October 27, 2023

The Honorable Bill Cassidy, MD
Ranking Member
Senate HELP Committee
Washington, DC 20510

RE: Request for Information – NIH Reform

Dear Ranking Member Cassidy,

The Infectious Diseases Society of America (IDSA) and the HIV Medicine Association (HIVMA) appreciate the opportunity to provide feedback to you and the Health, Education, Labor and Pensions (HELP) Committee regarding NIH reform. We represent more than 14,000 infectious diseases (ID) and HIV physicians, physician-scientists and other clinicians and public health professionals on the front lines of infectious disease and HIV research, prevention and treatment.

Our overarching concern is that the current capacity of ID and HIV physician-scientists is insufficient to meet our nation's needs. To effectively address the expanding scale and scope of infectious diseases and growing antimicrobial resistance, and to end the HIV epidemic, greater numbers of ID physicians and scientists dedicated to ID research are needed. A major role of the NIH, and specifically for infectious diseases, of the National Institute of Allergy and Infectious Diseases (NIAID), is to support the pipeline of ID and HIV physician-scientists who will become the future physicians and research leaders in our field. Unfortunately, the support of the NIH for career development awards has remained flat and many promising young physician-scientists leave the specialty because they don't see a path forward. For this and many other reasons, the specialty of infectious diseases, both adult and pediatric, has become less attractive. For example, in 2023, just over half of ID physician training programs, and only 43% of pediatric ID training programs were filled; by comparison, most other physician specialties filled nearly all their programs.[1] In addition, the supply of ID physicians is especially limited, including in rural and frontier areas. More than three-quarters of U.S. counties did not have a single ID physician in 2017.[2]

We need to train more ID physician-scientists to continue to address knowledge gaps and to develop the tools necessary to address emerging and re-emerging infectious diseases. This effort requires increased support from NIH for training grants (T-32s) and career development awards (K awards) for ID/HIV researchers. These programs are critical as they provide protected time for education and mentored training in the critical years for early career physician-scientists, enabling them to become the future leaders of ID/HIV research. Our inability to recruit and train enough ID physicians, including ID physician-scientists, will persist if insufficient support for early career scientists continues. A failure to make

[1] National Resident Matching Program, Results and Data, 2023 Appointment Year. Retrieved from https://www.nrmp.org/wp-content/uploads/2023/04/2023-SMS-Results-and-Data-Book.pdf
[2] Walensky RP, McQuillen DP, Shahbazi S, Goodson JD. Where Is the ID in COVID-19? Ann Intern Med. 2020 Oct 6;173(7):587-589. doi: 10.7326/M20-2684. Epub 2020 Jun 3. Retrieved from PMID: 32491920; PMCID: PMC7277486.

necessary investments now will yield dire consequences for the future of ID research and public health and limit the ID workforce.

Below, we offer recommendations and responses to your request for information regarding strategies to ensure NIH continues to support cutting-edge research and to modernize the agency so it is more transparent, nimble and forward-thinking. We welcome continued dialogue and collaboration with you and the HELP Committee on these topics.

Increasing the Pace of Science

Overarching Questions

1. ***How has the conduct and dissemination of science changed in recent years, particularly due to COVID-19? What role can NIH play in speeding up the pace of science and quickly disseminating high-quality research findings?***

There were significant advances in medical research due to COVID-19. Clinical trial and data analysis infrastructures were developed to support the research, development and optimal use of treatments for COVID-19 and to better understand COVID-19 immunity and management of long COVID immunity. For example, NIH launched the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) initiative that simultaneously invested in multiple, parallel approaches, allowing successful interventions to be identified much faster than using more traditional research methods. To launch clinical trials with candidate COVID-19 vaccines and monoclonal antibodies, the NIH developed a consortium called the COVPN (COVID-19 Prevention Network). The COVPN brought together the NIH-supported clinical trial centers that were set up to do HIV prevention and therapeutic studies, namely the AIDS Clinical Trials Group, the HIV Prevention Trials Network and HIV Vaccine Trials Network. Without access to these well-established networks of highly qualified clinical trialists and their staff the conduct of many studies would have been quite difficult if not impossible.

It is essential that Congress and NIH support and maintain this infrastructure so that it can be used to accelerate research on other infectious diseases and be ready to quickly address the next outbreak or pandemic.[3] Expanded NIH funding for these innovative platform-based approaches that allow simultaneous comparison of multiple intervention groups against a single control group for other infectious diseases will accelerate the pace of science and deliver results on clinical outcomes much faster. Just as we maintain FEMA and the Coast Guard at readiness, our scientific enterprise needs to stand ready for "bad weather."

6. ***What lessons can be learned from individual NIH Institutes and Centers (ICs) related to the conduct of clinical research? How can clinical trials be conducted more efficiently and effectively? What types of trials should NIH conduct, and what types are more appropriate for industry to undertake?***

The conduct of clinical trials that will lead to the FDA approval of a drug, vaccine or other biological needs to be done by highly trained individuals that are competent in good clinical trials practice. Clinical research drives new discoveries and innovations in health care. Federally supported infrastructure

[3] Titanji BK, Boulware DR, Bender Ignacio RA. Strategies for Expediting Clinical Trials in the Next Public Health Emergency. JAMA Health Forum. 2023;4(9):e233191. Retrieved from doi:10.1001/jamahealthforum.2023.3191

should provide an integrated framework to link individuals diagnosed with emerging infectious diseases to appropriate trials and encourage large-scale collaboration across many different types of facilities, including community hospitals and community health centers.

- Such an approach will increase the reach of trials of promising therapeutics to populations that are typically underrepresented in studies, including African American/Black, Latinx and Indigenous populations, children and adolescents, and adults aged 75 and older. This goal is best accomplished by performing studies on larger, more diverse populations, with a focus on settings outside the traditional urban tertiary care academic centers.
- Increasing access to clinical trials in rural areas should also be considered through this approach. These considerations increase access to treatments for patients in areas with limited medical care and expand the ability to rapidly gather data across a broader range of participants.

“Warm base” research refers to studies that not only gather data under a particular clinical research protocol but also serve the function of keeping trial sites in a state of readiness to undertake additional or future research and can be useful in ID clinical trials. Emerging infectious diseases threats require infrastructure and patient populations that can be rapidly leveraged to develop an understanding of a possible unknown pathogen and methods to prevent and treat it. Funding “warm base” research on existing infectious diseases creates this infrastructure. NIAID has supported collaborative government-to-government research in countries like Mexico and Indonesia that focused on different infectious diseases, such as acute febrile illness and respiratory diseases.

- Support for registries, biobanks and data queries — particularly for rare diseases — is desperately needed. This is crucial for advancing therapies for immunocompromised people for whom randomized clinical trials are not possible. Different trial instruments — e.g., registries, large observational studies (pragmatic and retrospective) conducted via EMR searches and randomized trials — need to be considered. In addition, modeling and novel statistical tools that reach answers faster should be considered.
- Vaccine and drug trials provide opportunities for collaboration with industry, including outreach to other disciplines to leverage trials to explore mechanistic hypotheses.
- The ACTIV program provided a model for public-private partnerships to increase trust and access to research across the U.S. and internationally while leveraging scientific innovation and support across several industry partners.
- Administrative burdens should be reduced to incentivize additional sites to engage in clinical trials, including rural and other sites that serve underserved populations. Without reasonable accommodations, the burden of participation may be too high to include these sites.

When COVID cases surged in 2020, clinical trial resources were rapidly repurposed, enabling COVID-19 studies. Similar efforts in the U.S. can leverage research on endemic infectious diseases, which can be rapidly repurposed to study future emerging infectious diseases. Ongoing research and clinical trials on infectious diseases such as COVID-19 or influenza can then be utilized to rapidly study and conduct emergency clinical trials for emerging respiratory viruses.

- Research that addresses intersections between public health, health disparities, environmental challenges, climate change and testing therapies and vaccines provides opportunities for specific settings.
- The National Center for Advancing Translational Science model used for COVID-19 research deserves consideration. It has the benefit of supporting Clinical and Translational Science Awards, which support training and collaboration between centers. This approach also supports training and mentorship of early career physician-scientists as part of the grant, which helps bolster the physician-scientist pipeline.
- Research should also be aimed at developing platforms for rapid deployment of diagnostic tests when facing a new pathogen so that we can more rapidly scale up testing capacity when a new threat emerges. Testing is critical to inform individual care and broader responses. Research investments should also focus on developing novel therapeutic options that would have activity against anticipated pathogens such as coronaviruses, influenza and bacteria, including multidrug-resistant ones.

Extramural Research Program

2. ***How do academic institutions typically fund the salaries of extramural investigators? What benefits and challenges come with this approach? How could this practice be reformed to better support the biomedical research workforce and ensure that NIH dollars, on a per project basis, accurately reflect the time commitments of each investigator and staff member?***

There is not a singular model for funding the salaries of extramural investigators. Some public universities require researchers to successfully obtain extramural (mainly NIH) grant funding to support ~50% of their salary. At many academic institutions, there is an expectation of >70% NIH (or other extramural) support. The rest is generally supplemented by their clinical work using a relative value unit (RVU)-based model (i.e., payment for the number of patients seen). This model is extremely challenging, particularly for junior investigators. The model also creates a disparity for physicians in medical specialties like ID that do not typically perform surgical procedures that generate greater RVUs. Furthermore, NIH places a cap on how much grantees can earn. The salary cap is unrealistic, is not commensurate with physician salaries and disincentivizes the pursuit of research as a career option. There needs to be greater collaboration between NIH and academic institutions so that the needs of the agency, academia and individual researchers are all addressed.

To attract and retain more ID and pediatric ID physician-scientists, salaries and protected time for research activities must increase and salaries must be competitive with those of clinicians. This is particularly true in ID, where procedure-based compensation is not available. According to data compiled by Medscape, ID ranks below all but four other specialties for annual compensation, including general internal medicine, despite the additional years of training.[4] This dissuades trainees from pursuing the ID specialty and ID research and limits the clinical and research workforce. NIH policies that require grantees and their institutions to honor granted research effort as protected time and ensure

[4] Medscape, 2023 Physician Compensation Report. Retrieved from https://www.medscape.com/sites/public/physician-comp/2023.

that salary for that protected time is commensurate with that of clinician colleagues is critical to retaining our ID physician-scientist workforce.

7. ***What specific factors cause individuals to leave the biomedical research workforce? How could common NIH funding mechanisms be revised to better recruit and retain high-quality investigators, including young investigators?***

Recently, IDSA and HIVMA were dismayed to see no increase in paylines for most early career grants at NIAID.[5] These low paylines, which have not increased in more than a decade, result in rejections of highly qualified applicants, further shrinking the already inadequate pipeline of ID physician-scientists, with long-term consequences for the field. Since obtaining NIH funding is critical to early career researchers, we are extremely concerned that there is not enough support for early career physician-scientists specializing in ID and HIV research. This greatly compromises ID and public health research. In addition, because of low paylines, most physician-scientists are constantly in fear of losing their positions or having to lay off staff and recurrently lay off and hire. This further disincentivizes early career researchers who would expect job security after many years of training.

In addition, grants should not be so onerous and time-consuming to prepare, given the very low payline and (relatively) small institute budgets for career development awards. Given very low paylines, IDSA and HIVMA members report that they have resubmitted applications multiple times to receive funding. This disincentivizes early career researchers from staying in the field. To recruit and retain talented physician-scientists in ID, there should be more funding for early career investigators, and it should be easier to obtain.

9. ***What role do institutions not affiliated with major research universities, such as other types of academic medical centers or community hospitals, currently play in the NIH ecosystem? How could these types of facilities be more effectively leveraged as research partners?***

Pragmatic trials networks (e.g., FDA Reagan Udall COVID-19 Diagnostics Evidence Accelerator, Sentinel, PCORnet, NIH Collaboratory), including networks that enroll pediatric populations, should be developed. This will increase engagement of front-line physicians and community clinicians in clinical trial research, especially if clinical trial infrastructures are in place. Specifically, from the time of trial inception, the federal government should involve clinicians, researchers and community members representing the population being studied or who have lived experience of the health issue.

Front-line physicians and other community clinicians should participate in trial planning. As active members and trusted figures in trial site communities, these individuals help build transparency and public trust in addition to improving clinical trial design. Additionally, they help expand potential trial participant pools, which can improve trial diversity and strengthen study findings. Investments should also be made in leveraging technology and telehealth platforms to support community-based trial sites. Models that link such institutions with larger, highly resourced institutions could be considered, provided they are built on equity and a collaborative model. The regulatory and administrative burden of pragmatic trials also needs to be rethought to make them more feasible, less expensive and more

[5] NIAID Paylines. Retrieved from https://www.niaid.nih.gov/grants-contracts/niaid-paylines.

responsive to current needs interfacing between clinical care and public health, especially for communities furthest from the benefit of cutting-edge medicine.

Like for industry (see above), what is needed is strategic planning and a thorough review of the research infrastructure, strengths and weaknesses of a given entity, opportunities for making an impact and mechanisms to cast the widest net to include all stakeholders who wish to participate and bring important skills.

Organizing NIH for Success

Statutory Structure and Functions

3. ***In your view, could NIH research dollars be better allocated within the agency's portfolio? Are there certain areas of research that are over-funded or under-funded? What strategy should Congress and NIH take in allocating resources to specific areas?***

IDSA and HIVMA believe that early career funding should be more broadly available to build the ID and HIV research workforce pipeline. Currently, early career grants are too competitive and are often given to more experienced researchers, while early career physician-scientists apply multiple times over several years before successfully receiving funding, with some leaving the field altogether because of difficulty securing funding.

In addition, IDSA and HIVMA support **$7.060 billion, including $608 million for antimicrobial resistance research at NIAID,** to spur ID research and secure its future by:

- Enhancing basic, translational and clinical research on resistance;
- Supporting training of new investigators to improve ID research capacity;
- Expanding clinical trial infrastructure to boost preparedness, therapeutics, vaccines and diagnostics;
- Developing a clinical trials network to reduce barriers to research on difficult-to-treat infections;
- Focusing on pragmatic research and implementation science to get clinical innovations into health care and the populations with least access.

We also support **$3.673 billion for HIV research** across NIH centers and institutes to continue the biomedical research and infrastructure that is the foundation for the diagnostic, treatment and preventive interventions available today for HIV (including achieving the goal of ending the HIV epidemic) as well as other health threats, including cancer, hepatitis C and emerging infectious diseases.

Decreases in NIAID funding would devastate our ability to respond to current and future infectious diseases threats and prevent us from achieving the goal of ending the HIV epidemic and addressing emerging infectious disease threats.

8. ***Please evaluate the success of NIH's public-private partnerships to date, such as the Partnership for Accelerating Cancer Therapies (PACT), Accelerating Medicines Partnership (AMP), Helping to End Addiction Long-Term (HEAL) Initiative and Accelerating COVID-19 Therapeutic Interventions***

and Vaccines (ACTIV). Do you see any differences in their effectiveness? If yes, what attributes do you believe make a public-private partnership more or less successful?

As discussed above, the ACTIV initiative was an important step forward by investing in multiple research approaches simultaneously, which allowed successful interventions to be identified much faster than using more traditional research methods. A successful public-private partnership requires investment from both sides and the ability to change direction nimbly based on promising scientific discoveries. One issue that needs to be addressed is intellectual property that results from research in such partnerships. While private companies typically have the capacity to provide significant funding for research, they also usually require ownership of the resulting data at the longer-term expense of the academic researchers and universities. Ensuring co-ownership of the results of such partnerships is key to their future success. In addition, greater NIH funding of clinical trials would help to ensure ownership of results by researchers, incentivizing greater involvement by physician-scientists.

Improving Transparency and Oversight

4. ***Would increasing audits and other oversight mechanisms have an overall positive or negative effect on the conduct of research?***

IDSA and HIVMA feel that responsible oversight of federally funded research must allow the ability for the U.S. to continue its leadership role in ID and HIV research. We anticipate that the updated NIH Grants Policy Statement, Section 15.2, regarding foreign grant recipients may place undue administrative burdens on the researchers, which could jeopardize essential international scientific collaboration. Global cooperation is critical to the study of ID as well as the prevention of, preparedness for and responses to outbreaks and pandemics.

IDSA and HIVMA urge NIH to continue to seek stakeholder input on this important topic. Policies with such a substantial impact on the scientific community require consultation among a broad array of stakeholders and should involve sufficient time for dialogue on intended and unintended impacts. IDSA and HIVMA recommend that NIH provide additional opportunities for stakeholders to give input, including listening sessions, prior to finalizing this proposed policy.

Additionally, scientific research on topics like gain of function is especially at risk of being stifled by stringent audits and oversight. This research is essential because it can help us understand potential human-pathogen interactions, assess their likelihood of emerging in a pandemic and inform preparedness efforts, including surveillance and developing medical countermeasures. While such research is inherently risky and requires strict oversight, there is also risk if it is not supported, leaving us unprepared for the next pandemic.

Undue oversight can dissuade researchers from pursuing these topics despite their importance in pandemic preparedness, vaccine development and medical countermeasure research. It is important to balance responsible oversight and a focus on biosafety practices with an environment wherein critical research is supported. In February 2022, the U.S. government charged the National Science Advisory Board for Biosecurity (NSABB) — which is comprised of members with significant expertise in science, research methodology, biosecurity and bioethics — with reviewing policies governing gain of function research and dual-use research of concern. IDSA and HIVMA support the work of NSABB to facilitate the

advancement of science with improved and appropriate guardrails. We encourage the HELP Committee to continue working with the scientific community to determine what policies or investments may be useful to help implement their recommendations.

In conclusion, existing threats and emerging diseases with pandemic potential require a ready workforce that can be mobilized to rapidly provide innovative research and solutions to protect the public. IDSA and HIVMA welcome continued collaboration on developing these important topics. If you have questions about these comments or would like to connect, please contact Eli Briggs, IDSA director of public policy, at ebriggs@idsociety.org, or Andrea Weddle, HIVMA executive director, at aweddle@idsociety.org.

Sincerely,

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President, IDSA

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