Creating the Health Advanced Research Projects Agency (HARPA)

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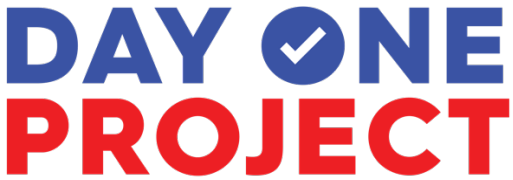

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Summary

The federal government can directly address the massive market failures at the center of our healthcare enterprise by establishing a new Health Advanced Research Projects Agency (HARPA)[1] modeled after the Defense Advanced Research Projects Agency (DARPA)—the agency the Department of Defense uses to build new capabilities for national defense.

The need for HARPA is twofold. First, developing treatments for disease is difficult and time consuming. HARPA will provide the sustained drive needed to push through challenges and achieve medical breakthroughs by building new platform technologies. Second, the U.S. healthcare system largely relies on the private sector to leverage national investments in basic research and develop commercially available treatments and cures. This model means that diseases for which investments are risky or downstream profit potential is low are often ignored. HARPA will step in where private companies do not, addressing market failures with direct investments that ensure that all patients have hope for a brighter future.

HARPA will leverage existing basic science research programs supported by taxpayer dollars, as well as the efforts of the private sector, to develop new capabilities for disease prevention, detection, and treatment and overcome the bottlenecks that have historically limited progress. To do this, we have to think and act differently about how we address human health challenges. HARPA would support research that directly affirms, refutes, or otherwise changes current clinical practice. It would do this using milestone-driven, time-limited contracts as the central mechanism for driving innovation. This will ensure efficiency, transparency, and optimize success.

1. Challenge and opportunity

Every year, the United States spends more than $3.4 trillion on healthcare and tens of billions of dollars on biomedical research. Yet we only have treatments for around 500 of the approximately 10,000 known human diseases.[2] 30 million people in the United States—half of whom are children—suffer from a rare disease for which no treatment has yet been developed.[3] There are no ongoing efforts to develop treatments or cures for the overwhelming majority of these diseases. That massive market failure is the big secret

[1] Development of the HARPA concept was supported by the Suzanne Wright Foundation. More information about this concept can be found at https://www.suzannewrightfoundation.org/harpa/ and https://www.harpa.org.

[2] Milken Institute, "Faster Cures", n.d., https://www.fastercures.org/about/fastercures/.

[3] Genetic and Rare Diseases Information Center, "FAQs about Rare Diseases", National Center for Advancing Trannslationnal Sciences, U.S. Department of Health & Human Services, n.d., https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases.

of the biomedical research enterprise and is simply unacceptable. We need bold action to correct this massive market failure and revolutionize how we attack disease.

In 1958, the United States created the Defense Advanced Research Projects Agency (DARPA) at the Department of Defense. This new government agency was designed to make pivotal investments in breakthrough technologies for national security and directly address market failures that were impeding innovation. The establishment of DARPA launched a new era in defense innovation that led to countless innovations, including the Internet, stealth aircraft, GPS-based precision navigation, night vision, autonomous vehicles, speech recognition, and robotic prostheses.

We need to take the same aggressive entrepreneurial approach to health innovation as we have in protecting our nation from foreign threats. Creating a new Health Advanced Research Projects Agency (HARPA) would fundamentally transform the way the United States approaches treating the majority of human diseases, and would directly address many of the shortcomings of our healthcare and biomedical research systems.

Imagine being able to predict and intervene before someone has a mental health crisis; diagnose cancers at their earliest stages when treatments are most effective; end deaths from antibiotic-resistant bacterial infections; and provide treatments for rare genetic diseases. That is the promise of HARPA.

By applying the same tools that DARPA uses to develop new capabilities for defense (Section 3), HARPA would be engineered to close the gap between basic research and real-world needs. HARPA initiatives would target the diseases that affect millions of Americans but are going unaddressed because of risk aversion and short-term, perverse incentives in academia and the private sector. These initiatives would be funded through large milestone-driven timeline limited contracts needed to take on transformational projects, and would be led by top experts recruited for focused stints at the agency. The result will be an institution designed from the ground up to finally solve the most pressing healthcare issues of our time: skyrocketing drug prices, the tragic shortcomings of our mental-health support systems, the opioid crisis, unconscionable waiting lists for organ donations, medical errors, and many more. DARPA enabled the United States to lead the world when it comes to defense innovation. HARPA will do the same for healthcare.

2. Function and structure

2.1 Function

Federal funding for medical research is primarily allocated though the National Institutes of Health (NIH). Through its $41 billion annual budget, NIH funds basic science and

clinical research through grants. Grants are typically awarded to individual projects at academic institutions. Collectively, these projects form the bedrock of our knowledge about biology, health, medicine, and disease.

Importantly, NIH is not designed to develop marketable disease treatments or cures or to develop new platform technologies that are intended to revolutionize medicine. NIH funding is used to support therapeutic and technology development, but not in a way that prioritizes quick, efficient commercialization of new discoveries. Moreover, NIH does not include a mechanism for ensuring commercialization. SBIR grants flail at the challenge of commercializing innovations with woefully inadequate funding. Simply put, the current path from NIH-funded basic science to applied research to viable commercial product is too slow, and it does not address massive market failures that define health research and development today, leaving many human diseases without dedicated efforts to uncover solutions. Funds for basic science and clinical research through grants—awarded to academic institutions that pursue particular, individual interests in discovery—are great for uncovering truths about biology, but are an extremely inefficient way to drive toward therapies that make their way into the clinic.

Private companies, on the other hand, only scale up and market economically viable therapies. Therapies that are potentially effective but have a limited market remain inaccessible to the public at large or come with astronomical price tags that patients simply cannot afford.

Effectively bringing new innovations to the market requires alternative approaches to the bottom-up grant funding common to NIH programs. Again, this is not to say that the NIH dollars are poorly spent. The dollars spent on research are essential to understanding health and disease. But an alternative model is needed to advance research toward the development of necessary technologies and treatments to cure disease.

HARPA would close these gaps. Just as NIH brings federal resources to bear on basic science and early-stage research, HARPA would bring federal resources to bear on applied science and later-stage development and deployment. HARPA would have three guiding functions:

(1) **Launch and manage large-scale health-research initiatives.** Although multiple federal entities[4] work on health research, there is little coordination among these

[4] Including NIH as well as the Department of Health and Human Services, the Department of Veterans Affairs, the Environmental Protection Agency, the Food and Drug Administration, the National Science Foundation, and others.

entities regarding research priorities, activities, or progress. HARPA would work with these entities—as well as with the private sector, academia, and states and localities—to launch and carry out targeted, multi-stakeholder research initiatives aimed at our most pressing underserved health challenges. Using milestone driven and timeline limited funding contracts, HARPA will be able to ensure rapid continuous progress. These initiatives would integrate the diverse capabilities of participating institutions to make real progress on persistent and pressing health problems.

(2) **Invest in transformational platform technologies.** HARPA's focus will be on projects that have direct impact on clinical care. Basic science tends to advance methodologically and incrementally. This partly reflects the nature of the field (one set of experiments informs the next) and partly reflects the nature of incentives in academia (moving too far and too fast away from an established knowledge base decreases the likelihood of publishable findings). By contrast, HARPA will only support transformative research that will substantially improve clinical practice and this is how potential impacts will be evaluated. Pushing for such platform technology breakthroughs is a high-risk, high-reward enterprise. HARPA will focus on the uncertain but potentially transformational medical technologies and therapies that tend to go underfunded today.

(3) **Support development of treatments and cures for *all* diseases.** All taxpayers contribute to federally funded medical research. But not all taxpayers reap the benefits. Relying on the private sector to bridge the gap between basic research and commercially available products means that those with rare or difficult-to-treat diseases are often ignored. HARPA will correct this market failure by supporting development of treatments and cures for *all* diseases—especially those that are being neglected by the existing healthcare ecosystem.

2.2 Structure

HARPA would be modeled on DARPA. DARPA is considered the "gold standard" for innovation and accountability within the federal government. DARPA is also distinct from other federal agencies that fund research and development in that it is focused on *building capabilities* rather than simply *advancing knowledge*. This unique mission requires DARPA to have a unique set of attributes and operating principles, including the following:

- **Contracts large enough to provide a critical mass of funding.** While most federal grants for academic research are on the order of tens to hundreds of thousands of dollars annually, DARPA funds projects at $1–$5 million per year. These large

contracts enable DARPA affiliates to pursue goals that would simply be out of reach at lower funding levels.

- **Minimal bureaucracy.** DARPA's entire staff consists of about 220 government employees. This includes DARPA's ~100 program managers (PMs), who collectively oversee about 250 research & development projects funded at total of about $3 billion per year. All actual research and development activities are conducted by public, private, and academic affiliates. DARPA's small staff size and flat organizational hierarchy makes the agency effective and nimble, able to move quickly on priority issues in a limited amount of time. Moreover, the fact that DARPA is not organized around disciplines allows PMs to pursue unconventional but productive cross-disciplinary collaborations.
- **No entitled constituencies.** While funding from other federal grant programs may only be accessible to certain recipient classes (*e.g.*, academic institutions), DARPA does not predetermine which types of institutions are eligible for funding. Funding projects at a wide variety of institutions—including universities, national labs, public and private companies, state and local government agencies—enables DARPA to access the full breadth of talent, expertise, ideas, and resources that the nation has to offer. For example, DARPA funding in the start-up community has yielded advances that may have been difficult or impossible to achieve in other sectors. DARPA uses flexible procurement tools like "Other Transaction Authority" to make it easy for small businesses and nontraditional defense contractors to participate in the agency's initiatives.
- **"Portfolio approach" to high-risk, high-reward efforts.** DARPA understands and accepts that frequent failure is the price of success when it comes to achieving transformational breakthroughs. DARPA PMs have the resources and authority to invest in multiple approaches to a given goal. DARPA proposals are openly competed, but PMs can strategically select the winners in a way that creates a diversified, risk-mitigating project portfolio.
- **Government control of contracts.** DARPA negotiates contracts that enable control over performance. Contracts specify milestones and "go/no-go" decision points to ensure that scientific progress is made in an efficient and timely manner. This enables PMs to better manage funded projects and to cut funding if a project is not yielding desired results.
- **Top-notch talent.** DARPA attracts world-class PMs recruited from academia, industry, and government agencies. DARPA benefits from expedited direct hiring authority for science and engineering experts.
- **High turnover.** PMs are hired for limited stints (generally 3–5 years), and there are no career PMs. This approach keeps DARPA talent fresh—ensuring that the agency is scientifically current and flexible to new avenues of investigation—and

fuels an urgency for PMs to "achieve success in less time than might be considered reasonable in a conventional setting."[5]

Many, if not all, of these characteristics could be carried over to HARPA. HARPA could also adopt DARPA's funding-management model. Under this model, all funding allocations would be left to the discretion of the HARPA Director while all funding oversight would be entrusted to HARPA PMs. Funds would be awarded as milestone-driven contracts that give PMs the capacity for early termination if a particular project is not yielding desired results. This almost never happens with traditional federal grants for research and development.

Because HARPA will differ in structure and function from traditional research-funding agencies, it is sensible for HARPA to have a reporting chain of command separate from NIH. We believe that HARPA would be best situated directly under the Secretary of Health and Human Services (HHS) or under the HHS Assistant Secretary for Health. The Biomedical Advanced Research and Development Authority (BARDA) provides precedent for placement directly under the Assistant Secretary for Preparedness and Response.[6]

3. Path to establishment

HARPA could be established under existing authorities, but, ideally, would be established through authorizing legislation and new appropriations. There are several steps the federal policymakers could take to kick-start the establishment process. First, the president could issue a Memorandum or Executive Order directing the HHS Secretary to develop a blueprint for HARPA's establishment as well as a strategic plan for HARPA's activities. These documents would include identification of priorities and goals; analysis of global markets, policies and production capabilities; structure and accountability; and initial funding recommendations. Ideally, they would be developed by a short-term Federal Advisory Committee (FAC)—comprised of top physicians, health researchers, and innovative thought leaders. It is important that the FAC include avenues for external input, including providing and promoting a public comments period and

[5] Defense Advanced Research Projects Agency, "About DARPA," U.S. Department of Defense, n.d., https://www.darpa.mil/about-us/about-darpa.

[6] After the anthrax attacks of 2001, Congress responded by creating BARDA, a new agency focused on the threat of biological, chemical, and nuclear terrorism. BARDA is responsible for procuring and developing countermeasures principally against bioterrorism, but also against chemical, nuclear, and radiological threats; pandemic influenza, and urgent health threats like antibiotic resistance and Ebola. BARDA could have been established within the Department of Defense or NIH, but Congress recognized that it would have to function differently than those agencies. BARDA was established to serve the needs of the American people, not just the military, and to focus on targeted threats, not just basic research. Congress therefore placed BARDA within HHS under the Office of the Assistant Secretary for Preparedness and Response.

convening stakeholder for a across the country. After these documents are developed, the president could urge Congress to deliver a bill establishing HARPA.

Alternatively, the [resident could include funds for HARPA in an annual budget proposal under the Assistant Secretary for Health or Assistant Secretary for Preparedness and Response. (If Congress appropriates those dollars, HARPA could be established without authorizing legislation.[7]) We believe that a minimum budget of $100 million for HARPA in its first year and $300 million in its second year would be sufficient to get the agency started and to establish high-impact programs, but to be truly transformational, the agency should ramp up to several billion in research expenditures annually. Throughout this process, the president should use high-profile speeches and events to publicly explain the need for HARPA, and to advocate for its creation.

4. Vision

With a DARPA-inspired structure, HARPA would achieve rapid translation of biomedical discoveries into patient-care capabilities. HARPA's mission and activities would be synergistic—not duplicative or competitive—with existing federal research efforts. In particular, HARPA would use fundamental scientific understanding developed with NIH support as a foundation for developing breakthrough medical advances.

HARPA would operate in a health ecosystem that includes biotechnology, pharmaceutical, and healthcare companies, venture capital and philanthropy, academic institutions, and government and regulatory agencies. HARPA would address two of the most prominent shortcomings of this ecosystem: (1) the aversion to failure that limits the willingness of academics and the private sector to pursue high-risk, high-reward projects, and (2) profit incentives that limit the willingness of the private sector to develop therapies for rare or difficult-to-treat diseases. HARPA would provide the capital and supportive, focused research environment needed for experts from all sectors to demonstrate "proof of principle" for various medical innovations. In doing so, HARPA will drive explosive growth in the number of technologies, treatments, and cures that cross the so-called "valley of death" separating lab-scale insights from commercially available products.

HARPA would focus on developing transformational technologies that fundamentally change the way we do health research and deliver care. By focusing on the development

[7] This is similar to how the Human Genome Project was funded. The National Human Genome Research Institute at the NIH was not authorized until after the Human Genome Project had completed. The project was completed because Congress appropriated dollars annually to the NIH for human-genome research through earmarks.

of tools and technologies to transform the way we approach diseases, HARPA can establish mechanisms that ensure wellness and curing disease are prioritized, while correcting the perverse incentives in the market that limit the country's ability to receive treatment.

There is a rich history of under-funding the development of such technologies even though they are often quickly engrained into the healthcare enterprise, making it difficult to imagine life without them. They enable breakthroughs that even inventors did not anticipate, create entire new fields of research, and often result in Nobel Prizes. They establish jumping-off points and serve as accelerants for progress. Such work is typically high-risk, high-reward and aims to build transformative capabilities rather than incremental discovery-based research that is commonly funded by the NIH. While NIH does a tremendous job of funding basic science and clinical research, HARPA will build new capabilities on the foundation that agencies like NIH and the Department of Veterans Affairs establish through their funding.

For instance, HARPA could drive the following:

- **Technologies that allow clinicians to identify and quantify every protein in a drop of blood,** completely transforming disease diagnosis, health monitoring, and care.
- **A next-generation diagnostic imaging machine** that makes it possible to detect a myriad of diseases at much earlier stages that is substantially cheaper, higher-resolution, and more portable than current MRI machines enabling broader use.
- **A cortical eye prosthesis** that communicates directly with the brain, making it possible to restore sight to the 7 million individuals (including 160,000 veterans) living with a visual disability in the United States.
- **New classes of antibiotics** to fight the enormous international public-health and economic threat posed by antibiotic-resistant bacteria.
- **A series of clinical trials for the most expensive marketed drugs,** aimed at developing alternative treatment regimens to improve outcomes by reducing toxicities while dramatically reducing treatment costs. Such de-escalation studies of marketed oncology drugs have been shown to improve outcomes and dramatically reduce costs to save billions of dollars.
- **A massive effort to repurpose already approved drugs for new applications.** There have only been about 2,400 drugs ever been approved for use in humans. Exploring new applications of drugs that are already known to be safe and effective—instead of only focusing on creation of new drugs—could save billions of dollars on research and development and uncover novel uses for drugs that are already known to be safe and effective for other indications.

5. Beyond health

It has not escaped our notice that the same market and institutional failures that created the valley of death and need for DARPA and HARPA exist in other areas of research and development. Our nation is facing unprecedented challenges associated with climate change and the need to provide a better world for all. We feel strongly that the federal government should establish additional Advanced Research Projects Agencies (ARPAs) to complement the efforts of other federal agencies and the private sector. Doing so would enable the government to take a leadership position in tackling monumental challenges.

We believe that, in addition to HARPA, the nation needs to establish capabilities in agriculture (AgARPA), the environment (EnARPA), and transportation/infrastructure (TARPA). Fleshing out the details for establishing each of these entities should fall upon the White House Office of Science and Technology Policy in coordination with the Office of Management and Budget, the President's Council of Advisors on Science and Technology (PCAST), and the leadership of the appropriate federal agencies. Creating these new capabilities will kickstart new industries, create the jobs of the future, and improve our ability to be better stewards of the Earth. Without them, the nation risks continuing its piecemeal approach to addressing our most pressing challenges, while slipping further behind other nations investing heavily in innovations aimed at solving these global challenges. Establishing ARPA capabilities across the federal government would create a network of forward-thinking agencies prepared to address intractable challenges, while building an extraordinary, lasting legacy.

About the authors

Michael Stebbins is a geneticist and public-policy expert who served as the Assistant Director for Biotechnology in the Obama White House Office of Science and Technology Policy. He is currently the President of Science Advisors, a science and health consulting firm he founded in 2018 to provide science, technology, and public-policy guidance to private companies, philanthropies, and non-profit organizations. While at the White House, Michael's work led to large initiatives across the federal government to address antibiotic resistance, protect pollinators, improve veterans' mental health, increase access to federally funded scientific research publications and data, promote the preferential purchasing of antibiotic-free meats, reform the regulatory system for biotechnology products, drive federal purchasing of bio-based products, and improve the management of scientific collections. Michael previously served as the Vice President of Science and Technology for the Laura and John Arnold Foundation, science advisor to the Obama Presidential Campaign, and on the Obama White House Transition Team. He is the former director of biology policy for the Federation of American Scientists and worked for U.S. Senator Harry Reid and at the National Human Genome Research Institute. Before coming to Washington, he was a senior editor at *Nature Genetics*.

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About the Day One Project

The Day One Project is dedicated to democratizing the policymaking process by working with new and expert voices across the science and technology community, helping to develop actionable policies that can improve the lives of all Americans, and readying them for Day One of a future presidential term. For more about the Day One Project, visit dayoneproject.org.