports, NIH program officers do not typically engage with researchers in a material way. NIH staff do not generally ask follow-up questions about the information contained in progress reports or otherwise demonstrate that the agency uses the reports for any specific purpose. Yet, these reports and other compliance activities require significant time and effort on the part of researchers to prepare.

This creates a significant oversight challenge: on the one hand, these findings demonstrate issues with the performance of certain funding recipients that need to be quickly identified and addressed. However, clearly existing grants oversight tools, such as annual progress reports, clearly create a disproportionate burden for researchers who are genuinely seeking to comply.

Moving forward, Congress and NIH should explore options to balance administrative burden with truly meaningful oversight tools. For example, in addition to the annual single audit (a process led by the funding recipient and focused on financial metrics), NIH could use a risk-based framework to commission randomized audits focused on compliance with award terms and conditions and research integrity issues. This approach could be balanced with consideration of streamlined recurring reporting for lower risk projects.

Box 3. HHS-OIG Reviews of NIH Grants Management and Oversight

In 2023, OIG issued three reports finding deficiencies with NIH's grants management processes. Specifically, OIG found:

1. NIH did not effectively monitor activities carried out by EcoHealth Alliance and its subaward recipient, the Wuhan Institute of Virology (WIV), including by ensuring the submission of progress reports and required laboratory records. OIG's review ultimately led HHS to propose the WIV for debarment.
2. NIH did not receive 81 out of 109 required audit reports from foreign award recipients. Of the 28 audit reports that were received, 10 required corrective action, but NIH only followed up within required timeframes for three out of the 10 recipients.
3. NIH generally did not comply with single audit review requirements, taking more than twice the allotted time to respond to findings that warranted corrective action. Government funding recipients with multiple awards are required to commission an annual audit (known as the "single audit") conducted by a third party to determine financial health and test internal controls. In some cases, NIH's delay likely jeopardized the agency's ability to take legal action in response to findings.

Conclusion

Since the enactment of 21st Century Cures, the scientific landscape has changed exponentially. Artificial intelligence and machine learning have advanced at an unexpectedly rapid pace, and their potential applications within biomedical research and health care are seemingly endless. The COVID-19 pandemic accelerated the adoption of telehealth and the digitization of public health data, shifted how we develop medical countermeasures, and proved the pace at which science can occur under the right circumstances. These trends underscore the importance of fully realizing the goals of prior legislative efforts. While we now have more opportunities to advance the health and wellbeing of the American people through biomedical innovation, the risks of failure—whether by failing to harness research opportunities, the erosion of the domestic biomedical research workforce, the proliferation of low-quality research, or poor oversight that threatens public trust in science—are greater than ever before. I look forward to working with all interested stakeholders and my colleagues on the HELP Committee to harness this opportunity to strengthen NIH for the next generation of Americans.