

August 16, 2024 (revised September 1, 2024)

The Honorable Cathy McMorris Rodgers
Chair, Energy & Commerce Committee
U.S. House of Representatives
Washington, D.C. 20515

Re: “Reforming the National Institutes of Health: Framework for Discussion”; Revised Comment Letter

Dear Chair McMorris Rodgers,

On behalf of the Healthspan Action Coalition (HSAC), we are pleased to comment in this letter on the proposed reform of the National Institutes of Health set forth in the Energy and Commerce Committee’s June 2024 “*Reforming the National Institutes of Health: Framework for Discussion*” (referred to in this letter as the “Framework”). To comment on the Framework, we undertook the four-part analysis set forth in Exhibit 1 attached to this letter. We have summarized that analysis in this letter to facilitate its review by the Committee.

The Healthspan Action Coalition is a not-for-profit organization dedicated to assisting legislators and other policymakers focused on funding and overseeing healthspan research and development.¹ Our membership includes over 180 healthcare professionals, advocacy groups, and companies engaged in the life science, medical, and healthcare sectors.² The Coalition stands committed to advancing healthspan research and related policymaking.

We view healthspan research policy *generally* as a quality of life matter relevant to every stage of human life, and *specifically* as a set of policies related to supporting healthy aging and preventing age-related diseases. As such, healthspan research is relevant to each current National Institute and National Center (each an “IC”; collectively the “ICs”) and each IC following the reorganization contemplated by the Framework. This view of healthspan aligns with an important concept articulated in the Framework: “*By encouraging each IC to utilize a holistic life stage approach, our goal is to eliminate the demographic- or disease-specific siloed nature of the current structure and ensure each IC is considering the whole individual and all populations across the entire lifespan.*”³

Consistent with this reference to “a holistic life stage approach...across the entire lifespan”, we define “healthspan” as the period of a person’s life spent in good health, free from chronic diseases and disabilities. As such, healthspan research reaches beyond science and technology to matters that are socioeconomic in nature.⁴ This definition of “healthspan” contrasts with that of “longevity”, with the latter concentrated on the absolute length of a person’s life as a biological matter, from birth to death, and with less attention to quality of health or socioeconomics, except to the extent of the economic benefits of longevity.⁵ Part 3 in Exhibit 1 contains more detail on this comparison of healthspan and longevity.

As a preface, and to underscore the seriousness of reorganizing NIH, we must acknowledge that, notwithstanding the various structural and policy reforms described in the Framework from which NIH can benefit, NIH still stands as the world’s foremost institution for life, medical, and healthcare scientific research. Evidence of

¹ <https://healthspanaction.org/about-us/>

² For a list of coalition members, see <https://healthspanaction.org/healthspan-action-coalition/>. The members of the Coalition’s leadership and advisory team who participated in the preparation of this letter and the attached exhibit include Executive Director Bernard Siegel, Chief Operating Officer Melissa King, Director of Policy Research and Education Eve Herold, Senior Advisor for Industrial and Regulatory Policy Alan Jakimo, and Internet Director Kevin McMahon.

³ This sentence appears as the second penultimate sentence in the second paragraph under the heading “Background” in the “Structural Reform” section of the Framework.

⁴ See, e.g., Kaeberlein M. “How healthy is the healthspan concept?” *Geroscience*. 2018 Aug;40(4):361-364. Epub 2018 Aug 6. PMID: 30084059; PMCID: PMC6136295. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6136295/>

⁵ See, e.g., Cordeiro, J.L. and Wood, D. *The Death of Death*. Copernicus Books. 2023.

this preeminence includes the fact that as of October 2, 2023, 171 Nobel laureates had conducted their research intramurally at NIH and/or extramurally with NIH funding at a plethora of academic and other research institutions.⁶

We reference funding here because of NIH's quite substantial annual budget. According to the Framework, NIH's proposed funding for FY2024 is \$48.2 billion. The magnitude of this amount, coupled with decades-old issues arising with the Public Health Service Evaluation Set-Aside mechanism (the "Evaluation Set-Aside") as described in the Framework, and other issues described in the Framework, lead inexorably to the Framework's driving force: *Congress stands at a pivotal moment in planning and constructing the policy-oriented groundwork necessary for NIH to maintain and extend its position of prominence in life, medical, and health science research.*

We seek in this letter to underscore that NIH's structure, policies, operating procedures, and research funding priorities must align with the goal of nurturing and extending healthspan. While we bring our healthspan legislative policymaking advocacy to this letter, our comments reach beyond healthspan. This is reflected in the four parts of our analysis set forth in Exhibit 1, viz.:

- Part 1:** Historical Context of the Framework
- Part 2:** Policymaking Analysis of Explicitly Stated Reforms in the Framework
- Part 3:** Additional Policymaking Considerations
- Part 4:** Strengths/Weaknesses/Opportunities/Threats Related to Framework Reforms

In the balance of this letter, we summarize the major points in each of these four parts.

Part 1: Historical Context of the Framework

The history of NIH and its predecessors consists of at least 12 significant acts of Congress and one significant executive branch action, each of which is listed in Figure 1A in Exhibit 1. The first entry in this list is the 1798 Act for the Relief of Sick and Disabled Seamen. The list in Figure 1A may be incomplete, but depending on the years in which any additional laws were enacted or additional executive branch actions were taken, an expanded list could further support the technical point that, as a statistical variable without reference to any substantive legislative policymaking, the time between successive laws relating to NIH could be one to eight years overdue (with a median of five years) for significant organizational and managerial reformation by Congress.

Part 2: Policymaking Analysis of Explicitly Stated Reforms in the Framework

In Part 2, in order to provide our comments on specific structural and policy reforms proposed in the Framework, we employ a data structure derived from the "2 x 3" matrix diagram of the Framework presented in the Committee Chair's notice announcing the publication of the Framework. Using this structure, we have summarized our comments as follows:

Structural Reforms

Consolidation of Institutes and Centers (ICs) from 27 to 15: We concur that this 44% reduction in the number of ICs following the reorganization envisioned in the Framework should improve inter-IC coordination and reduce siloing. But successful improvement of such coordination and reduction of siloing will require not only reorganization in the form of IC consolidation, but also active management. Without active management, the magnitude of the contemplated consolidation presents risks of overlooking important details and inadvertently missing special areas of research. These risks can be addressed through: (i) a carefully planned and phased implementation for the consolidation; and (ii) continuous monitoring and dynamic management of substantive elements of the consolidation and anti-siloing policy. Finally, notwithstanding the benefits of increased innovation resulting from increased collaboration in an anti-siloed environment, there may be occasions from time to time when healthy competitive programs within NIH or funded by NIH could be helpful.

⁶ NIH. "Who we are." <https://www.nih.gov/about-nih/who-we-are/history>

Adoption of a “holistic life stage” approach focused on the “whole individual and all populations across the entire lifespan,” with elimination of the “demographic- or disease-specific siloed nature of the current structure”: This policy should impart a healthspan sensitivity to each of the 15 ICs resulting from the reorganization and the projects those ICs fund and oversee. To gain the understanding of this policy necessary for its successful implementation, a series of studies, seminars, and workshops on how to nurture a “holistic life stage across the entire lifespan” policy across the entire NIH may be warranted. Also, to further support implementation of this policy, consideration should be given to requiring grant proposals to any IC to describe how the applicable proposed research would support the policy of a holistic life stage approach across the entire lifespan.

Enhanced coordination, interdisciplinary collaboration, and transparency: To achieve this objective, it may be helpful to identify specific mechanisms for enhancing coordination and transparency and metrics for identifying and assessing the comparative value of projects arising from coordination and transparency. To identify areas ripe for enhanced coordination and transparency, consideration may be warranted for establishing advisory panels specifically for identifying such areas; and using various digital intelligence tools to help identify such areas.

Policy Reforms

1. Mission & Leadership

Introducing term limits for IC directors. We agree that term limits can prevent stagnant leadership. Consideration, however, should be given as to whether any exceptions should be allowed from time to time, and if so, how such exceptions would be administered and overseen.

Leadership Mentoring: To avoid stagnancy, existing leaders must be actively mentored in the subject of leadership transitions. Executive transition programs at schools of business administration may be helpful for such an effort.

Enhancing financial transparency and accountability: We agree that financial transparency is crucial for public trust and requires robust oversight mechanisms. Consideration may be warranted for developing digital intelligence tools that can support such mechanisms.

Enhancing Interdisciplinary Collaboration through Thematic Research Clusters: Thematic research clusters would exhibit four attributes: (1) topical specificity and comprehensiveness; (2) interdisciplinary in reach; (3) conducive to integration of research and application; and (4) collaboratively designed and implemented. Healthspan science requires a multidisciplinary approach that combines insights from biology, medicine, public health, and the social sciences. Initial thematic research clusters in the healthspan field could include: definition of healthspan metrics; and understanding of gene/protein interaction networks that influence healthspan.

As a matter of national security, safeguarding NIH-funded research from undue foreign influence and interference: We agree on the vital importance of implementing stringent national security reviews of any project that involves international collaboration and/or NIH funding of research to be conducted outside the United States and by non-U.S. nationals within the United States. This entails a mandate to incorporate national security reviews into the grant review process. This mandate must be carefully managed so as not to discourage international collaboration from which the U.S. can benefit. As part of this subject, clear policies should be adopted in support of identifying and mitigating potential conflicts of interest.

Improving NIH's response to emerging challenges through enhancing coordination, supporting high-risk research, and fostering innovation. The proposed reforms aimed at creating a more agile and responsive NIH capable of addressing complex health challenges should include: establishment of trans-NIH initiatives for interdisciplinary collaboration; support for public-private partnerships to leverage additional resources and expertise; and implementation of digital intelligence tools to analyze data and optimize research strategies.

2. Funding

Repealing the PHS Evaluation Set-Aside amendment (the “Evaluation Set-Aside”) to improve funding transparency: As originally implemented, the Evaluation Set-Aside established in 1970 was to have provided a mechanism by which NIH could fund activities designed to evaluate NIH research projects for purposes of informing Congress about NIH projects to facilitate Congress’s oversight of NIH’s public health initiatives and outcomes and improving related policies when necessary or advisable. Even if the 1970 Evaluation Set-Aside did not work as originally intended by Congress,⁷ its original intent has continuing validity. Thus, assuming the existing Evaluation Set-Aside is repealed, as contemplated by the Framework, thought should perhaps be given to a replacement mechanism that will generate information that allows Congress to perform its policymaking role with respect to NIH and in the manner suggested by the General Accounting Office in 1993.⁸

Implementing measures to prevent waste and fraud and research misconduct: Estimates of fraud and abuse in the overall U.S. healthcare sector have ranged from 3% to 10%, representing approximately \$130 billion to \$450 billion annually.⁹ Consistent with this alarming estimate, in 2023, the NIH Office of Extramural published data on incidence of misconduct in extramural research funded by NIH. This data showed a precipitous increase, from an annual average of 98.3 (+/- 16.2) during the five years ending in 2017, to 554.0 (+/- 18.4) during the four years ending in 2022.^{9A} This five-fold increase in allegations of misconduct over the past ten years is more than troubling. The Framework should include efforts to understand the reasons for this increase and policies aimed at reducing misconduct on research funded by NIH.

3. Grants

Supporting innovative research is essential, but the grant review process must be transparent and free from bias. The Framework notes the dichotomy between two types of grant proposals: those from lesser known scientists that are “innovative, though potentially riskier” and those seeking to achieve “incremental advancements on proven ideas” from “more well established [scientists], usually at later stages in their careers, with a demonstrated record of success.” NIH must be able to allocate funds for both types of proposals. We believe that digital intelligence can be of value to achieve rationale and balanced funding of both types of proposals.

Prohibiting risky gain-of-function research of concern /dual use research of concern (GOFROC/DURC). The concerns expressed in the Framework regarding GOFROC/DURC are not new. While gain-of-function research (GOFR) and dual use research (DUR) have led to important fundamental insights into the biology, ecology, and pathogenesis of viruses,¹⁰ but as noted in the Framework, significant species-level existential risks inherent in GOFROC/DURC must be addressed

⁷ See, e.g., General Accounting Office, “Report to the Chairman, Committee on Labor and Human Resources, U.S. Senate”, April 8, 1993, <https://www.gao.gov/assets/pemd-93-13.pdf>. (“Although some of the PHS evaluation set-aside supported studies of the implementation and effectiveness of federal health programs, we find that it has been less effective than it could have been in providing information to the Congress on PHS programs.”)

⁸ *Id.* (“The major factors limiting the ability of the evaluation set-aside to respond to congressional needs for information are (1) the use of a portion of the set aside funds for projects that are not evaluations of PHS programs and (2) the failure to synthesize and communicate evaluation results regularly to the Congress.”)

⁹ See, e.g., Drabiak K. and Wolfson, “What Should Health Care Organizations Do to Reduce Billing Fraud and Abuse?”, *AMA Journal of Ethics*, March, 2020. <https://journalofethics.ama-assn.org/article/what-should-health-care-organizations-do-reduce-billing-fraud-and-abuse/2020-03>

^{9A} Lauer, M. “Trends in Extramural Research Integrity Allegations Received at NIH.” *Extramural NEXUS*. NIH Office of Extramural Research. March 22, 2023. <https://nexus.od.nih.gov/all/2023/03/22/trends-in-extramural-research-integrity-allegations-received-at-nih/>

¹⁰ Subbarao, K. “Gain-of-Function Research: Background and Alternatives.” *Potential Risks and Benefits of Gain-of-Function Research: Summary of a Workshop*. National Research Council; Institute of Medicine. National Academies Press (US); 2015 Apr 13. <https://www.ncbi.nlm.nih.gov/books/NBK285579/>

through appropriate and optimal regulation. This regulation must clarify what types of experiments are of concern and ensure that NIH's oversight of GOFR/DUR grant proposals and resulting grants are improved to address these concerns without hindering essential scientific research. As part of this pursuit, digital intelligence tools need to be examined for their potential use to balance the benefits and risks of GOFR/DUR.

Encouraging interdisciplinary partnerships between NIH ICs and external organizations: Similar to other thematic areas of research, interdisciplinary collaboration on healthspan research is essential to address the complex factors influencing healthspan. Accordingly, in respect of healthspan research, NIH must sponsor interdisciplinary partnerships between and among universities, private sector entities, and international research institutions to leverage additional resources and expertise.

Following the table in Figure 2C in Part 2 in Exhibit 1, we address at length two significant proposed reforms in the Framework:

- Repeal of the PHS Evaluation Set-Aside
- Proposed Replacement of National Institute on Aging with National Institute on Dementia

Part 3: Additional Policymaking Considerations

Part 3 of the analysis of the Framework in Exhibit 1 covers policymaking considerations that, while not addressed explicitly or at length in the Framework, nevertheless warrant express or further treatment by the Committee in any sequel to the Framework. These additional considerations arise particularly in the context of the last sentence in the Policy Reform Background section of the Framework, *viz.*: “The twin imperatives of maintaining the country’s position of global scientific leadership, while also addressing past misconduct illustrates the need for a wholesale, robust review and reform of NIH policy programming, and activities, as well as a comprehensive organizational restructuring.”

Part 3 in Exhibit 1 presents four such areas for express or further treatment:

- Leveraging Digital Intelligence (aka “Artificial Intelligence”)¹¹
- Reforms to the Bayh-Dole Act of 1980 consistent with the Framework
- Alternative Organizational Structures for Implementing the Framework Reforms
- Coverage of Longevity Research in any Revised Framework and Corresponding Bills

With respect to the fourth of these bullet points, to address the legitimate concerns of those commentators who posit a materially adverse loss of longevity research funding by NIH if the National Institute on Aging is transformed into a National Institute on Dementia, it may make sense for the Committee to include in any revisions to the Framework and corresponding bills an express plan for porting to the ICs comprising the reorganized NIH the expertise and experience currently residing within NIA on longevity research outside of Alzheimer’s disease, Parkinson’s Disease, and dementia. Such porting should be consistent with, and driven by, the expertise and experience on longevity research that already exists outside NIA, as illustrated in Figure 3 in Exhibit 1.

Part 4: Strengths/Weaknesses/Opportunities/Threats Related to Framework Reforms

In Part 4 of the analysis in Exhibit 1 we provide a preliminary Strengths/Weaknesses/Opportunities/Threats matrix for the Framework. We utilized generative digital intelligence models to create this matrix. This “SWOT” analysis may be helpful to the Committee as the legislative policymaking process entailed by the Framework proceeds.

¹¹ In analyzing the Framework, we made extensive use of multiple large language models to generate text and provide numerical data. In many cases, this text and numerical data was cite-checked, but also edited by us. Where direct quotes generated by these models is set forth in this letter and Exhibit 1, we so indicate. All of this text and numerical data needs to be considered as indicative until comprehensive cite- and fact-checking are fully completed.


Conclusion

The Framework proposed by the Committee outlines significant changes aimed at improving the efficiency, innovativeness, transparency, and responsiveness of the NIH to challenges faced in the life, medical, and health sciences. Integrating healthspan science and advocacy into these reforms is crucial to ensure that NIH's structure, policies, and research priorities are aligned with the goal of extending the years of healthy life enjoyed by each American. Indeed, as the Committee states on the cover page of the Framework: *The Time is NOW to Build a Stronger NIH for the Future.*

* * *

Thank you for the opportunity to contribute to this vitally important endeavor to reorganize and reform the NIH — an endeavor that is likely overdue simply as a matter of the passage of time and substantively necessary and advisable if NIH is to continue to serve in the coming decades as the world's preeminent center of life, medical, and health science research.

Respectfully,



Bernard Siegel
Executive Director

HEALTHSPAN ACTION COALITION

Exhibit 1

An Analysis of the U.S. House of Representatives Energy & Commerce Committee Framework for Discussion relating to Reforming the National Institutes of Health

This Exhibit presents the analysis performed by the Healthspan Action Coalition (“HSAC”) in order to provide comments to U.S. House of Representatives Energy and Commerce Committee (the “Committee”) with respect to its June 2024 release titled “Reforming the National Institutes of Health – Framework for Discussion” (the “Framework”).

The analysis of the Framework presented in this Exhibit consists of four parts, including:

- Part 1:** Historical Context of the Framework
- Part 2:** Policymaking Analysis of Explicitly Stated Reforms in the Framework
- Part 3:** Additional Policymaking Considerations
- Part 4:** Strengths/Weaknesses/Opportunities/Threats Related to Framework Reforms

Part 1: Historical Context of the Framework

The Framework illustrates that the 118th Congress stands at what may be a pivotal moment in Congress’s funding and oversight of NIH – adding to a succession of similarly important waypoints in the long history of NIH and its predecessors. This history, beginning only ten years after New Hampshire became the ninth of the initial 13 states to ratify the U.S. Constitution in 1788, thereby leading to the commencement of operations of the United States as a federal republic in 1789, consists of at least 12 significant acts of Congress and one significant executive branch action, each of which is listed in Figure 1A.

The list in Figure 1A consists of these 12 laws and one executive branch action explicitly referenced in the Framework, as well as additional laws the subjects of which are at least implicitly covered in the Framework or historically significant with respect to the operation of NIH. The first of these laws and actions is the 1798 Act for the Relief of Sick and Disabled Seamen (which established the Marine Hospital Service (MHS)); and the last is the American Recovery and Reinvestment Act of 2009 (Congress’s response to the Great Recession from December 2007 through June 2009).

The last column in Figure 1A contains the timespan in number of years between the two events in each successive pair of events, beginning with the pair represented by (x) the 1798 Act for the Relief of Sick and Disabled Seamen and (y) the 1887 establishment by the MHS of the Hygienic Laboratory on Staten Island in the City of New York.

Figure 1B presents two series of statistics on the distribution of the timespans listed in Figure 1A. For each series, these statistics include: the number and median of timespans in the distribution; the 25% and 75% quartiles in the distribution; and any outliers. The box chart in Figure 1C graphically presents these two series of statistics. As the box chart illustrates, the first series of time spans, which includes all 12 pair of events, contains an outlier, *viz.*, the 89 year timespan between the 1798 Act for the Relief of Sick and Disabled Seamen and the 1887 formation of the Hygienic Laboratory. The second series of time spans excludes that outlier.

Using the statistics for the second series we projected the year following the last event in the Figure 1A list (i.e., the signing into law of the American Recovery and Reinvestment of 2009) that the next major act of Congress should have been likely to have occurred. Adding to 2009, the 25% quartile of 7 years between acts of Congress relating to NIH, and the 75% quartile of 14 years, suggests that, without reference to substantive reforms, some sort of major reformation/reorganization of NIH should have been enacted by Congress sometime between 2016 (calendar year 2009 PLUS the 25% quartile of 7 years) and 2023 (calendar year 2009 PLUS the 75% quartile of 14

years).¹² Using the median of 10 years, reorganization of NIH would be five years overdue (calendar year 2009 PLUS the median of 10 years).

Thus, strictly as a technical timing matter, and without reference to any substantive legislative policymaking, NIH is overdue by one to eight years (with a median of five years) for significant organizational and managerial reformation. In this respect, NIH is just like any other entity that must be continually revitalized through reorganization and reform.

We readily acknowledge that the list in Figure 1A may be incomplete.¹³ Accordingly, adding laws and/or executive branch actions of major import to the statistical timespan analysis in Figures 1B and 1C could, depending on the years in which any such additional laws or executive branch actions were signed into law or undertaken, lengthen or shorten the median and interquartile statistics on which we base the observation of a Congressionally legislated reorganization of NIH being overdue.

Figure 1A. Major Acts of Congress and Executive Branch Comprising NIH History

Year	Act of Congress / Executive Branch Action	Significance	Years after Last Major Action
1798	Act for the Relief of Sick and Disabled Seamen (1 Stat. 605; July 16, 1798)	By establishing the Marine Hospital Service (MHS), Congress recognizes that the health of U.S. commerce depends on the health of its merchant marines.	-
1887	Establishment of Hygienic Laboratory	Laboratory established within the MHS, an often regarded as the origin of NIH.	89 years
1902	“An Act to increase the efficiency and change the name of the United States Marine-Hospital Service” (Pub.L. 57-226, 32 Stat. 712; July 1, 1902)	“The care of sick and disabled seamen and all other duties now transferred, required by law to be performed by the Marine-Hospital Service shall hereafter be performed by the Public Health and Marine-Hospital Service, and all funds and appropriations now provided by law for use by the Marine-Hospital Service and all properties and rights pertaining to said service shall be available for use for like purposes and in like manner...”	15 years
1912	“An Act To change the name of the Public Health and Marine-Hospital Service to the Public Health Service, to increase the pay of officers of said service, and for other purposes.” (Pub.L. 62-265, 37 Stat. 309; August 14, 1912)	In addition to change of name to PHS, this Act authorizes PHS to “study and investigate the diseases of man and conditions influencing the propagation and spread thereof, including sanitation and sewage and the pollution either directly or indirectly of the navigable streams and lakes of the United States, and it may from time to time issue information in the form of publications for the use of the public.”	10 years
1930	Ransdell Act “An Act To establish and operate a National Institute of Health, to create a system of fellowships in said institute, and to authorize	“The roots of this act extended to 1918, when chemists who had worked with the Chemical Warfare Service in World War I sought to establish an institute in the private sector to apply fundamental knowledge in chemistry to problems of medicine. In 1926, after no	18 years

¹² It is interesting to note that the 25% quartile of the time between events variable is seven years. Seven years is also the duration of time set forth in the NIH Reform Act of 2006 between evaluations as to Congress’s need to exercise its authority to reorganize NIH. See footnote 19 *infra*.

¹³ For a legislative chronology of NIH, see <https://www.nih.gov/about-nih/what-we-do/nih-almanac/legislative-chronology>.

Year	Act of Congress / Executive Branch Action	Significance	Years after Last Major Action
	the Government to accept donations for use in ascertaining the cause, prevention, and cure of disease affecting human beings, and for other purposes Hygienic Laboratory renamed as National Institute of Health (Pub.L. 71-251, 46 Stat. 379; May 26, 1930)	philanthropic patron could be found to endow such an institute, the proponents joined with Louisiana Senator Joseph E. Ransdell to seek federal sponsorship. The truncated form in which the bill was finally enacted in 1930 reflected the harsh economic realities imposed by the Great Depression. Nonetheless, this legislation marked a change in the attitude of the U.S. scientific community toward public funding of medical research.” ¹⁴	
1937	<p align="center">National Cancer Institute Act of 1937</p> <p>“An Act to provide for, foster, and aid in coordinating research relating to cancer; to establish the National Cancer Institute; and for other purposes.” (Pub.L. 75-244, ___ Stat. ___; August 5, 1937)</p>	“That for the purposes of conducting researches [sic], investigations, experiments, and studies relating to the cause, diagnosis, and treatment of cancer; assisting and fostering similar research activities by other agencies, public and private; and promoting the coordination of all such researches and activities and the useful application of their results, with a view to the development and prompt widespread use of the most effective methods of prevention, diagnosis, and treatment of cancer, there is hereby established in the Public Health Service a division which shall be known as the National Cancer Institute.”	7 years
1944	<p align="center">Public Health Service Act</p> <p>(Pub.L. 78-410, 58 Stat. 682; July 1, 1944)</p>	“An Act to consolidate and revise the laws relating to the Public Health Service, and for other purposes.”	7 years
1970	<p>“Title IV – Evaluation of Health Programs”, Sec. 401(a), Inserting new Section 513 to PHSA (referred to as the “PHS Evaluation Set-Aside”) (Pub.L. 91-296, 58 Stat. 709, June 30, 1970)</p>	“...allows the Secretary to use up to 1 percent of the appropriations for programs authorized under the Public Health Service Act and related acts for the evaluation of PHS programs.[fn] Because it is not linked to a specific request for information, the legislative language authorizing the PHS evaluation set aside gives considerable latitude to the Secretary of HHS. The legislation neither specifies what kinds of information the evaluations should generate nor requires HHS to communicate the results of the information to the Congress. However, Senate Report No. 91-667 indicates that the intent of the PHS set-aside is to develop information about the effectiveness of federal health programs in order to inform legislative deliberations.” ¹⁵	26 years
1971	<p align="center">National Cancer Act of 1971</p> <p>“An Act To amend the Public Health Service Act so as to strengthen the National Cancer Institute and the National Institutes of Health in order more effectively to carry out the national effort against cancer.”</p>	The act represented... what President Nixon described as the ‘war on cancer,’ ... the nation’s second leading cause of death. The act granted authority to the Director of NCI to plan and develop a National Cancer Program that included NCI, other research institutes, and other federal and non-federal programs. It established the procedure for submitting NCI’s annual budget, called the “bypass budget,” which is transmitted directly from the NCI director to the	1 year

¹⁴ <https://history.nih.gov/display/history/WWI+and+the+Ransdell+Act+of+1930>

¹⁵ General Accounting Office, *supra*, note 7.

Year	Act of Congress / Executive Branch Action	Significance	Years after Last Major Action
	(Pub.L. 92-218, 85 Stat.; December 23, 1971)	President and Congress. ... It also established the President’s Cancer Panel, a three-member panel that submits an annual report to the President and holds periodic public hearings. Finally, the act provided additional funding for NCI to establish 15 new cancer research centers, local cancer control programs, and an international cancer research data bank.” ¹⁶	
1980	Bayh-Dole Act (Pub.L. 96-517, 94 Stat. 3015; December 12, 1980)	“It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.” ¹⁷	9 years
1993	NIH Revitalization Act of 1993 (Pub.L. 103-43, 108 Stat. 4607; June 10, 1993)	“...reauthorized certain expiring authorities of the NIH; mandated establishment of the Office of Research Integrity in DHHS; lifted the moratorium on human fetal tissue transplantation research; mandated inclusion of women and minorities in clinical research protocols; created in statute the Office of Alternative Medicine, the Office of Research on Women’s Health, the Office of Research on Minority Health, the Office of Biobehavioral and Social Sciences Research, and the National Center for Human Genome Research; mandated establishment of an intramural laboratory and clinical research program on obstetrics and gynecology within NICHD and the National Center on Sleep Disorders Research in NHLBI; codified in statute the establishment of the Office of AIDS Research, and strengthened and expanded its authorities, including authorizing OAR receipt of all appropriated AIDS funds for distribution to the ICs; authorized the establishment of an NIH director’s discretionary fund; provided the director, NIH, with	13 years

¹⁶ <https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-cancer-institute-nci#:~:text=August%20%2C%201937%E2%80%9494The%20National,government’s%20place%20in%20cancer%20research.>

¹⁷ Bayh-Dole Act, Chapter 38, Section 200 (“Policy and Objective”); codified in 35 USC Sec. 200.

Year	Act of Congress / Executive Branch Action	Significance	Years after Last Major Action
		extramural construction authority; required from extramural construction funds a \$5 million set aside for Centers of Excellence; mandated establishment of the IDeA program; required the NCI to conduct the Long Island breast cancer study; authorized establishment of scholarship and loan repayment programs for individuals from disadvantaged backgrounds; changed the designation from center to institute for NINR and from division to center for the Division of Blood Resources, NHLBI; and provided other new NIH authorities and directives. ¹⁸	
2006	<p align="center">NIH Reform Act of 2006</p> <p>“An Act To amend title IV of the Public Health Service Act to revise and extend the authorities of the National Institutes of Health, and for other purposes.” (Pub.L. 109-82, 120 Stat. 3675; January 15, 2007)</p>	<p>“National Institutes of Health Reform Act of 2006 - Title I: NIH Reform - (Sec. 101) Amends the Public Health Service Act to reauthorize and reorganize the National Institutes of Health (NIH), including by: (1) renaming NIH agencies as national research institutes or national centers; (2) establishing a Division of Program Coordination, Planning, and Strategic Initiatives (the Division); and (3) placing specified offices within the authority of the Division, including the Office of AIDS Research and the Office of Dietary Supplements. Allows the Director of NIH to establish additional offices or administrative units within the Division. Sets at 27 the maximum number of national research institutes and national centers that NIH may have. Authorizes the Director, with the approval of the Secretary of Health and Human Services, to reorganize the offices within the Office of the Director if the Director determines that the management and operation of NIH programs and activities would be more efficiently carried out. Sets forth process for any future reorganization.</p> <p>Requires the Secretary to establish an advisory council within NIH to be known as the Scientific Management Review Board to: (1) provide advice not less than once every seven years regarding the use of the authority to reorganize NIH; (2) determine whether and to what extent the organizational authorities should be used; and (3) issue recommendations. Requires that changes recommended by the Board be made, unless the Director objects. Provides for congressional review of any reorganization of NIH, including the addition or elimination of any national research institutes or national centers.”¹⁹ [<i>emphasis not in original</i>]</p>	13 years

¹⁸ <https://history.nih.gov/display/history/Legislative%2BChronology>.

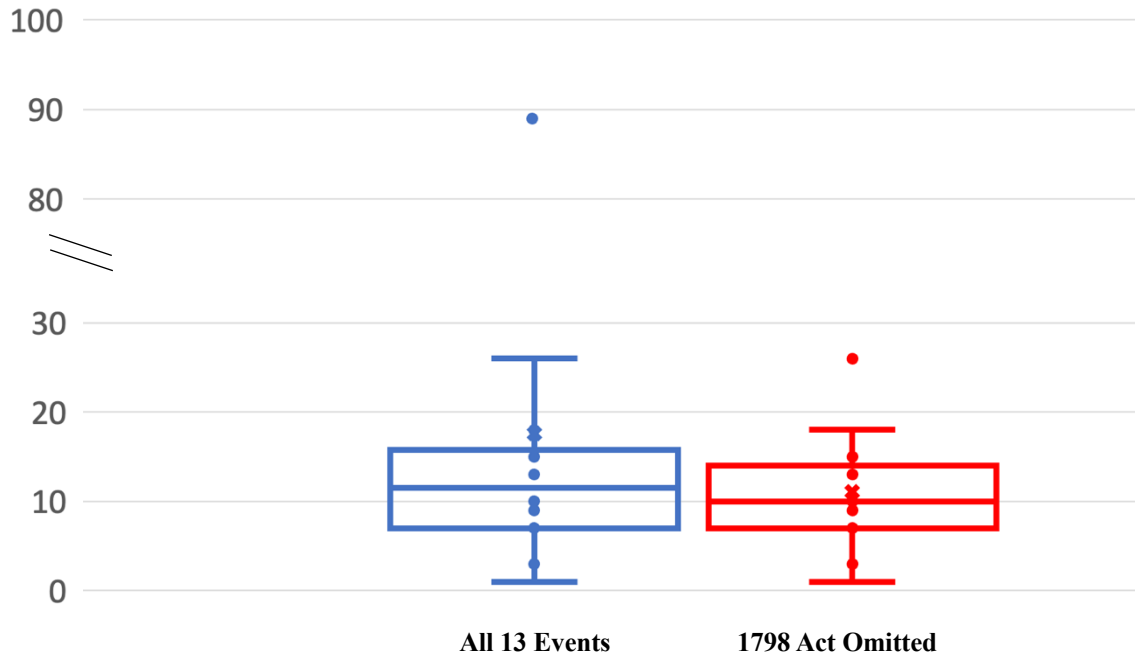
¹⁹ Congressional Research Service, “Summary: H.R. 6164 – 109th Congress (2005-2006)”. <https://www.congress.gov/bill/109th-congress/house-bill/6164> (Noting the reference to “seven years” in this

Year	Act of Congress / Executive Branch Action	Significance	Years after Last Major Action
2009	American Recovery and Reinvestment Act of 2009 Pub.L 111-5, 123 Stat. 115 (February 17, 2009)	Provides \$8.2 billion of additional funding for FY 2009 to the NIH Office of the Director, with \$7.4 billion to be transferred to the ICs and to the Common Fund under PHSA 402A(c)(1) in proportion to appropriations otherwise made thereto.	3 years

Figure 1B. Timespan Statistics

	All 13 Events	Excluding First Event
# of timespan pairs	12	11
Median	11.5	10
25% quartile	7	7
75% quartile	15.75	14
Outliers	89 years	26 years

Figure 1C. Box Chart Illustrating Timespan Statistics

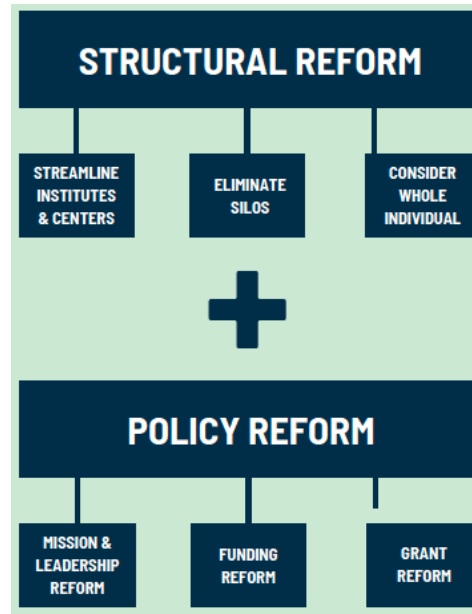


summary and “7 years” as the 25% interquartile in the statistical analysis presented in Figures 1B and 1C.)

Part 2: Policymaking Analysis of Explicitly Stated Reforms in the Framework

The Framework proposes a series of reforms at NIH aimed at enhancing innovative research output, efficiency, transparency, and responsiveness to the life, medical, and health science needs of the American people. The structural and policy aspects of these reforms are diagrammed at a high level of generality in the Committee Chair’s announcement of the Framework.²⁰ We have copied that diagram in Figure 2A.

Figure 2A. High-level Diagram of Framework Reforms



By turning the diagram in Figure 2A counterclockwise by 90 degrees, we have extended its 2 x 3 matrix structure to organize our substantive comments on the Framework. This counterclockwise quarter turn rotation is illustrated in Figure 2B.

Our intent in constructing the table in Figure 2C is twofold:

First, we wanted to comment on the Framework in a visually organized way consistent with the Committee’s visually oriented approach illustrated in Figures 2A and 2B.

Second, we wanted to suggest to the Committee that its diagrammatic approach illustrated in Figures 2A and 2B has the potential to serve as a data structure that facilitates (i) cataloging and analyzing comments received in respect of the Framework, and (ii) application of one or more machine learning tools (e.g., cluster analysis and supervised learning) to support analysis of comments received by the Committee in respect of the Framework. (We welcome the Committee’s questions about such applications of digital intelligence to analyzing comments on the Framework.)

²⁰ Hon. Cathy McMorris Rodgers, U.S. House of Representatives Energy & Commerce Committee Chair, “Reforming the National Institutes of Health Framework for Discussion.” June 2024. https://d1dth6e84htgma.cloudfront.net/NIH_Reforms_Framework_Pager_f94f6eac2c.pdf

Figure 2B. Figure 2A Diagram Turned Counterclockwise by 90 Degrees.

Type of Reform	Proposed Reform	Rationale for Reform	Items for Potential Further Consideration
Structural	Streamline ICs	Proposed Reforms 1...n	...
	Eliminate Silos	Proposed Reforms 1...n	...
	Consider Whole Individual	Proposed Reforms 1...n	...
Policy	Mission & Leadership Reform	Proposed Reforms 1...n	...
	Funding Reform	Proposed Reforms 1...n	...
	Grant Reform	Proposed Reforms 1...n	...

Figure 2C. Substantive Comments in respect of the Proposed Reforms in the Framework

Type of Proposed Reform	Proposed Reform	Rationale for Proposed Reform	Items For Possible Further Consideration
<i>Structural</i>	<p>Consolidation of Institutes and Centers (ICs) from 27 to 15.</p> <p>Reduce siloing.</p>	<p>Should reduce inter-IC redundancy.</p> <p>Supports improved inter-IC coordination, with the aim of achieving a correlated reduction in siloing.</p>	<p>While reducing the number of ICs by 44% should significantly address siloing, this phenomenon can still plague the ICs remaining after the consolidation. Success at anti-siloing requires not only reorganization in the form of consolidation, but also active management to optimize the potential output from the substantially reorganized NIH.</p> <p>In addition, the magnitude of the consolidation presents risks that the consolidation may (i) oversimplify the diverse extramural and intramural research needs to the detriment of the life, medical, and health science sectors and other myriad stakeholders in healthcare, and (ii) potentially neglect special areas of research.</p> <p>These risks can be addressed through: (i) a carefully planned and phased implementation; and (ii) continuous monitoring and dynamic management of substantive elements of the consolidation.</p> <p>NOTE: Notwithstanding the benefits of increased innovation resulting from increased collaboration in an anti-siloed environment, there may be occasions from time to time where a healthy competitive exercise can be helpful.</p>

Type of Proposed Reform	Proposed Reform	Rationale for Proposed Reform	Items For Possible Further Consideration
	Adoption of a “holistic life stage” approach focused on the “whole individual and all populations across the entire lifespan,” with elimination of the “demographic- or disease-specific siloed nature of the current structure”.	This approach can imbue every IC and the projects they fund and oversee with a sensitivity to healthspan.	<p>Implementing a holistic life stage approach with a sensitivity to healthspan across the series of ICs following the consolidation described in the Framework will be hard to achieve without a deep and broad, transparent understanding of healthspan policymaking. A series of analytical studies, seminars, and workshops on how to nurture this approach across the entire NIH may be warranted.</p> <p>This approach should include a requirement that grant proposals include information on how healthspan sensitivity is programmed into the research so proposed.</p>
	Enhanced coordination, interdisciplinary collaboration, and transparency.	Should increase the frequency of innovative discoveries and inventions of significance to healthcare.	<p>To achieve this objective, it may be helpful to develop an easy-to-learn series of “Standard Operating Procedures”, that cover:</p> <ul style="list-style-type: none"> (i) specific mechanisms for enhancing coordination and transparency; (ii) metrics for identifying and assessing the comparative value of projects arising from coordination and transparency. <p>To identify areas ripe for enhanced coordination and transparency, consideration may be warranted for:</p> <ul style="list-style-type: none"> (i) establishing advisory panels specifically for identifying such areas; and (ii) using various digital intelligence tools to identify such areas. <p>Healthspan science inherently requires a multidisciplinary approach, combining insights from biology, medicine, public health, and social sciences.</p> <p>Thematic research clusters exhibit four criteria: (1) topical comprehensiveness; (2) interdisciplinary in reach; (3) conducive to integration of research and application; and (4) collaboratively designed and implemented.</p>

Type of Proposed Reform	Proposed Reform	Rationale for Proposed Reform	Items For Possible Further Consideration
			Examples of initial thematic research clusters in healthspan field include: definition of healthspan metrics; and understanding of gene/protein interaction networks that influence healthspan.
Policy Reform – 1. Mission & Leadership	Introducing term limits for IC directors.	Term limits can prevent stagnant leadership. NIH, just like other entities that must be continually revitalized through reorganization and reform in order to allow new ideas relevant to the time periods in which they arise, must be able to pass the torch of leadership from generation to generation, lest the following admonition from Max Planck be lost on us: “A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it.” ²¹	Implement mentored programs for leadership transitions. Consideration may be given as to whether any exceptions would be allowed, and if so, how they would be administered and overseen.
	Enhancing financial transparency and accountability.	Financial transparency is crucial for public trust and requires robust oversight mechanisms.	Consideration may be warranted for developing digital intelligence tools that can support robust oversight mechanisms.
	Enhancing Interdisciplinary Collaboration	Establishing thematic research clusters.	Healthspan science inherently requires a multidisciplinary approach, combining insights from biology, medicine, public health, and social sciences.
	National Security: Safeguarding NIH-funded research from undue foreign influence and interference.	Implementing stringent national security reviews is necessary but should not discourage international collaboration.	Mandate foreign grant reporting and incorporate national security reviews into the grant process. Develop clear policies to identify and mitigate potential conflicts of interest

²¹ Planck, M. *Scientific Autobiography and Other Papers*, trans. F. Gaynor (New York, 1949), pp. 33-34, as quoted in Kuhn, T.S., *The Structure of Scientific Revolutions*, 50th Anniversary Edition (p. 151), The University of Chicago Press. Kindle Edition. (“Death” in this context should be viewed institutionally as departure from a position of leadership, which does not necessarily entail death in the biological sense.)

Type of Proposed Reform	Proposed Reform	Rationale for Proposed Reform	Items For Possible Further Consideration
	Improving NIHs Response to Emerging Challenges: Enhancing coordination, supporting high-risk research, and fostering innovation.	The proposed reforms aim to create a more agile and responsive NIH capable of addressing complex health challenges.	Establish trans-NIH initiatives for interdisciplinary collaboration. Encourage public-private partnerships to leverage additional resources and expertise. Implement digital intelligence tools to analyze data and optimize research strategies.
Policy Reform – 2. Funding	Repealing the PHS Evaluation Set-Aside law (the “Evaluation Set-Aside”) to improve funding transparency. (See discussion below.)	Original intent of Evaluation Set-Aside was to provide a mechanism by which NIH could obtain information for Congress to aid Congress in its policymaking oversight and improvement of public health initiatives and outcomes. This original intent notwithstanding, several significant issues with administration of the Evaluation Set-Aside are discussed in the Framework.	The original intent of the Evaluation Set-Aside may still make sense. Assuming it is repealed in accordance with the proposal to do so in the Framework, consideration should perhaps be given to a replacement mechanism that will generate information for Congress that allows Congress to perform its policymaking, funding, and oversight roles with respect to NIH.
	Implementing measures to prevent waste and fraud and research misconduct.	Estimates of fraud and abuse in the overall U.S. healthcare sector have ranged from 3% to 10%, representing approximately \$130 billion to \$450 billion annually. ²² In 2023, NIH Office of Extramural published data on incidences of misconduct in extramural research funded by NIH. This data showed a precipitous increase from an annual average of 98.3 (+/- 16.2) to 554.0 (+/- 18.4). ²³	The five-fold increase in allegations of misconduct over the past ten years is troubling. The Framework should include efforts to understand the reasons for this increase and policies aimed at reducing this problem.
Policy Reform – 3. Grants	Supporting innovative research	Supporting innovative research is essential, but the grant review process must be transparent and free from bias.	Allocate specific funds for high-risk, high-reward research projects.
	Prohibiting risky gain-of-function research	[See discussion in letter to which this Exhibit 1 is attached regarding GOFROC/DURC research.]	The GOF/DUR field requires regular review and updating of grant policies to adapt to emerging science and

²² National Health Care Anti-fraud Association. “The Challenge of Health Care Fraud.” <https://www.nhcaa.org/tools-insights/about-health-care-fraud/the-challenge-of-health-care-fraud/>

²³ Lauer, M. “Trends in Extramural Research Integrity Allegations Received at NIH.” Extramural NEXUS, NIH, March 22, 2023. <https://nexus.od.nih.gov/all/2023/03/22/trends-in-extramural-research-integrity-allegations-received-at-nih/>

Type of Proposed Reform	Proposed Reform	Rationale for Proposed Reform	Items For Possible Further Consideration
			scientific, medical, and public health needs.
	Establishing independent review entities		Assure the grant review process includes independent and diverse reviewers.
	Encouraging partnerships between NIH ICs and external organizations.	Collaborative efforts are essential to address the complex factors influencing healthspan.	Consider NIH sponsoring partnerships between and among universities, private sector entities, and international research institutions to leverage additional resources and expertise.
	Provide grants for interdisciplinary healthspan research projects.		Consider allocating specific funding of grants in the interdisciplinary field of healthspan research, with the aim of fostering a comprehensive approach to extending healthy life years.

Proposed Repeal of Evaluation Set-Aside

As noted in the table in Figure 2C, the Framework points to unsuccessful administration of the 1970 amendment to Section 241 of the Public Health Service Act authorizing the “PHS Evaluation Set-Aside” (the “Evaluation Set -Aside”). In response to a question intended to corroborate the Framework’s criticism of the Evaluation Set-Aside, GPT-4o notes:

First, the Evaluation Set-Aside has been criticized for lacking clear guidance on how the set-aside funds should be used, which led over the course of decades to inconsistent application of those funds and sometimes ineffective evaluations.

Second, challenges have arisen in assuring that evaluations mandated by the Evaluation Set-Aside have been comprehensive and communicated effectively to Congress. Evaluations have often not synthesized results across program areas, limiting their usefulness in providing a holistic view of program effectiveness.

Assuming that the Evaluation Set-Aside is repealed, Congress in the context of enacting that repeal will need to address whether any aspects of the evaluations contemplated by the Evaluation Set-Aside should be legislatively mandated and improved. For example, in any replacement for the Evaluation Set-Aside, explicit guidance should be provided on the permissible uses of any evaluation funding provided in the replacement, assuring such funds are directed towards meaningful assessments of program implementation and effectiveness. This would involve clarifying the intended use of funds in the replacement legislation and requiring annual reports summarizing evaluation findings. Furthermore, enhancing the synthesis and communication of evaluation results by program area could improve their utility for Congress. By implementing these changes in the Evaluation Set-Aside replacement legislation, the efficacy of using funds for evaluation to inform Congress about the effectiveness of federal health programs could be significantly improved, leading to better oversight and program enhancements.

Proposed Replacement of National Institute on Aging with National Institute on Dementia

Dementia forms a family of several neurodegenerative diseases, the most prevalent of which is Alzheimer’s Disease. Demographic and research expenditure data for dementia varies by source, year, dollar type (constant or current), and population under study. For example, a RAND Corporation study²⁴ published in *The New England Journal of Medicine* in 2013 showed that an “estimated prevalence of dementia among persons older than 70 years

²⁴ Michael D. Hurd, et al., “Monetary Costs of Dementia in the United States”, *N Engl J Med*, 2013;368:1326-1334.

of age in the United States in 2010 was 14.7%” and that “[t]he yearly monetary cost per person attributable to dementia was either \$56,290 ... or \$41,689 ..., depending on the method used to value informal care.” Multiplying these amounts per individual by the prevalence data for the 71-plus years of age population in the United States, “suggest[ed] that the total monetary cost of dementia in 2010 was between \$157 billion and \$215 billion”, with “Medicare [paying] approximately \$11 billion of this cost”.

Turning from dementia generally to Alzheimer’s Disease specifically, the 2013 RAND study estimated that the monetary costs in the U.S. in 2010 attributable to Alzheimer’s Disease were \$109 billion. Illustrating the point about variability in the demographic and expenditure data, for the same year, as reported in the RAND study, the Alzheimer’s Association estimated the monetary costs were \$172 billion, 58% higher than what RAND found such amount to be. Legislative policymaking in the context of such variability presents challenges.

Notwithstanding the increasing number of therapeutics approved by the U.S. Food and Drug Administration for treating Alzheimer’s Disease and its symptoms, it is beyond the pale to believe that the U.S., or any other country, has in just 10 years addressed the depth and breadth of the impact of dementia reported in the 2013 RAND study. Indeed, the continuing need to address the prevalence and cost of dementia is illustrated in the July 1, 2024 web publication by the U.S. Centers for Medicare and Medicaid Services introducing the “Guiding an Improved Dementia Experience (GUIDE) Model”.²⁵ This publication highlights that in 2023 dementia affected more the 6.7 million Americans (approximately 2% of the U.S. population), with this number projected to increase to 14 million by 2060. The driving policies for the GUIDE Model are establishing “a standard approach to care, including ... caregiver training, education, and support services” aimed at “allow[ing] people with dementia to remain safely in their homes for longer” and “enhanc[ing] health equity by ensuring that underserved communities have equal access to the model intervention.”

Additionally, calling a National Institute primarily engaged in performing and funding research on dementia the “National Institute on Aging” may be a misnomer, as the field of research on aging is fundamentally broader than the field of research on dementia.

Accordingly, by reason of the above demographic and lexical logic, it is easy to justify formation of a National Institute on Dementia, provided that longevity-related diseases other than Alzheimer’s and other forms of dementia heretofore covered by the National Institute on Aging are covered elsewhere in the ICs remaining after the reorganization contemplated by the Framework. This proviso is consistent with the Framework’s statement that “[b]y encouraging each IC to utilize a holistic life stage approach, our goal is to eliminate the demographic- or disease-specific siloed nature of the current structure and ensure each IC is considering the whole individual and all populations across the entire lifespan.”

Beyond the substantive concept reflected above as to replacing the National Institute on Aging with the National Institute on Dementia, several administrative points need to be addressed. First, as noted above, any sequel to the Framework should explicitly address how NIH will fund research on longevity-associated diseases and conditions other than dementia, geriatric care generally, and the overall health and well-being of older adults. If not carefully implemented, closing the NIA could lead to a gap in research and support for these other critical areas, potentially neglecting the holistic needs of the aging population – which such holistic approach across the entire life span is a necessity stated explicitly in the Framework. Additionally, the transition from a broad-based institute to a specialized one might disrupt ongoing research and funding structures, potentially slowing progress in areas that do not fall under the dementia umbrella.²⁶

In sum, the establishment of a National Institute on Dementia could adversely affect aging research, which is inherently interdisciplinary and interconnected. Aging is a complex process that involves various biological, social, and environmental factors, and isolating dementia research might overlook the broader context in which these diseases develop. This could limit the potential for comprehensive solutions that address the root causes of aging-

²⁵ Centers for Medicare and Medicaid Services, “Guiding an Improved Dementia Experience (GUIDE) Model,” <https://www.cms.gov/priorities/innovation/innovation-models/guide>

²⁶ The point in this sentence came to our attention in a response to a prompt to GPT-4o.

related health issues. Balancing the need for specialized dementia research with the broader objectives of aging research will be crucial to ensure that the diverse needs of the aging population are met effectively.²⁷

Part 3: Additional Policymaking Considerations

In this Part 3, we turn to policymaking considerations that are not addressed explicitly or at length in the Framework, but that may warrant consideration by the Committee. These additional matters arise particularly in the context of the last sentence in the Background section of the Framework, *viz.*: “The twin imperatives of maintaining the country’s position of global scientific leadership, while also addressing past misconduct illustrates the need for a wholesale, robust review and reform of NIH policy programming, and activities, as well as a comprehensive organizational restructuring.”

The four matters we address in this Part 3 include:

- leveraging digital intelligence²⁸
- reforms to the Bayh-Dole Act of 1980 consistent with the Framework
- alternative organizational structures for implementing the Framework reforms
- coverage of longevity research in any revised Framework and corresponding bills

Leveraging Digital Intelligence (aka “Artificial Intelligence”)

Similar to other sectors within industry, commerce, government, and academic and other not-for-profit research institutions, NIH’s intramural and extramural research operations can benefit substantially from digital intelligence tools. We use the term “digital intelligence” to mean the field of computer science first called “artificial intelligence” in 1956 at a conference at Dartmouth University,²⁹ and which rose out of the cybernetics field pioneered by Norbert Wiener et al. during the 1940s,³⁰ as well as Alan Turing’s work in the late 1940s and early 1950s on computing machinery and intelligence.³¹ The benefits of applying digital intelligence to NIH’s research operations will likely become increasingly evident over coming years as it contributes to an emerging series of ongoing discoveries and inventions in life, medical, and health science and related technologies. The digital intelligence tools currently available include large language models evidencing “generative artificial intelligence” (GAI); and these tools may begin expanding to platforms evidencing cognitive skills, referred to as “artificial general intelligence” (AGI), in the last years of the 2020s.³²

Several LLM-enabled GAI platforms have been trained on large, relevant datasets to identify trends, predict outcomes, and optimize research and development strategies for various diseases and disorders. At least one company has succeeded at using a GAI tool to discover, as a target, a common pathway responsible for a family of diseases with similar sequelae, and a second GAI tool to engineer a small molecule drug aimed at that target, cutting substantially the time from discovery to commencement of clinical studies of the drug targeted at one of the diseases in that family of diseases. Clinical studies of this drug are underway on two separate continents.³³

²⁷ The point in this sentence came to our attention in a response to a prompt to GPT-4o.

²⁸ In analyzing the Framework, we made extensive use of multiple large language models to generate text and provide numerical data. This text and numerical data was cite-checked and edited by us. Where direct quotes of that text is set forth in this letter and Exhibit 1, we indicate the source thereof.

²⁹ See “The History of Artificial Intelligence”, History of Computing CSEP 590A, University of Washington, December 2006. <https://courses.cs.washington.edu/courses/csep590/06au/projects/history-ai.pdf>

³⁰ See Wiener, N. “Cybernetics”. *Scientific American*, Vol. 179 No. 5 (November 1948).

³¹ AI-PRO. “The History of AI: From Turing’s Theories to ChatGPT’s Breakthroughs.” <https://ai-pro.org/learn-ai/articles/the-history-of-ai-from-turings-theories-to-chatgpts-breakthroughs/>

³² See, e.g., Kurzweil, R. *The Singularity is Nearer*. Penguin Publishing Group. Kindle Edition; and <https://www.metaculus.com/questions/3479/date-weakly-general-ai-is-publicly-known/>.

³³ See NCT05938920 and NCT05975983, each named “Study Evaluating INS018_055 Administered Orally to Subjects With Idiopathic Pulmonary Fibrosis”), in clinicaltrials.gov.

Given the likely impact of Digital Intelligence on NIH, especially as reorganized in the manner envisioned in the Framework, the Committee may find it more than just helpful, and perhaps imperative, to expand the Framework to include digital intelligence policymaking. This policymaking would potentially cover several functions for which digital intelligence could play a valuable role in NIH's operations, including: (i) enhancing data analysis and interpretation; (ii) increasing the efficiency of administrative tasks; (iii) supporting collaborative research; (iv) advancing gender and diversity initiatives; (v) enhancing training and education; and (vi) if and when permitted after the implementation of appropriate confidentiality safeguards, assisting in peer review and grant evaluation.

Regarding the sixth of these functions, at a high level of generality in need of further clarification, NIH prohibited its peer reviewers from using digital intelligence in December 2021 in NIH Office of the Director Notice # NOT-OD-22-044 (the "'044 Notice")³⁴. This OD notice states that, "[c]onsistent with the agency's responsibility to protect applications, information, and data related to NIH peer review contained in [NIH's data] systems", the following activities are prohibited:

"Accessing, or attempting to access, a secure government computer system used to support the NIH peer review process by any individual who has not been authorized by the NIH DFO in charge of that review meeting, or assisting such an individual gain access to a system;

Engaging in unauthorized or improper use of these systems, applications, data or information contained therein, including communicating, delivering, transmitting, or causing to be communicated, delivered, or transmitted, or attempts to communicate, deliver, transmit or cause to be communicated, delivered or transmitted to any person not entitled to receive such information;

Sharing or assisting in the sharing of government-issued login credentials and/or passwords with, or granting access to, any individual, organization, or other entity, in gaining access to a secure government computer system used to support the NIH peer review process.

In NOT-OD-23-149, released on June 23, 2023 (the "'149 Notice"), the Office of the Director clarified that the GAI prohibition set forth in the '044 Notice extends to NIH scientific peer reviewers "using natural language processors, large language models, or other generative Artificial Intelligence (GAI) technologies for analyzing and formulating peer review critiques for grant applications and R&D contract proposals."³⁵ The '149 Notice further states that NIH is revising its "Security, Confidentiality, and Non-disclosure Agreements for Peer Reviewers" to clarify this prohibition.

The '149 Notice offers a simple rationale for prohibiting reviewers from using digital intelligence tools, to wit: "AI tools have no guarantee of where data are being sent, saved, viewed, or used in the future, and thus NIH is revising its Confidentiality Agreements for Peer Reviewers to clarify that reviewers are prohibited from using AI tools in analyzing and critiquing NIH grant applications and R&D contract proposals."³⁶

One way to address the confidentiality requirements of NIH's peer review program in the context of applying GAI to peer review of grant proposals would be for NIH to design, develop, and maintain a GAI model for exclusive use by NIH and its peer reviewers. This would require collaboration among various stakeholders, including NIH officials and counsel, GAI developers, cybersecurity specialists, hyperscaled cloud providers, data scientists, peer reviewers, and grant proposers. The timeline for developing a secure and efficient LLM for NIH's exclusive use could span 18 to 24 months. The cost of developing a custom LLM could vary widely, ranging from

³⁴ Office of the Director, NIH, "Maintaining Security and Confidentiality in NIH Peer Review: Rules, Responsibilities and Possible Consequences", NOT-OD-22-044, December 30, 2021. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-044.html>

³⁵ Office of the Director, NIH, "The Use of Generative Artificial Intelligence Technologies is Prohibited for the NIH Peer Review Process." NOT-OD-23-149. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-23-149.html>

³⁶ Id.

several million to tens of millions of dollars, depending on the complexity and scale of the project.³⁷ While significant in amount, we suspect that the value of such an NIH-only LLM would exceed its cost.

The training library for an LLM for exclusive use by NIH and its peer grant reviewers would need to include a vast array of scientific literature, previous grant applications, patent applications and issued patents, clinicaltrials.gov and its non-U.S. counterparts, and anonymized peer review data to assure the model can understand and generate relevant content without compromising confidentiality. The data used for training would need to be carefully curated to exclude sensitive or proprietary information, and the GAI tool would need to be hosted on secure, NIH-controlled servers to prevent unauthorized access and data breaches. This approach aligns with NIH's commitment to maintaining the integrity of the peer review process.³⁸

In addition to confidentiality concerns, any NIH LLM would need to address concerns relating to safe, secure, and trustworthy development and use of digital intelligence. The October 30, 2023 Executive Order 14110 addresses many of these as tasks on which many different U.S. government executive branch agencies are currently working.³⁹

Relationship of Framework to Bayh-Dole Act of 1980

The Framework does not explicitly mention by name the Bayh-Dole Act of 1980, but does refer to the need to enforce financial disclosure and transparency requirements “for appropriate reporting and disclosure of royalty payments and other third-party financial benefits, including support from and affiliations with foreign institutions”. In the footnote to this reference to royalty payments, the Framework cites “H.R. 7853 Royalty Transparency Act”. This bill was introduced on April 2, 2024 and was referred to the House Committee on Oversight and Accountability and the House Committee on the Judiciary. If enacted and signed into law, this bill would require federal executive branch employees to disclose the amount of royalties they receive from licenses to their inventions granted by the federal government pursuant to Section 209 of the Bayh-Dole Act of 1980, as amended.^{39A}

For 44 years, the Bayh-Dole Act has provided invaluable support for the development and commercialization of a long line of medically important, innovative medical products (including small molecule drugs, biologics, cell and gene therapies, and medical devices). This support notwithstanding, the Bayh-Dole Act currently faces several challenges revolving around its continued implementation and interpretation. Key issues are reported to include: balancing between public and private interests; NIH's exercise of its march-in rights when the requirements of Bayh-Dole are not met (e.g., manufacturing of covered products in the U.S.); government recoupment of its investments in R&D from companies that market highly profitable products based on inventions licensed to them under Bayh-Dole; and the impact of Bayh-Dole on university research. As noted by GPT-4o, “[t]hese challenges highlight the ongoing debate about how to balance the benefits of the Bayh-Dole Act with the need to ensure that the public interest is adequately protected, particularly in sectors like pharmaceuticals where the implications for public health and access to medicines are significant.”

These challenges to continued implementation and interpretation of Bayh-Dole may be sufficiently important to include in the wide-ranging study of NIH contemplated by the Framework.

³⁷ Miller, K. “A New Approach Trains Large Language Models in Half the Time.” Human -Centered Artificial Intelligence, Stanford University. June 26, 2023. <https://hai.stanford.edu/news/new-approach-trains-large-language-models-half-time>

³⁸ GPT-4o authored this paragraph.

³⁹ Office of the President. “Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence”. Executive Order 14110. 88 FR 75191, November 1, 2023.

^{39a} Footnote 15 of the Framework cites H.R. 7853. The Senate version thereof, S. 3664, was introduced in the Senate on January 25, 2024. See <https://www.congress.gov/bill/118th-congress/senate-bill/3664?q=%7B%22search%22%3A%22s+3664%22%7D&s=1&r=1>. Section 209 of the Bayh-Dole Act of 1980 (codified in 35 U.S.C. Section 209) provides for licensing of federally-owned inventions, which section was substantially amended by Section 4 (Licensing Federally Owned Inventions) of the Technology Transfer Commercialization Act of 2000 (Pub. L. 106-404, 114 Stat. 1742).

Alternative Organizational Structures for Implementing the Framework Reforms

The current NIH structure, with its 27 ICs, has been criticized for being overly complex and siloed, leading to inefficiencies, redundancies, and other problems, as described in the Framework. As a macro approach to this set of problems, the Framework proposes consolidation of NIH from 27 ICs to 15 ICs. Implementing this consolidation will present a significant managerial challenge. To achieve success, the Committee may want to consider two or more different organizational approaches for subsets of ICs and subsets of research within any single IC. Some of these approaches are described below.⁴⁰

Federated Model with Enhanced Coordination: The current organizational approach to each IC acting largely independently from the other ICs but with enhanced coordination through a central coordinating body. This structure could preserve the specialized expertise and experience of each IC while improving overall coordination and reducing redundancies.

Matrix Structure: With a matrix organizational structure, researchers (both intramural and extramural) with specific functional expertise and resources form one dimension of the matrix and specific projects form the other dimension. As projects arise, various sets of researchers and their resources from one or more ICs would be assigned to those projects. This would promote interdisciplinary research and enhance flexibility in resource allocation. Matrix structures are characterized by a dual reporting system, with each researcher reporting to two managers: a functional manager who oversees functionally oriented tasks and responsibilities; and a project manager who directs project-specific activities.

A matrix organization offers the following advantages: cross-functional teams; flexibility and adaptability; varying balance of power between functional and project dimensions; improved resource utilization; enhanced communication; and increased flexibility.

Disadvantages of a matrix organization include: complexity; potential for conflict between the two dimensions; and too time-consuming to effectively manage.

A matrix organization could serve as a foundation for the following two structures:

Thematic Research Clusters: Somewhat like a matrix organization, thematic research clusters are based on related health issues and scientific domains. Each cluster would facilitate coordinated research efforts within it, and be engineered to reduce duplication and enhance efficiency.

Modular Structures: This organization approach would call for implementation of modular structures where ICs can be dynamically reconfigured based on emerging scientific needs and priorities. This enhances flexibility and adaptability, allowing the NIH to respond quickly to new scientific challenges.

Regional Research Hubs: Regional research hubs that concentrate on specific health issues relevant to their geographic areas could be established. These hubs could address regional health disparities and assure that research is relevant to local populations.

Coverage of Longevity Research in any Revised Framework and Corresponding Bills

We return here to two principal terms defined in the letter to which this Exhibit 1 is attached: longevity and healthspan. To generate definitions for each of these two terms, we submitted the following prompt to the large language model GPT-4o running on the Perplexity.ai platform: “Define “longevity” and “healthspan”. Explain the difference between these two terms.”

The model responded to this prompt as follows (with some wordsmithing edits from us):

⁴⁰ The content in this section was generated by GPT-4o and edited by us.

“Longevity” refers to the length of time an individual lives, often surpassing the average life expectancy. It encompasses not just the total number of years lived but also implies living those years in a manner that is healthier and more fulfilling than average[1][2].

“Healthspan”, on the other hand, is the period of life spent in good health, free from chronic diseases and debilitating conditions. It emphasizes the quality of life and living years with full physical and mental functionality[1][3].

Differences Between Longevity and Healthspan

Aspect	Longevity	Healthspan
Definition	Total number of years lived	Number of years lived in good health
Focus	Quantity of life	Quality of life
Measurement	Life expectancy or lifespan	Healthy years without chronic disease
Goal	Extending life duration	Extending life quality and functionality
Factors	Genetics, healthcare, lifestyle	Lifestyle choices, healthcare, disease prevention
Outcome	Living longer	Living healthier, potentially longer

While both longevity and healthspan research are important, they address different aspects of aging. Longevity research aims to extend the number of years lived, whereas healthspan emphasizes maintaining health and functionality during one’s life. Healthspan research seeks to minimize the gap between lifespan and healthspan, which can be around 9 to 10 years, where individuals might live with poor health[1][2]. Prioritizing healthspan involves adopting lifestyle changes that promote physical, mental, and social well-being, thus potentially increasing both healthspan and lifespan[2][4].

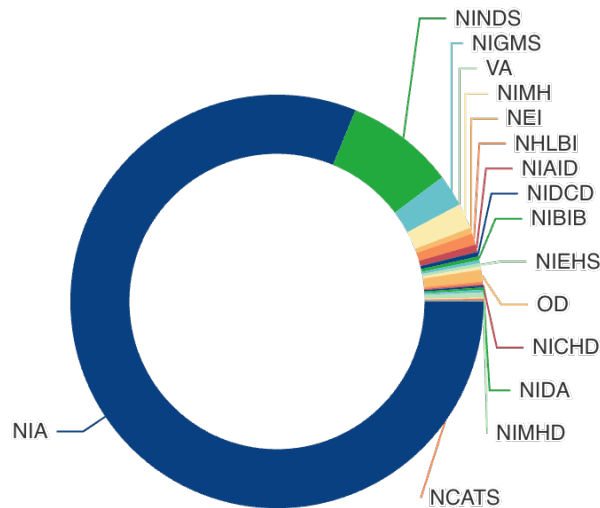
Citations:

- [1] <https://www.medichecks.com/blogs/longevity/what-s-the-difference-between-lifespan-and-healthspan>
- [2] <https://fortune.com/well/2023/04/15/healthspan-may-be-more-integral-to-your-well-being-than-lifespan-how-to-lengthen-it/>
- [3] <https://genflowbio.com/healthspan/>
- [4] <https://www.mdvip.com/about-mdvip/blog/healthspan-vs-lifespan-understanding-key-differences>

Based on these two definitions, and the structure of NIH prior to any reorganization of the magnitude contemplated by the Framework, it is rational to posit that while healthspan research is relevant to each IC, longevity research is specifically relevant to the National Institute on Aging. Moreover, while longevity research intersects with research on dementia, longevity research is not contained wholly within the field of dementia research. Indeed, this is reflected in the chart set forth in Figure 3. This chart, which was generated by the NIH rePORTER platform, indicates the relative amount of funding for FY2024 active research funding across the existing ICs and certain other federal agencies for research grants selected by the following search string applied to the Project Title, Project Terms, and Project Abstracts fields for the research grant dataset underlying NIH rePORTER:

longevity AND NOT (Alzheimer’s OR Parkinson’s OR dementia)

Figure 3. Relative FY 2024 Funding Amounts by NIH ICs on Longevity (excluding Alzheimer’s Disease, Parkinson’s Disease, or dementia)



The chart in Figure 3 indicates that NIA administers 81.2% of FY2024 NIH funding for longevity grants that do not include the terms “Alzheimer’s”, “Parkinson’s”, or “dementia” in the Project Title, Project Terms, and Project Abstracts fields for research grants in the NIH rePORTER dataset.

Accordingly, the chart in Figure 3 gives credence to comments in respect of the Framework that may be provided to the Committee from various organizations to the effect that if NIA is replaced with a National Institute on Dementia, there will be a materially adverse impact on NIH funding for longevity research. On the other hand, the fact that 18.8% of FY2024 funding for longevity research is being provided by ICs other than NIA indicates that there is at least some current coverage for longevity research at NIH beyond NIA.

To address the legitimate concerns of those commentators who posit the loss of longevity research funding by NIH if NIA is transformed into the National Institute on Dementia, it may make sense for the Committee to include in the sequel to the Framework and any bills resulting therefrom an express plan for porting to the remaining ICs the expertise on longevity research outside of Alzheimer’s disease, Parkinson’s Disease, and dementia.

Part 4. SWOT Analysis of Proposed NIH Reforms

With the support of GPT-4o, we generated a Strengths/Weaknesses/Opportunities/Threats matrix for the Framework. This SWOT matrix may be helpful to the Committee, with adjustments to be made as the legislative policymaking process entailed by the Framework proceeds.

Strengths

- *Consolidation of ICs:* Streamlining operations by reducing the number of ICs from 27 to 15 can enhance coordination and reduce siloing and redundancy.
- *Enhanced Financial Transparency:* Introducing measures for financial transparency and accountability can build public trust and assure responsible use of funds.
- *Support for Innovative Research:* Allocating funds for high-risk, high-reward research projects can drive breakthroughs in biomedical science.

Weaknesses

- *Risk of Oversimplification:* Consolidating ICs may lead to the neglect of specialized research areas and diverse health needs.
- *Leadership Transition Challenges:* Implementing term limits for IC directors could result in the loss of experienced leaders and disrupt ongoing research initiatives.
- *Potential Funding Inflexibility:* Repealing the PHS Evaluation Set-Aside might limit the NIH's ability to respond to emerging public health challenges.

Opportunities

- *Interdisciplinary Collaboration:* The reforms can foster greater interdisciplinary collaboration, essential for addressing complex health issues, such as aging and chronic diseases.
- *Public-Private Partnerships:* Strengthening partnerships with the private sector can leverage additional resources and expertise, accelerating the translation of research findings into practical applications.
- *Integration of Healthspan Research:* Emphasizing healthspan in research priorities and funding decisions can lead to significant improvements in the quality of life for aging populations.

Threats

- *Implementation Challenges:* The success of the reforms depends on careful implementation to avoid disruptions and assure that the diverse research needs are met.
- *Resistance to Change:* There may be resistance from within the NIH and the broader research community to the proposed structural and policy changes.
- *National Security Concerns:* Stringent national security reviews, while necessary, should not discourage valuable international collaborations.