Intent on bolstering the “Beau Biden Cancer Moonshot” of the 21st Century Cures Act, President Biden has been advocating for an Advanced Research Projects Agency for Health (ARPA-H) within the US National Institutes of Health (NIH). The mission of ARPA-H would be to “drive transformational innovation in health research and speed application and implementation of health breakthroughs.” Were ARPA-H to materialize, it would constitute the second and only federal advanced research agency established since the 1958 founding of its namesake, the Defense Advanced Research Projects Agency (DARPA). In support of this high-risk and high-reward initiative, the President’s fiscal year 2022 discretionary budget request calls for the appropriation of $6.5 billion.

Coming on the heels of the rapid sequence development of the SARS-CoV-2 mRNA vaccines, ARPA-H may no longer be dismissed as a pipe dream. Instead, as the COVID-19 pandemic has proven, the combination of commitment, resources, and talent can markedly accelerate the translational pace of fundamental discoveries. In this Viewpoint, we review the mission of ARPA-H, explore its overlap with the NIH, consider its congressional reception, and discuss its likely legislative vehicles.

Advancing ambitious translational goals for health will doubtlessly require a distinctive culture and an organizational structure that is performance-based, milestone-driven, and timeline-sensitive. The vetting of potential innovative projects by ARPA-H will not be the domain of academic peer reviewers as is the custom at the NIH. Instead, funding decisions will be made by experienced term-limited ARPA-H program managers. Commitment of applicants to teamwork, collaboration, and interdisciplinarity are likely to be especially prized. Successful investigators spanning academia, not-for-profit organizations, industry, and other governmental agencies will be rewarded with contracts subject to ongoing scrutiny. Promising “blue sky” ideas worthy of funding will have the potential to transform entire areas of medicine and health beyond what is immediately realistic or attainable. Often large in scale, these bold, high-risk projects stand to give rise to new high-payoff technologies and therapies. As articulated by Collins and colleagues, ARPA-H, modeled after its intrepid namesake, DARPA, is to “accelerate biomedical breakthroughs” and by so doing, “shape the future of health and medicine.”

The ultimate success of ARPA-H will require that the program be afforded authority and independence, that managers be allowed to fail, that research targets be chosen wisely, and that the technologies developed be commercialized by industry. Moreover, success will require that “program managers can wander intellectually and follow their noses, but not so broad that you try to boil the ocean.” Going forward, ARPA-H will be assisted by a federal advisory panel entrusted with facilitating interagency coordination and idea generation.

As envisioned by the Biden administration, ARPA-H would be a semi-autonomous entity within the NIH and the US Department of Health and Human Services. Were ARPA-H to be established as a stand-alone NIH institute, it would constitute the 22nd such construct. Either way, ARPA-H “will complement NIH’s existing research portfolio, providing an agile and flexible arm to advance biomedical science quickly and robustly.” How the health-transforming portfolios of ARPA-H and the NIH are to be harmonized remains to be determined, as noted by the Congressional Research Service. The Common Fund of the NIH, a bench-to-bedside portfolio of high-risk innovative endeavors with the potential for extraordinary influence is a case in point. Yet another example of potential interagency overlap is with the National Center for Advancing Translational Sciences, which is focused on innovation in medical product development. The Accelerating Medicines Partnership...
of the NIH must also be considered in this context. A public-private partnership intent on transforming the current model for developing new diagnostics and treatments, the Accelerating Medicines Partnership is comprised of the US Food and Drug Administration, multiple biopharmaceutical and life science companies, and not-for-profit organizations. Finally, consideration would have to be given to the overlapping reality of DARPA-funded biotechnology projects that are to be carried out at the NIH.

As suggested by the Congressional Research Service, Congress would do well to carefully deliberate the prospect of establishing ARPA-H. Congress may also choose to use this opportunity to reexamine the role that the federal government should play in the commercialization of biomedical products. While some have suggested it might be better for Congress to increase support to NIH or other existing programs rather than build ARPA-H, it is important to recognize that the DARPA model is really a very different undertaking, for better and worse. DARPA is well-known for its fail fast mentality, which encourages successive “acid tests” so that its managers can make cutthroat decisions about how to balance a relatively small dollar portfolio of projects and when to stop investing. While this approach may be well suited for some health care innovations in which disruption is key, many high-value health goals may require longer evaluation and incubation periods. A somewhat different issue is that DARPA traditionally does not take intellectual property or other returns on its initial investment or push for ethical licensing. Debates regarding intellectual property, trade secrets, and global access to COVID-19 vaccines suggest that this may be an element of the DARPA model that could use some tweaking. There is also the question of how to measure success or failure and adjust course if needed. Needless to say, the government can always choose to cease funding ARPA-H if it falls short, but the political reality is that withdrawing support may be easier said than done. For this reason, it is worthwhile for leaders to formulate and publicly commit to appropriate metrics for measuring the success of ARPA-H.

If Congress votes to support the establishment of ARPA-H, they will have to consider which legislative vehicle is best suited for the purpose. One possible vehicle is the Elijah E. Cummings Lower Drug Costs Now Act (HR 3), Title VII, which provides specific funds for innovation projects at the NIH. Similar considerations might apply to the Endless Frontier Act (HR 2731), which seeks to strengthen “U.S. leadership in critical technologies through basic research in key technology focus areas,” as well as the commercialization thereof. The language for ARPA-H is likely to be included in the Cures 2.0 Act being cosponsored by US Representatives Diana DeGette (Democrat from Colorado) and Fred Upton (Republican from Michigan).

It was in June of 2019, at a campaign stop in Iowa, that then-presidential candidate Biden first mentioned the prospect of an ARPA-H. Making a pledge to a crowd of supporters, Mr. Biden said, “If I’m elected president, you’re going to see the single-most important thing that changes America. We’re gonna cure cancer.”

At the time of this writing, the realization of this vision remains a work in progress. The draft of the Cures 2.0 bill, the most likely legislative vehicle for ARPA-H, has yet to be formally introduced to Congress. Notably, however, the Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 2022 (HR 4502), home to $3 billion in ARPA-H funding, passed the US House of Representatives on July 29, 2021. If it becomes a reality, ARPA-H will focus on time-limited projects that are intent on “revolutionizing how we prevent, treat, or cure a range of diseases, including cancer, infectious diseases, Alzheimer’s disease, and others.” Stated differently, ARPA-H will “focus on solving practical problems that foster breakthroughs to serve patients equitably.” All indications are that ARPA-H will make a substantial difference in the creative and scientific energy of the nation. It is a change whose time has come.
ARTICLE INFORMATION

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REFERENCES