



**Association of
American Medical Colleges**
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July 19, 2021

The Honorable Diana DeGette
U.S. House of Representatives
Washington, DC 20515

The Honorable Fred Upton
U.S. House of Representatives
Washington, DC 20515

Dear Representatives DeGette and Upton:

On behalf of the Association of American Medical Colleges (AAMC), thank you for your bipartisan, longstanding leadership on legislation to promote, develop, and deliver more cures, therapies, diagnostics, and preventive interventions to patients, families, and communities. We appreciate the opportunity to respond to your June 22nd Request for Information (RFI) on the Advanced Research Projects Agency for Health (ARPA-H) proposal as part of your 21st Century Cures 2.0 discussion draft (for ease of reference, we are submitting separate comments on other components of the discussion draft in another letter).

The AAMC is a not-for-profit association dedicated to transforming health through medical education, health care, medical research, and community collaborations. Its members are all 155 accredited U.S. and 17 accredited Canadian medical schools; more than 400 teaching hospitals and health systems, including Department of Veterans Affairs medical centers; and more than 70 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools and teaching hospitals and their more than 179,000 full-time faculty members, 92,000 medical students, 140,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences.

AAMC-member institutions are major centers of cutting-edge medical research, with scientists and clinicians at medical schools and teaching hospitals conducting over 50% of extramural research funded by the National Institutes of Health (NIH). These anchor institutions foster an environment of discovery that has laid the scientific groundwork for nearly every major medical intervention in practice today – including transplants, immunotherapies for cancer, laparoscopic surgery, the currently authorized COVID-19 vaccines, and countless other diagnostics, medications, vaccines, and other countermeasures – and that continues to promote the latest advances in medicine.

In addition to their integral role in advancing discovery, our members provide the world's most advanced and expert patient care informed by the latest innovations in fundamental and clinical research. In partnership with their physician faculty from affiliated medical schools, AAMC-member teaching hospitals represent 5% of all hospitals but provide 25% of the nation's medical and surgical intensive care beds, 36% of cardiac intensive care beds, 61% of pediatric intensive care beds, 98% of comprehensive cancer centers, and 69% of all Level 1 Trauma Centers. Our members are well established and respected regional referral centers and centers for tertiary care. They also provide treatment for a disproportionately high percentage of Medicare and Medicaid beneficiaries, as well as for those who are uninsured.

In other words, our member academic medical centers not only play a fundamental role in creating the breakthroughs of the future, they also are actively putting such innovations into practice for a diverse array of patients. Their seat at this nexus of research and care delivery gives the experts internally at AAMC and at our member medical schools and teaching hospitals a unique perspective both on the urgency with which patients and their providers seek new and more effective treatments, as well as the challenges and opportunities to accelerate our progress. We have drafted our comments to the ARPA-H RFI through this lens.

In particular, we wish to emphasize the importance of ensuring that the establishment of ARPA-H would complement and would not detract from the NIH as it is currently configured. We are grateful for the longstanding, strong bipartisan support for NIH in Congress, including in the fiscal year (FY) 2022 spending bill recently approved by the House Appropriations Committee, and that the President's FY 2022 budget request also proposes a bold funding level for NIH overall. Through ongoing, robust support for the foundational work that NIH funds at academic medical centers and other laboratories across the country, scientists can continue to gain ground against daily and emerging health threats facing patients, communities, and people everywhere. The President's proposal – including the establishment of ARPA-H – holds the potential to be truly transformative in driving medical and health advances, but only if coupled with a reliable and substantial commitment to the fundamental basic science work that has been the basis for every major breakthrough improving the lives of patients around the globe.

While healthy growth in NIH as it is currently configured is necessary to achieve the goals of ARPA-H, many stakeholders also have acknowledged that there is opportunity to fill voids unmet by NIH's current authorities and practices. As lawmakers and the Administration consider how ARPA-H might supplement and build upon the work currently supported by NIH, we urge you to keep in mind the principles underlying the scientific processes that have served the NIH as the world's gold standard for decades.

For example, many have expressed an interest in expediting decision-making regarding which research projects to fund, prompting proposals to bypass peer review of individual projects at ARPA-H in favor of approvals from ARPA-H project managers. To facilitate the success of such an approach and promote an appropriate level of oversight, the AAMC recommends establishing a committee that would have the authority to review portfolios at 6- or 12-month intervals and to evaluate progress on the selected projects. This recommendation would enable ARPA-H project managers with primary discretion with respect to funding decisions, reflecting the cultural reforms and efficiencies that many have suggested for the new initiative; at the same time, it also would offer the opportunity for staff to benefit from the diversity of expertise within academics and industry and for ARPA-H to offer assurances to lawmakers and the public that the necessary "checks" are in place to ensure resources are being expended wisely.

In addition to the recommendations outlined above, we are pleased to respond to the specific questions in the RFI. We welcome the opportunity to continue engaging with you as we gather input from leaders at our member institutions and proposals around ARPA-H become more refined.

In calling for the creation of ARPA-H, President Biden has cited the success of the Defense Advanced Research Projects Agency (DARPA) and expressed his belief that ARPA-H should be similar. Please provide specific details on which aspects of DARPA ARPA-H should replicate and why this would lead to similar success.

Ideally, ARPA-H will leverage the greatest strengths of both the ARPA model (as seen in DARPA and ARPA-Energy) and the NIH as it is currently configured. For example, adopting the DARPA approach of appointing a term-limited director and program managers presents an opportunity to regularly promote new ideas and vantage points within ARPA-H. The inclusion of program managers from different sectors who can bring expertise outside of the biomedical sciences also could facilitate the development of novel approaches to bear upon challenges in health. With the appropriate talent, oversight, and input (as we discuss further below in response to the question regarding transparency), ARPA-H could offer new avenues for broaching impactful and novel research projects that cannot be achieved elsewhere, including under NIH's current configuration, by empowering these program managers to oversee high-risk, high-reward projects in a similar fashion to other ARPAs.

At the same time, it is important to recognize that the DARPA model is not perfectly applicable to all opportunities in biomedical research. The largest shortcoming to an analogy between DARPA and ARPA-H is the timelines. Many biomedical research projects require a much longer time commitment to reach meaningful milestones relative to work on engineering projects and defense work. To fulfill their purposes most clinical trials are inherently slow. Opportunities to expedite such work safely through policy or process changes are marginal, the COVID-19 experience notwithstanding.

For ARPA-H to be successful, the expectations for the new initiative must be realistic about these limitations. Rigid project timelines that are grounded in the experience of the physical sciences will be counterproductive. The dynamic nature of biomedical science suggests that there should be some level of elasticity built into the goals. Defining appropriate milestones will be important in determining reasonable expectations for projects' (and the initiative's) success – if the goal is to deliver a tangible “product” to patients on an accelerated timeline, it will be important to consider the impact of barriers beyond the auspices of NIH and ARPA-H, such as liability concerns and the challenge of meeting meaningful clinical endpoints.

An additional consideration as you evaluate the utility of the DARPA model is how best to promote diversity, equity, and inclusion. Countless studies have shown that diversity across multiple dimensions enriches science. The AAMC strongly supports efforts NIH has implemented in recent years to improve diversity, equity, and inclusion within the biomedical research workforce, including policies to promote gender parity, the recently launched UNITE initiative to address structural racism, and programs that enhance the geographic distribution of our nation's medical research infrastructure. The nature of the DARPA model concentrates eligibility for resources on a limited pool of investigators. If such a model is replicated at ARPA-H, it will be critical to understand the impact on the workforce.

Likewise, identifying strategies to support the research pipeline will also be key. The time-limited nature of ARPA projects does not facilitate training opportunities, and it is not clear that early-stage investigators will be well-positioned to compete in such an environment.

To ensure it has the biggest impact, on what activities or areas should ARPA-H focus? What activities or areas should ARPA-H avoid?

The activities and areas of ARPA should be decided through consultation with the experts in the scientific and health communities, as well as other federal agencies and sectors. The areas of focus should be responsive to the greatest unmet needs in health, as well as taking into consideration projects that are high-risk, require an interdisciplinary or multi-sector approach to succeed, or those that need a “last-mile” effort for completion that has not been achieved through traditional approaches.

Because proposals to date have emphasized time-limited projects as a core characteristic of ARPA-H, the initiative likely will have the greatest success in advancing projects like diagnostics, treatment modalities using devices, potentially vaccines (because of the ability to use biological markers like antibody levels). In contrast, drug development is typically a multi-year process. This lengthy, slow process is not just the result of NIH peer review; industry does no better at speeding drug approvals. The process is inherently deliberate out of necessity. While we recognize and support the need to pursue bold, ambitious new targets to defeat cancer, diabetes, Alzheimer’s, and other specific threats, we note that the ARPA approach may be most impactful in advancing platforms and technologies with applicability across science.

Some assert ARPA-H’s ability to operate independently and transparently will be essential to its success. Do you agree? If so, what is the best way to design ARPA-H in order to accomplish this?

ARPA-H should retain a balance of independence in its structure and decision-making within the government, but it also should be responsive to external consultation from the broader research community. As described above, developing an external committee of scientific and other experts to assess annually or semi-annually the viability of projects underway not only will enhance oversight of the initiative, it also will strengthen the scientific rigor. Such a panel will grant the ARPA-H director and program managers primary responsibility for driving the initiative’s agenda and permit ARPA-H to operate nimbly, while also helping to prevent ARPA-H from being isolated from the breadth of expertise beyond awardees and federal scientists. ARPA-H should also be transparent throughout the lifecycle of a project, including its process for hiring program managers and defining areas of interest, the review process and makeup of reviewers, and the milestones expected at certain points in the research timeline.

How should ARPA-H relate to, and coordinate with, existing federal entities involved in health care-related research and regulation?

The fundamental research being conducted by the NIH should play an essential role in informing the work of ARPA-H. The outputs of NIH-funded research are a fundamental starting point for our understanding of health and disease, and coordination between NIH and ARPA-H will be very effective in identifying gaps in our understanding or the most pressing challenges we face. Other avenues of collaboration include the Food and Drug Administration, Centers for Disease Control and Prevention, and Centers for Medicare and Medicaid Services, to ensure that ARPA-H is tackling issues along the spectrum of health, to include population health and care delivery. Coordination with other federal agencies also will help guard against unnecessary duplication of work, ensuring instead that ARPA-H is building upon existing internal and extramural research.

What is the best way to ensure ARPA-H has a mission, culture, organizational leadership, mode of operation, expectations, and success metrics that are different than the status quo?

The creation of ARPA-H and its organizational structure and function should be an evidence-based process that looks at the specific gaps and challenges in the current health ecosystem. The utilization and implementation of a strong evaluation process as well as clearly defined metrics of success will be key factors in supporting ARPA-H's ability to complete projects outside of current capabilities. Along with all of these factors, we would like to emphasize the importance of equity and inclusion in the ARPA-H mission, in the way the organization is created, how program managers are selected, and which projects ARPA-H undertakes.

How should ARPA-H work with the private sector?

The greatest potential in ARPA-H is to enhance collaboration between industry and academia by catalyzing partnerships that leverage the expertise and assets of both entities. The private sector can bring key expertise to the work of ARPA-H, particularly in recognizing the potential of the health and technology nexus and opportunities for bringing new products to market/ensuring that products developed are usable and scalable. Academic medical centers offer incomparable practical knowledge with respect to patient populations and datasets, health care operations, and foundational science. Many AAMC-member institutions have experience with this model of collaborations between academia and industry, and creating additional environments and opportunities for both entities to partner on high-risk, high-reward projects through ARPA-H can help streamline an otherwise inefficient and clumsy process where cultural differences and knowledge gaps of one entity about the other have the potential to stall progress.

What is the appropriate funding level for ARPA-H? How do we ensure ARPA-H funding does not come at the expense of traditional funding for the National Institutes of Health?

It will be critical to ensure that Congress provides any funding for ARPA-H through a separate stream that supplements the funds for the NIH's base, and that the budget for NIH remains on a stable path of above-inflation growth, as Congress wisely has ensured for the last six years. As noted above, ongoing investment in NIH-supported basic research forms the building blocks of our understanding of health and disease and will allow ARPA-H to contribute to the work of translating discoveries into innovative strategies for prevention, treatments, and cures. With NIH currently only able to fund roughly 1 in every 5 proposals it receives – even with Congress's extraordinary support in recent years – we are unquestionably bypassing potentially transformative science simply as a function of our current investments in the NIH's base.

Establishing the appropriate firewall to avoid diverting resources from core NIH functions will be critical to prevent erosion in support for the fundamental science underlying ARPA-H's success. A distinct funding approach for ARPA-H also would allow lawmakers and the Administration the flexibility to make adjustments to the initiative in future years as necessary, without affecting NIH's base. The mission and estimates of associated expenses to achieve that mission should drive the funding level for ARPA-H.

The AAMC greatly appreciates the bold funding level in the FY 2022 spending bill approved July 15th by the House Appropriations Committee for the NIH overall. The spending bill includes robust growth in NIH's core functions across the agency, while also providing a solid foundation to establish ARPA-H in its first year. Striking this balance to ensure robust growth in NIH's base in

tandem with any investments in ARPA-H moving forward should continue to be a top priority, and we encourage you to work with appropriators to identify the optimal mechanisms to achieve this shared goal.

Thank you for considering these perspectives as you move forward with the Cures 2.0 process. We look forward to working with you, your colleagues, and the administration to fulfill the goals of ARPA-H and our shared commitment to innovation and scientific discovery.

Sincerely,

A handwritten signature in black ink that reads "Karen Fisher". The signature is written in a cursive, flowing style.

Karen Fisher, JD
AAMC Chief Public Policy Officer