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ACCELERATING INNOVATION FOR BETTER HEALTH

A MITRE FRAMEWORK SUPPORTING THE PROPOSED ADVANCED RESEARCH PROJECTS AGENCY FOR HEALTH (ARPA-H)

Executive Summary

The federal government has made significant investments in a variety of domains to improve our nation's healthcare ecosystem. These investments have ranged from health information technology and patient-centered outcomes research, to expanded insurance coverage and a ten-year reauthorization of the National Institutes of Health (NIH) that reinforced Congress' ongoing commitment that the U.S. continue to lead the world in funding ground-breaking biomedical research.

Thanks to such federal investments—and a robust commercial biomedical research and development sector—the United States has a strong foundation for rapidly advancing health innovation in ways that benefit all people. President Biden has proposed, in his Fiscal Year 2022 budget,[1] to create an Advanced Research Projects Agency for Health (ARPA H), a proposed agency within the NIH that would accelerate biomedical breakthroughs with "the potential to transform important areas of medicine and health for the benefit of all patients and that cannot be readily accomplished through traditional research or commercial activity."[2]

This report describes the ecosystem improvements that will support ARPA-H's success, and the role that ARPA-H could play in measuring innovation gaps, prioritizing societal needs, and attracting private capital alongside public funding. It outlines specific recommendations for the organization's underlying legal authorities, governance, and coordination of its policies and activities with other federal agencies and nongovernmental sectors. In addition, this report details a biomedical innovation framework, developed by MITRE, that proposes a system-level approach for accelerating biomedical innovation across the Department of Health and Human Services (HHS). Our framework was envisioned to support an integrated, efficient, and equitable health innovation pipeline energized by the federal government—a vision that the emergence of ARPA-H may substantially fill and move in exciting directions. The perspectives offered throughout this paper are informed by MITRE's decades-long experience supporting the Defense Advanced Projects Agency (DARPA's) research and development, operating six federally funded research and development centers (FFRDCs), and investing in MITRE innovation for the public good.

Vision

ARPA-H is established with the appropriate funding, authorities, and cross-agency collaboration priorities to:

- Lead a national conversation about unmet health needs.
- Identify critical innovation gaps and accelerate major biomedical breakthroughs with the support of a biomedical innovation framework.
- Apply federal authorities and resources—and create incentives to align private resources—to encourage the research and development required to generate biomedical breakthroughs that will improve health for all people across the nation.

Authorize Autonomy and Focus on Outcomes

To ensure that ARPA-H can realize this vision, focus the ARPA-H portfolio to consider health equitable outcomes, partnering with the Centers for Medicare and Medicaid Services (CMS) Innovation Center and a broad group of stakeholders to advance multi-payer initiatives to give providers and patients the tools they need to manage care and costs. Authorize ARPA-H with autonomy to establish an independent research agenda, manage a portfolio of projects with milestones and performance measures, and use other transactions authorities to accelerate decision making and optimize use of public funds.

MITRE's System-Level Biomedical Innovation Framework

The MITRE Corporation has designed a framework with recommendations to accelerate health innovation to improve health outcomes for all people using an evidence-based, data-driven process fueled by interconnected electronic health information. These recommendations leverage a framework that describes the critical roles ARPA-H could play to measure innovation gaps, prioritize societal needs, and attract private capital alongside public funding. The recommendations consider the organization's underlying legal authorities, governance, and coordination with other federal agencies and nongovernmental sectors.

1. **MEASURE.** Measure the health innovation ecosystem by developing and applying standardized measures for the health innovation ecosystem, and creating an executive-level dashboard that permits ARPA-H decisionmakers to model the pipeline of health innovations, evaluate scenarios to inform regulatory and funding decisions, and project impact on health outcomes, value, and access.
2. **DEFINE.** Define federal government priorities using a data-driven method to identify innovation gaps, communicate priorities transparently using Target Product Profiles, and use payment policy in federal programs such as Medicare and Medicaid to apply "pull" incentives to encourage innovators to fill other pressing gaps.
3. **ALIGN.** Align policies, practices, priorities, and objectives with an executive-level Policy Committee; ARPA-H engagement across sectors, interests, and communities; and a "front door" path for innovators to foster partnerships.
4. **FINANCE.** Enable ARPA-H to attract private capital to federal government innovation priorities by constructing innovation investment funds, creating a secondary market for products with favorable outcomes that were deprioritized due to lower profit, and partnering with social impact investors.
5. **DIGITIZE.** Position ARPA-H to benefit from a coordinated, digital ecosystem that supports increased access to, and ultimate use of, information for an equitable view of health that empowers individuals and communities.

About MITRE

MITRE is a not-for-profit organization chartered to work in the public interest for a safer and healthier world.

Since 1958, MITRE has operated federally funded research and development centers (FFRDCs) and performed both research and development and technical support for the Defense Advanced Research Projects Agency (DARPA). Since 2012, MITRE has operated the Centers for Medicare & Medicaid Services (CMS) Alliance to Modernize Healthcare FFRDC (Health FFRDC), working across the Department of Health and Human Services (HHS) to stand up innovative programs and implement major legislative and policy changes.

Recent MITRE contributions to accelerating health innovation include:

- Since 2016, MITRE has been advancing thought leadership on a **Strategy for Accelerating Biomedical Innovation**. With input from government, academic, not-for-profit, and private-sector partners, MITRE devised and patented a way to measure the performance of the biomedical innovation ecosystem, using a system level approach to move innovation at the pace of science.
- MITRE supported the **Office of the Assistant Secretary for Health (OASH) to develop a data driven method to identify innovation gaps** by convening experts, identifying metrics such as public health burden and societal costs, and signaling to the private sector HHS's priorities for filling gaps.
- MITRE convened the **COVID-19 Healthcare Coalition**, with close to 1,000 private organizations combining expertise and resources, that uses a "decision dashboard" as a "source of truth" to track pandemic-related trends and assess progress against Coalition objectives such as alleviating constraints in the supply chain for masks, ventilators, and diagnostic test components.
- MITRE supported the **National Institutes of Health's (NIH's) Rapid Acceleration of Diagnostics for COVID-19 (RADx)**,), which compressed a multi-year commercialization process into six months using performance-based contracts defined by time and regulatory milestones, a fast cycle for application review, and autonomy to redirect funds.
- MITRE, the American Society of Clinical Oncology, Inc. (ASCO®) and its nonprofit subsidiary, CancerLinQ LLC, among others, developed **minimal Common Oncology Data Elements (mCODE™)** to standardize and advance the interoperability of digital health data and help move toward a standard health record. MITRE and several other member organizations currently lead the Common oncology data element eXtensions Health Level Seven International Fast Healthcare Interoperability Resources Accelerator (**CodeX HL7 FHIR Accelerator**) to apply open-source structured data elements for oncology electronic health records to specific use cases and enable smarter data in the fight against cancer.
- MITRE published a **National Strategy for Digital Health**[3] in 2021 at the recommendation of the MITRE Health Advisory Committee, a group of visionary senior-level executives established to guide MITRE, and the Health FFRDC it operates, in identifying innovative solutions to transform the national health and human services enterprise.
- MITRE also recently published a **10-Point Action Plan: Sustaining a Biopharma Industrial Base for a More Secure Nation** with recommendations to mitigate risks from high-consequence events.

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Introduction

Foundation for Accelerating Biomedical Breakthroughs

The federal government has made significant investments in a variety of domains to improve our nation's healthcare ecosystem. These investments have ranged from health information technology and patient-centered outcomes research, to expanded insurance coverage and a ten-year reauthorization of the National Institutes of Health (NIH) that reinforced Congress' ongoing commitment that the U.S. continue to lead the world in funding ground-breaking biomedical research. Thanks to such federal investments—and a robust commercial biomedical research and development sector—the United States has a strong foundation to improve health in ways that benefit all people.

The White House[4] with NIH leaders[5] recently proposed to build on this foundation by creating a new agency, the Advanced Research Projects Agency for Health (ARPA-H), "to develop breakthroughs—to prevent, detect, and treat diseases like Alzheimer's, diabetes and cancer."[6] If authorized by Congress, the creation of ARPA-H would be a major step toward a future that will "accelerate the pace of breakthroughs to transform medicine and health"[7] through rapidly removing barriers that hinder how we solve vexing health challenges, creating new approaches that could bring better, more affordable innovation from lab bench to bedside and beyond.

Potential areas of transformative research driven by ARPA-H include: the use of the mRNA vaccines to teach the immune system to recognize any of the 50 common genetic mutations that drive cancer; development of a universal vaccine that protects against the 10 most common infectious diseases in a single shot; development of wearable sensors to measure blood pressure accurately 24/7; and leveraging of artificial intelligence technology to advance care for individual patients and improve detection of early predictors of disease.[8]

Despite major advances in health and healthcare, there remain significant opportunities that need a new kind of champion to speed up solutions to improve outcomes for uniquely difficult diseases, and to address deeply entrenched issues that impact health equity. The Milken Institute and FasterCures have noted that there are over 10,000 diseases, yet only 500 treatments.[9] A study by the National Organization of Rare Disorders found that of the 600 orphan products the Food and Drug Administration (FDA) has approved to treat rare diseases, three-quarters treat one condition—having no other uses—while more than 90 percent of rare diseases have no FDA approved treatments.[10] NIH publicly reports its spending on 292 categories of research and disease areas, which also hold major opportunities for game-changing breakthroughs.[11]

Moreover, the COVID-19 pandemic laid bare the disparities in outcomes for populations depending on social determinants of health (SDOH), affirming the evidence that only 20 percent of modifiable health outcomes can be attributed to clinical care.[12] The remaining 80 percent of health outcomes can be attributed to SDOH, "the conditions in which we are born, live, learn, work, play, worship, and age."[13]

While the need for immediate solutions is great, there are critical "innovation gaps" or barriers between the basic biomedical research enterprise at the NIH and the product development performed in the private biotechnology market. The White House and NIH describe the main hurdles: 1) the risk is too high, cost is too large, or timeframe is too long; 2) the focus is too

applied for academia; 3) the need exists for complex coordination across multiple parties; 4) the near-term market opportunity is too small to justify private investment; and/or 5) the goal is too broad for one company to do and fund alone.[14] Moreover, our nation needs a way to ensure that health equity is central to innovation, including ideating novel ways to advance health equity and amplify resilience.

Potential of ARPA-H

ARPA H, if enacted by Congress, represents a critical opportunity to accelerate biomedical breakthroughs. The White House[15] and NIH[16] provide compelling, feasible features for new ways of "doing science" required for a DARPA-like approach within the NIH. These features include "bold goals with big potential impact over incremental progress," a flat organizational structure with short-term program managers empowered to take risks unafraid of failure, time-bounded projects, an agency director with high degrees of independence and authority, and a senior leader ensuring the centrality of health equity. (These features align well with those identified as critical to DARPA's success by that agency's former Director and Deputy Director in a 2013 article in *Harvard Business Review*.[17]) Along with these requirements, the White House and NIH describe a major opportunity to develop/enhance critical collaborations outside of the NIH—across agencies that hold the potential to transform how the federal government partners not only among themselves, but also with the academic medical research sector, communities, and the life sciences industry.

The federal government's role in biomedical innovation ecosystem is complex, as it spans financing basic biomedical research and collection of data from clinical trials, the authority to permit market approval of new health technologies such as prescription drugs and medical devices, and the financial responsibility for health services for millions of people across the nation. Much like federal agencies may have related yet divergent priorities that will need to be aligned for ARPA-H to succeed, so too will the competing priorities of researchers who measure performance in tenure and publications, life science entrepreneurs who are responsible to shareholders, patient advocates with focused interests, and payers seeking value and managing a population. Encouraging collaboration among groups that have both different agendas and priorities—and sometimes a lack of trust—requires leadership, financial incentives that are sufficient to drive behavior change, and common frameworks for measuring improvements in the speed of innovation and population outcomes.

> "IF AUTHORIZED BY CONGRESS, THE CREATION OF ARPA-H WOULD BE A MAJOR STEP… RAPIDLY REMOVING BARRIERS THAT HINDER HOW WE SOLVE VEXING HEALTH CHALLENGES, CREATING NEW APPROACHES THAT COULD BRING BETTER, MORE AFFORDABLE INNOVATION FROM LAB BENCH TO BEDSIDE AND BEYOND."

MITRE could not agree more that "**the potential opportunity is extraordinary**." Accelerating biomedical

innovation is one of the major aims of MITRE's Federally Funded Research and Development Center (FFRDC). Sponsored by the Centers for Medicare & Medicaid Services (CMS) on behalf of Department of Health and Human Services (HHS), the Health FFRDC serves as an objective advisor to all HHS organizations and other federal agencies with health and human services missions. As operator of the Health FFRDC, MITRE mobilizes experts and convenes stakeholders to accelerate and expand the impact of government programs to reinvent health systems, enhance the care experience, and protect and promote health and well-being. Formally established under Federal Acquisition Regulation Part 35.017, FFRDCs meet special, mission-driven, long-term research and development needs and operate in the public interest, free from conflicts of interest.

In our role as operator of the Health FFRDC, MITRE supports all operating and staff divisions of HHS as well as other federal agencies, state and municipal governments, and public charities. MITRE focuses on achieving key outcomes in health and human services through the Health FFRDC include: Improving Health and Social Equity, Empowering Patients and Clinicians, Improving Global Health Security, and Increasing Access to and Quality of Care. This mission is well-aligned with the vision for ARPA-H presented by the White House and NIH leadership.

The purpose of this white paper is to share a system-level framework for accelerating health innovation previously developed by MITRE, and how this framework might support the success of ARPA-H. MITRE's Framework for Accelerating Biomedical Innovation includes details for how ARPA-H might measure innovation gaps, prioritize unmet needs, align federal government organizations along the pathway from bench to bedside and beyond, and attract private capital alongside public funding. Consistent with the publication of MITRE's recent Call to Action: A National Strategy for Digital Health, the white paper highlights the fundamental role of digital health and the free flow of health data and evidence to inform decision makers within the proposed ARPA-H and the medical research ecosystem broadly. We hope these additional considerations, which build on what has been described by the White House and NIH, might contribute to ARPA-H's promise to move beyond current major innovation gaps and catalyze a major acceleration in the research and development required to "create breakthrough innovations that serve an entire health ecosystem and all populations."[18]

Essential Components for ARPA-H's Success

An important goal of ARPA-H is to catalyze biomedical breakthroughs to advance health and well-being that are broadly accessible to all people across the nation. New health breakthroughs—no matter how sophisticated from a technology standpoint—will not improve population health if their delivery is inequitable or their cost is prohibitive.

The White House and NIH take an important stance by proposing that "ARPA-H should have a senior leader responsible for ensuring that issues of equity are considered in all aspect of ARPA-H's work."[19] With this perspective, the ARPA-H portfolio will have the opportunity to aim its ground-breaking research in domains that may make considerable strides toward outcomes that advance health equity.

ARPA-H should develop its health innovation research agenda, build its portfolio of projects, and decide

which projects to fund, terminate, or scale over time based on their contributions to the overall goal of a more equitable, accountable, affordable healthcare system, partnering with the CMS Innovation Center and a broad group of stakeholders to advance multi-payer initiatives to give providers and patients the tools they need to manage care and costs.

MITRE agrees with the White House and NIH leaders that ARPA-H's ability to achieve the desired outcomes depends on the new agency having autonomy and independence. Congress and HHS leaders should create ARPA-H as a new organization, with a new culture and way of doing business, grounded in NIH expertise and relationships but unbound by preexisting rules and administrative processes. ARPA-H's leaders should encourage a healthy appetite for risk to empower project managers and contract officers to run fast, break things, and not fear retribution. ARPA-H leadership should adopt agile approaches to "fail fast"—rapidly test and adjust development over time toward desired outcomes.

Recently, NIH demonstrated features of taking risk, a sense of urgency, and independence in standing up the Rapid Acceleration of Diagnostics for COVID-19 (RADx) program, which sought to solve a critical challenge—the need for millions of COVID-19 diagnostic tests—in a compressed timeframe of months, rather than years. The program emphasized speed, merged best practices from business and academia, used performance-based contracts with clearly defined milestones and frequent reviews by a panel of experts, and was empowered to cancel projects that were not meeting milestones.[20]

Two final, but important, components for Congress to consider in authorizing ARPA-H are: 1) permitting project managers to reallocate funds from less-promising to more-promising projects, without seeking consensus and approvals; and 2) flexibly applying federal contracting authorities (like other transactions authority) to accelerate decision making and optimize use of public funds.

MITRE'S System-Level Framework for Accelerating Biomedical Innovation

MITRE has designed a Biomedical Innovation Framework to support a system-level approach for accelerating health innovation across the Department of Health and Human Services (HHS). Our framework was envisioned to facilitate an integrated, efficient and equitable health innovation pipeline energized by the federal government—a vision that the emergence of ARPA-H may substantially fill and move in exciting directions (see Figure 1). The United States possesses all of the ingredients needed to fuel that pipeline. What has been lacking, until now, is a transparent view of the federal government's goals in this endeavor, the tools to measure progress toward those goals, and leadership to focus and unite disparate efforts across the public and private sectors. The COVID-19 pandemic presented an opportunity to accelerate biomedical innovation when actions are aligned around a clear goal, shared measures of success, and desired outcomes. The framework provides a blueprint to replicate and scale those successes: to align major HHS agencies (e.g., NIH, FDA, CMS) to create a powerful engine for progress and ideas, leading to innovative, safe, and effective biomedical products and services that fill existing gaps, improve outcomes, reduce disparities, and permit continuous innovation through four steps and a foundation of digitization:

MEASURE: Collect data on unmet needs and equity and establish a dashboard to create transparent and readily available information about the biomedical innovation pipeline.

DEFINE: Prioritize innovation gaps, communicate goals, and create incentives to advance biomedical innovation that efficiently addresses unmet public health needs.

ALIGN: Align organizations, policies, and funding across key HHS internal stakeholders and the private sector to foster collaboration.

FINANCE: Engage modern finance tools routinely used in the private sector to help establish markets for government priority biomedical innovations.

DIGITIZE: Position ARPA-H to benefit from a coordinated, digital ecosystem that supports increased access to, and ultimate use of, information for an equitable view of health that empowers individuals and communities.

The MITRE framework features elements that align well to the public information about ARPA-H's potential mission and structure. In the sections that follow, we describe each element of this framework and provide recommendations for how its principles align to and may advance the efficacy of ARPA-H by helping to define, measure, align, and finance its work to accelerate biomedical breakthroughs.

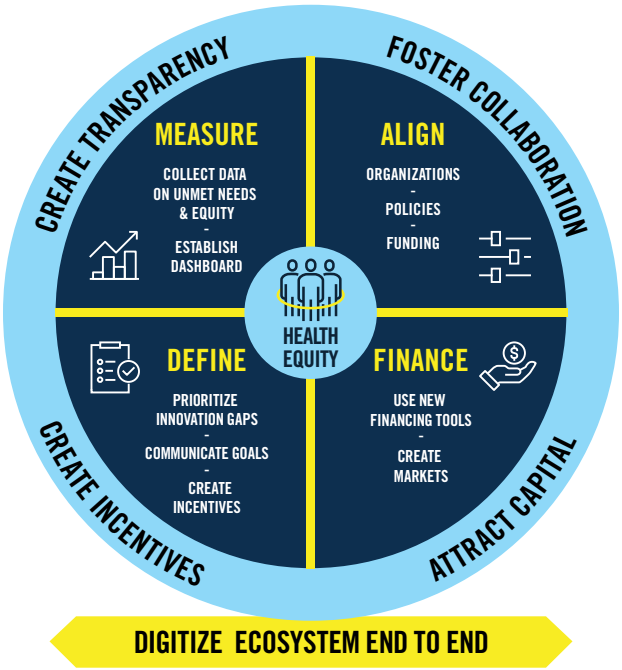

FIGURE 1. MITRE'S BIOMEDICAL INNOVATION FRAMEWORK: MEASURE, DEFINE, ALIGN, FINANCE, & DIGITIZE.

1. **MEASURE**

   Measure the health innovation ecosystem by developing and applying standardized measures for the health innovation ecosystem, and creating an executive-level dashboard that permits ARPA-H decision makers to model the pipeline of health innovations, evaluate scenarios to inform regulatory and funding decisions, and project impact on health outcomes, value, and access.

   Context:

   Central to the federal government's ability to manage innovation is having visibility into the pipeline and the ability to forecast the impacts of federal government decisions, a capability the federal government currently lacks. Data on pipeline products is closely held by life sciences companies. Standard metrics are not universally adopted; some metrics for important outcomes, such as health equity, must be created. The potential return on investment (ROI) from private investment decisions reflects both the high risk of scientific failure and the uncertainty of reimbursement from payers, including the federal government.

   ARPA-H's mission will drive the collective achievement of breakthroughs through work that relies on multiple stakeholders. The new agency, as well as HHS senior leadership, will benefit from the development of a standard metrics framework and executive-level dashboard for the health innovation pipeline that brings together data and outcomes across stakeholder perspectives. Adding a modeling capability (e.g., akin to the National Health Expenditures projections) could help ARPA-H evaluate the potential risks and rewards of pipeline investment decisions from a health equity perspective. It could also evaluate the impact of HHS handoffs and evaluate scenarios that could accelerate innovation, such as FDA-CMS parallel review or coverage with evidence development, for their impact on public health outcomes, healthcare system metrics, federal government costs, net present value, and domestic manufacturing capacity.

   "ARPA-H… WILL BENEFIT FROM THE DEVELOPMENT OF A STANDARD METRICS FRAMEWORK AND EXECUTIVE-LEVEL DASHBOARD FOR THE HEALTH INNOVATION PIPELINE THAT BRINGS TOGETHER DATA AND OUTCOMES ACROSS STAKEHOLDER PERSPECTIVES."

   Such a dashboard would help all stakeholders—including biomedical researchers, academic medical centers, life sciences companies, families and communities—understand what innovations are in the pipeline, have an agreed-upon set of metrics to assess the societal value of innovations, and connect data from early research and development through commercial market into a central model. The framework and criteria could be publicly stated, creating transparency about the government's priorities in healthier people and smarter spending, and include interactive views tailored as appropriate to the audience.

   ARPA-H's support for the continued development of data infrastructure and adoption of data standards for data collection and data sharing,

such as Fast Healthcare Interoperability Resources (FHIR), would enable integration of public and private data sources. Were such standards adopted at state and local levels and the data integrated into the dashboard, states and local governments could evaluate the impact of health innovations on local and marginalized populations at the community level.

Protocols for federated data collection will facilitate participation by large numbers of health systems, which can then be linked with high level, centralized dashboards on key outcomes of interest. This method is now being deployed in the MITRE-led effort to study the effectiveness of monoclonal antibodies to treat COVID-19 variants. Applying similar techniques with federal government data and commercial health sector data would lead to a fully connected health innovation insights dashboard.

Recommendations:

- HHS leadership should build an executive-level dashboard that integrates public and private data on the end-to-end health innovation pipeline to permit a unified view over a long-term horizon. The dashboard and underlying modeling capability should aspire to include both the breadth and depth of available public and private data sources, including claims data, electronic health record data, and non-traditional sources such as environmental and economic trend information which may impact health.
- HHS should continue to lead the development and use of open-source software and information standards and data infrastructure. Through ARPA-H's work, the federal government can lead adoption of key standards being developed today, including measures of SDOH such as the Centers for Disease Control and Prevention's (CDC's) Social Vulnerability Index,[21] and establish a foundational framework and platform for health standards that measure outcomes, societal value, and equity.
- HHS leaders should use the dashboard to visualize and model impacts of decisions on key measures of health equity, including individual and population health. The dashboard would provide actionable situational awareness and evidence to support federal government decisions by forecasting their impact on public health outcomes, healthcare system metrics, federal government costs, net present value, and domestic manufacturing capacity. The dashboard would help policymakers view the health innovation pipeline (e.g., therapeutics under development) to collectively streamline efforts and identify gaps. The dashboard would highlight roadblocks and barriers (policy, market incentives, funding) that hamper innovation and could model actions to remove roadblocks (e.g., aligning FDA and CMS review, funding infusion for NIH research).
- ARPA-H should use its platform to support pilot projects that enable the data pipeline, test alternative payment models, and bring innovative interventions to underserved communities. Funding and supporting pilot projects are critically important to enable adoption and broader implementation. Many vendors and other organizations cannot adopt new standards until there is general acceptance of the standard and pilots have been completed, but it is hard to gain that necessary level of acceptance without early testing and feedback, as the standards

are not generally accepted. Aligning ARPA H–funded projects with engagement in the testing and adoption of standards can speed and scale research across the ecosystem.

2. **DEFINE**

Define federal government priorities using a data-driven method to identify innovation gaps, communicate priorities transparently using Target Product Profiles (TPPs), and use payment policy in federal programs such as Medicare and Medicaid to apply "pull" incentives to encourage innovators to fill other pressing gaps.

Context:

As described in "Measure," the federal government can develop a data-driven method to identify innovation gaps to inform prioritization of HHS investments, including those of ARPA-H. As innovation gaps are identified, ARPA-H will take on a series of pressing issues but clearly cannot take on all issues needing attention. The broader federal government can play a parallel role harnessing its market power as an innovation buyer to direct innovation toward defined areas of need, increasing its return on investment by integrating this research into centralized decision making and pipeline management. In other words, ARPA-H can align with and benefit from CMS' transformation from a passive payor to an innovation driver, "pulling" biomedical innovation forward in critical areas where there are large disability-adjusted life year burdens borne by beneficiaries, and healthcare costs borne by taxpayers.

The COVID-19 pandemic highlighted the ability of the federal government to rapidly mobilize resources toward areas of unmet public health need and innovation gaps. In a global pandemic, the societal needs were many and obvious: strategies for treating COVID-19, diagnostic tests that could be used in a variety of settings, and ultimately a vaccine. Moving forward, ARPA-H leaders will prioritize which innovation gaps are high priorities for federal government investment, while attracting private funds to others.

In the case of SARS-CoV-2 and COVID-19, technology developed in response to Zika and Dengue was quickly leveraged to address the new emerging pandemic (e.g., ongoing funding for messenger ribonucleic acid (mRNA) technology resulted in an "on the shelf" product that was further tailored to a SARS-CoV-2 vaccine). By working with multiple companies that had the capability to produce parts of Moderna's mRNA vaccine, the federal government was able to construct a supply chain capable of producing this vital product at scale. Federal COVID-19 Response has increased coordination across the federal government to enhance communications and relationship management with industry.

ARPA-H's mission could also be advanced, and the overall ecosystem improved, by the federal sector better integrating and advancing data science and data standardization—issues foundational to the ability to leverage data efficiently towards multiple contexts. The Health Level Seven International (HL7) Fast Healthcare Interoperability Resources (FHIR) Accelerators are examples of cross-sector efforts in this regard. For example, CodeX (Common oncology data element eXtensions) HL7 FHIR Accelerator consists of a community of organizations that are collaborating to improve data interoperability across the industry, notably by extending the mCODE™ data standard to specific

oncology use cases. CodeX members such as Pfizer, UnitedHealthcare, American Cancer Society Cancer Action Network, Varian, MITRE, American Society for Radiation Oncology, and others are working together to build a sustained and supportive community to test, implement, and improve the mCODE™ data standard.

Through a mutual vision to improve care coordination for cancer patients, the CodeX FHIR Accelerator has been a critical platform to facilitate the teamwork of several public, private, and government agencies in their pursuit to enable smarter use of data in the fight against cancer. While focused on cancer, CodeX has laid the groundwork for a framework and infrastructure that can be expanded to other critical health areas such as Alzheimer's disease, and further informs how we might realize the vision of a Standard Health Record. Collaborative efforts like mCODE™ and CodeX often uncover innovation gaps and can help define additional areas of need.

Over the past decade, Congress has enacted—and CMS has implemented—significant financial incentives for healthcare providers to adopt electronic health records (about $32.7 billion in the Health Information Technology for Clinical and Economic Health Act of 2009 alone).[22] The Center for Medicare and Medicaid Innovation (CMMI), established to transform the healthcare system by reducing program spending while preserving or enhancing quality of care,[23] has been funded by $20 billion since its inception. In its first decade, CMMI has engaged nearly one million healthcare providers serving about 26 million patients. CMMI and other CMS efforts have advanced the adoption of value-based care, which now accounts for about 40 percent of Medicare fee-for-service payments, 30 percent of commercial payments, and 25 percent of Medicaid payments.[24] Those payments depend, in part, on using interoperable electronic health records and reporting measures of quality and outcomes.

Experience during the COVID-19 pandemic, in which the use of preventive and non-emergency healthcare services dropped precipitously, has shown that providers participating in value-based payment programs were better positioned to respond than those relying solely on fee-for-service payments, both in terms of their financial viability (e.g. shared savings, capitation), and infrastructure (e.g., contact tracing, outreach to high-risk patients, and support for coordinated and virtual care).[25] A refreshed strategy for the CMMI's next ten years envisions a health system that achieves equitable outcomes through fewer models and ensuring that more providers serving low- and modest-income, racially diverse, and/or rural populations can

"CODEX HAS LAID THE GROUNDWORK FOR A FRAMEWORK AND INFRASTRUCTURE THAT CAN BE EXPANDED TO OTHER CRITICAL HEALTH AREAS …, AND FURTHER INFORMS HOW WE MIGHT REALIZE THE VISION OF A STANDARD HEALTH RECORD."

engage in them; CMMI and CMS will continue to drive high-quality, affordable, person-centered care, built through "multi payer alignment on clinical tools, outcome measures, payment, and policy approaches."[26]

CMMI can be a key partner for ARPA-H to commercialize and scale the innovations it develops in the context of advanced payment models. By doing so, government payers will be better prepared to anticipate and plan advances that will emerge through precision medicine and other discovery in the coming years—advances that hold great promise but with associated costs that could make them prohibitive for many individuals and systems. NIH leaders have already outlined one potential idea, to use new manufacturing processes to create patient-specific cancer immunotherapies less costly ("from $100,000s to $1,000s"[27]). ARPA-H can serve as coordinating force to ensure that there is a whole-of-government approach to investing in innovation and synching successful preventions and treatments with value-based payment paradigms and flexibilities.

Recommendations:

ARPA-H's mission will be most effective if the federal sector continues to advance the biomedical and health ecosystem in ways that help to define and articulate where to focus breakthrough innovations:

- ARPA-H will be supported in its mission to identify and drive at biomedical innovation gaps through the development of a sustainable data-driven prioritization method that includes an inclusive array of populations (e.g., underserved and un-/underinsured communities) and contexts (e.g., needed medical interventions, solutions advancing health equity, process enhancements). The proposed ARPA-H's leaders should assess the value of filling these gaps using multiple dimensions of value based on the stakeholder and decision context; these assessments should consider multiple perspectives (e.g., patients, healthcare sector with time costs, society) and decisions (e.g., coverage, access) to ensure a holistic and inclusive view of the value of possible innovation.
- HHS leaders should make insights and priorities public to incentivize innovation toward areas of public health need. This can be through launching large-scale initiatives, such as the Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) initiative and All of Us Research Program, publishing Target Product Profiles (TPPs), and using flexible contracting authorities, including other transaction authority (OTA) and multi-year procurement with performance based milestones to direct potential solutions to fill high-priority innovation gaps.
- Support ARPA-H's convening authority to work with CMS and other federal agencies to incentivize developing and implementing the breakthroughs through payment decisions, prize authorities, advance purchase commitments, and other financial incentives (e.g., tax policy, research funding). Federal government can create "pull incentives" for needed innovations through offering certainty that there will be market demand.
  - CMS leadership can leverage reimbursement decisions to grant special payments, such as the New Technology Add On Payment and designation as an Advanced Diagnostic Laboratory Test, to direct innovation by creating a market for innovative products that address federal government priorities.

  - Performance-based contracts or prize competitions could be awarded for products aimed toward TPPs to incentivize innovation in categories that typically have not attracted sufficient private investment. Performance based contracts would have defined milestones to assess if further development of, or exiting from, an idea is most valuable, thereby saving time and capital on products that will not achieve the desired outcomes.
- The medical research projects funded by ARPA-H and performed by its partners should align with the design of alternative payment models (APMs) to measure the desired changes in health outcomes, while rewarding efficient delivery of new innovations and equitable access for all people.
- ARPA-H can partner with APMs to identify opportunities for innovative care delivery models. Those partnerships could include states, self-insured employers, commercial payers, and Medicare and Medicaid. Existing authorities of CMMI can be applied to create these partnerships.

3. **ALIGN**

Align policies, practices, priorities, and objectives with an executive-level Policy Committee; ARPA-H engagement across sectors, interests, and communities; and a "front door" path for innovators to foster partnerships.

Context:

The federal government can position ARPA-H to play three critical roles that will align resources across the federal government and take better advantage of resources from the private sector.

First, the federal government can position ARPA-H as a "nerve center" for capacity building. The system level, interconnected digital health infrastructure of the future—built on governance, standards, and interoperability requirements—will require leadership from the highest levels of the federal government. State and local governments, public health departments, hospitals and health systems, community-based organizations, life science innovators and payers must be brought along to align their systems and processes within this new paradigm. Leadership, investment, and education will all be necessary.

Second, HHS could establish an executive-level Policy Committee with visibility across operating and staff divisions to identify potential opportunities, make introductions, foster collaboration between entrepreneurs and payers on pilot projects, and bring attention to regulatory and reimbursement barriers that stymie innovation. The Policy Committee could determine how to develop a "front door" for "matchmaking" between venture capital, research projects, interested stakeholders, and potential partners for proof-of-concept projects. With a digital nerve center and a visible front door, ARPA-H will be positioned to not only take on specific high-risk, high-reward projects, but also to foster collaboration and accelerate innovation for critical needs that may not be funded by ARPA-H.

Third, ARPA-H can be responsible for ensuring its funded research projects have coordinated data management strategies for obtaining, securing, protecting, and sharing critical real-world data (RWD) to permit use of the data for other research questions, including the application of artificial intelligence. Expansions of the approaches to RWD

developed during the COVID-19 pandemic could shorten development timelines for innovations by modernizing clinical trials, creating infrastructure to turn RWD into real world evidence (RWE) for discovery, and ensuring innovators understand the different evidentiary standards for regulatory and payment consideration. Inclusive partnerships that include diverse populations and organizations, such as minority-owned institutions and small businesses, can link information on SDOH and sources of community social support. Other novel partners and funding sources, such as the CDC Foundation and biopharmaceutical companies, could help connect community organizations to clinical trials enrollment and other patient-support opportunities.

Innovative approaches advanced during COVID-19 can replicate and scale; ARPA-H can apply them to address other challenges in oncology and other therapeutic areas. Such approaches include:

- Advance the use of novel clinical trial designs, such as platform trials, decentralized trials, and drug repurposing.
- Develop open data platforms that foster rapid scientific advances, including data and metadata management and the integration of disparate data in cloud-based systems.
- Incentivize precompetitive data sharing among biopharmaceutical companies.
- Improve patient access, enrollment, and centeredness in healthcare with reduced disparities through telehealth and virtual enrollment.

Importantly, partnerships with industry were critical to success with COVID-19 vaccines and diagnostic tests. The RADx program used a platform trial design to study several devices in the context of a single disease in an ongoing manner. The study included a master protocol and consent, standard templates, and modular amendments that permitted rapid institutional review board reviews.[29]

NIH leveraged the Point-of-Care Technologies Research Network, developed to drive the development of point-of-care diagnostic technologies for sexually transmitted diseases, among others, to stand up RADx within five days of Congress' enacting the CARES Act.[30] Importantly, this included new mechanisms for companies to get the guidance and support they needed from regulators and public contracting experts in an efficient manner.

"BY PARTNERING ACROSS GOVERNMENT AND WITH STAKEHOLDERS, ARPA-H CAN HELP TO DRIVE INNOVATION"

A novel partnership between the NIH, RADx project teams and executive project managers, and the FDA has featured a series of weekly coordinating meetings over the past year, sharing FDA's latest thinking on key issues and NIH's priorities for review of RADx applications.[31]

The Biodefense Industrial Base (BDIB) is the collection of companies that provide the needed capacity and capabilities to produce, distribute, and sustain needed countermeasures, pharmaceuticals, equipment, and other supplies. NIH, the Biomedical Advanced Research and Development Authority (BARDA), FDA, and the Department of

Defense all work with components of the BDIB at various stages of the product lifecycle, but there are often missed handoffs and unclear relationships with commercial entities. In addition, there is no routine engagement between these companies and the federal government throughout the product lifecycle. The federal government can build on the success of the Federal COVID-19 Response (FCR, formerly Operation Warp Speed) in working with companies across the U.S. Biodefense Industrial Base (BDIB), creating clarity of purpose for both government and industry, and harmonizing government investment and objectives within industry partnerships.

Over the next decade, CMS and CMMI plan to partner with payers, purchasers, providers, patient advocates, community-based organizations, and state Medicaid programs to move the healthcare system forward to achieve equitable outcomes through high-quality, affordable, person-centered care. By partnering across government and with stakeholders, ARPA-H can help to drive innovation toward that goal.

Recommendations:

- HHS leadership can facilitate ARPA-H's success and enhance the overall innovation ecosystem by creating a streamlined executive-level Policy Committee that includes executive leaders from each of the HHS operating divisions, including Agency for Healthcare Research and Quality (AHRQ), the Assistant Secretary for Preparedness and Response (ASPR), CDC, CMS, FDA, the Health Resources Services Administration (HRSA), NIH, and more. It should have the authority to make cross-cutting decisions that align agencies' activities when necessary to facilitate innovation. The committee might also be vested with the authority to use ARPA-H experience to make cross-cutting decisions that improve the federal government's broader health innovation pipeline.
- This Policy Committee could build upon the RADx and BDIB models setting HHS or federal government level policies that facilitate handoffs across operating divisions (e.g., implications of institutional review board decisions on clinical trials, alignment of evidentiary standards for regulatory and payment determinations, advancing adoption of data standards and interoperability, and modernizing data sharing and privacy), provide necessary access and communication across agencies, and ensure alignment toward common objectives and milestones.
- A Policy Committee could identify and proactively mitigate potential roadblocks that slow down promising research, while sending clear signals to stop investing in projects that have a basis in unproven or unreproducible science. It could align and clarify guidance on expectations for meeting regulatory review requirements or obtaining sustainable payment from patients, healthcare systems, or third-party payers, as appropriate.
- Congress should establish a mechanism for the Policy Committee to work with interested stakeholders and the relevant Committees of jurisdiction to obtain technical corrections or waivers that will align policy and facilitate regulatory review and market access for ARPA-H projects.
- The White House and NIH acknowledge that ARPA-H should "engage with the broader biomedical community." One opportunity would be to establish a broad stakeholder panel to

provide input in the design, implementation, and continuous improvement of innovation pipeline and priorities, particularly incorporating input and values relevant to creating health equity. The panel could include representatives of the biomedical, research, healthcare, and financial industries. Patient advocates are a critical stakeholder group in discussions of value assessment and the tradeoffs of different frameworks for assessing it.[32] Further, FDA is required to report on the use of patient experience data in regulatory decision making, especially focusing on the review of patient experience data and information on Patient-Focused Drug Development tools, in reviewing applications for new drugs and biologics.[33]

- HHS leadership should build capacity to harness the U.S. health innovation ecosystem to perform entrepreneurial education, encourage entrepreneurship, and educate innovators on the commercialization process. This could be done in tandem with ARPA-H's development, and using lessons learned from the COVID-19 pandemic.
  - HHS can support economic development and innovation by facilitating partnerships between innovators and the federal government that allow innovators to directly work with FDA and CMS to gain specific guidance of what to expect for a given innovative product and to serve as a channel for individual Q&A.
  - These standard practices for ongoing and timely feedback would speed development discussions and scale to the entire health innovation pipeline, making it more nimble, responsive, and harmonized to eliminate waste and repetition.
  - Investing in the overarching alignment processes and management will amplify the capabilities and investments of ARPA-H and, therefore, make the transition from technology to scale faster and easier. The federal government would decrease the risk of innovation and increase investment in defined innovation gaps by defining the process and end outcome for innovators.
- ARPA-H's authorities should support work with industry to conduct research, transition research into products, and scale production.
  - A critical role for ARPA-H is to improve coordination across government in order for the projects it champions to be bold and innovative, and to not get stymied. This represents an opportunity for HHS leadership to send clear signals to the market on priority innovation gaps and unmet health needs, and create durable changes needed—and modeled through ARPA-H—to how the federal sector supports biomedical breakthroughs.
  - An executive-level Policy Committee should include a subcommittee focused on biopreparedness and securing the industrial base.

4. **FINANCE**

   Enable ARPA-H to attract private capital to federal government innovation priorities by constructing innovation investment funds, creating a secondary market for products with favorable outcomes that were deprioritized due to lower profit, and partnering with social impact investors.

Context:

Balancing risk and reward is at the core of financial decision making. If the expected financial return exceeds the risk-adjusted cost, then the investment may be well justified to a commercial enterprise. The challenge is that development of safe and effective therapeutics, devices, and other health innovations is a long, risky, and expensive process. The risk-reward profile of many innovations that society needs is not aligned with for-profit objectives or fiduciary responsibilities to shareholders and other investors.

In testimony to the House Appropriations Committee, Health Subcommittee, in May 2021, NIH Director Dr. Francis Collins stated that "Our confidence that NIH is ready has been greatly advanced by our experience in addressing the COVID-19 pandemic—[including] building a venture capital model for assessing SARS-CoV-2 diagnostic technologies…"[34] This experience shows that the federal government can change the risk-reward profile through ARPA-H actions to match publicly funded research projects with private funders who can ensure continuity of the research when government funding ends and multiply the impact of limited public funds. For COVID-19 innovation, the federal government assumed a great deal of financial risk by investing in development and pre-committing to price and purchase volumes, invoking emergency authorities to compel private action, and covering and paying for vaccines and therapeutics for a large population in need. This increased the expected returns to private sector involvement. Some current and future opportunities in this vein are described below as examples of how modern finance mechanisms can be used for the public good.

Recommendations:

To increase the impact of federal government investment, Congress can authorize ARPA-H to employ finance tools to attract private capital to federal government innovation priorities. Specific policies that would facilitate this include:

"… THE FEDERAL GOVERNMENT CAN CHANGE THE RISK-REWARD PROFILE THROUGH ARPA-H ACTIONS … [TO] MULTIPLY THE IMPACT OF LIMITED PUBLIC FUNDS."

- Create and/or participate in novel investment vehicles (e.g., the "ARPA-H Fund") to fund innovations in federal government priority areas.
  - Develop an investment fund for innovations in federal government priority areas with a waterfall payout structure, offering lower payouts / capped returns for federal government and not-for-profit organizations (e.g., foundations, patient groups) and higher payouts / returns to for-profit investors.[35] This design could insulate market investors from losses, changing the risk-return profile, creating incentives to invest, and multiplying the impact of limited federal government funds.
  - Establish a megafund for federal government priority areas to draw large amounts of capital from both equity and bond markets, accelerating longer-term investment that do not depend on continued annual appropriations.[36] A megafund allows segmentation of classes of investments based upon risk tolerance and would include both

equity and collateralized debt in the form of research-backed obligations.[37, 38, 39] This model would bring together private capital and federal government sponsorship to attract institutional and bond investors. Federal government funding could be limited. It would likely require new authorities for the federal government to create the required structures to attract private capital.[40]

- Catalyze secondary markets to continue development of "deprioritized innovation" in the biomedical pipeline.[41]
  - Some products in the biomedical pipeline have a lower expected return on investment, and companies will not develop them further. Often developed with federal government funding, they will be lost to science and patients as "deprioritized innovation."
  - ARPA-H could partner with industry to stimulate and sustain secondary markets for deprioritized innovation in therapeutic areas with a need for greater equity and high public health impact.
  - ARPA-H could establish a public-private partnership model as a clearinghouse for deprioritized innovation to allow their transfer to other entities (e.g., government labs, not-for-profit drug developers, virtual drug developers).
  - ARPA-H could sponsor a database of deprioritized innovation to increase liquidity of markets.
  - Tax incentives could encourage out-licensing or donations of assets to entities with different risk return requirements (e.g., patient groups, nonprofits), who would develop them. Tax incentives could also encourage the creation of entities such as not-for-profit spinoffs.
- Encourage and participate in social impact investment initiatives to solve public health challenges in collaboration with for-profit and not-for-profit social enterprises.
  - Social impact investments are made with the intent to generate positive, meaningful social and environmental impact alongside a financial return.[42] Over the past decade, substantial advancements have propelled the social impact investment market and multiplied the power of using private capital for good in society.
  - Health is an area ripe for social impact investing and encouraging solutions for health equity and addressing SDOH. Foundation, association, and private sector–led social impact funds are increasingly offering grants, low-cost loans, mezzanine finance, equity ownership, and other solutions to provide access to capital for social enterprises, as well as offer support in the form of expertise and connections that can scale programs.[43, 44, 45]
  - ARPA-H can partner with the social impact investing community to create and/or co-invest in social impact funds focusing on health equity and SDOH, collaborate in investment programs that offer private returns for public outcomes (e.g., social impact bonds), and support and partner with organizations providing market infrastructure (e.g., B Labs, which certifies B Corporations with social performance goals).
  - These efforts would extend the benefits from government efforts in other non-health social impact investment (e.g., the Small Business Administration's Small Business Investment Company Impact Fund) into health-related domains.[46]

5. **Digitize**
   Position ARPA-H to benefit from a coordinated, digital ecosystem that supports increased access to, and ultimate use of, information for an equitable view of health that empowers individuals and communities.

   Context:

   One critical need in the health ecosystem is the infrastructure to manage an ever-increasing flow of data—including patients' medical records, financial transactions related to providing care, the pipeline of private research and development efforts and portfolio of publicly-funded projects, and information on outcomes for individuals and populations that can help understand SDOH and advance health equity. ARPA-H could benefit from an interconnected, end-to-end digital ecosystem to accelerate the collection, analysis, and use of RWD and RWE in health research.

   The growth of digital health technologies could present new opportunities for HHS in its support of ARPA-H. As described in MITRE's *A National Strategy for Digital Health,* digital health is the convergence of health related sciences and digital technologies that empowers people and populations to manage their health and well-being. Digital health capabilities are redefining the delivery of healthcare, management of public health, and our understanding of health itself—and we need to think strategically to create the changes we need to see.

   Defining a national strategy for digital health is critical to ensure that digital technologies are not just "layered" on top of the current system, which is costly, inequitable for many, and often yields poor health outcomes. Federal agencies and other stakeholders are making significant investments in new tools; methods for capturing, providing, and using data; and innovative ways to provide health services. Yet there is no agreement on a national set of priorities to guide this multitude of innovators toward common goals and priority outcomes.

   Recommendations:

   MITRE's *A National Strategy for Digital Health* includes several recommendations that point to the central role of digital health in achieving ARPA-H's goals:

   - Develop digital technologies to empower individuals to manage their health and well-being safely and securely.
     - Digital devices and systems are needed for collecting and using data to enable coordinated, holistic, and integrated care. They must equip individuals and providers with meaningful information and enable greater engagement of individuals in their health and

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wellness. Foundational to meeting this goal is ensuring that individuals own their data and possess sufficient digital health literacy to use it.
    - HHS' continued work on adopting policy and legal changes necessary to give individuals ownership of their health data, supporting digital health literacy, growing methods and data to understand the impacts of digital health approaches, and developing components that will further mature the nation's precision medicine capability will be needed to ensure ARPA-H research can benefit from the digital health ecosystem under development.
- Create data exchange architectures, application interfaces, and standards that put data, information, and education into the hands of those who need it, when they need it, reliably and securely.
    - ARPA-H can support the digital transformation of health by ensuring that its funded projects assume adherence to the Office of the National Coordinator for Health Information Technology (ONC) regulations on interoperability of health information and the prohibition on information blocking. Over time, an interoperable base of RWD can permit robust observational data studies and ensure representation from groups who are underrepresented in clinical trials, for example. Health interoperability and adoption of data standards permit innovation in new tools and services that apply artificial intelligence and machine learning. Through partnering with health systems that are already using standardized electronic health records to meet requirements for Medicare and Medicaid payment, ARPA-H can help drive the adoption of these frameworks through the research it funds in health systems.
- Foster a digital health ecosystem that delivers timely access to information to inform public health decision making and action.
    - ARPA-H can catalyze new breakthroughs in knowledge and technology, but ultimately impact on patients depends on those innovations diffusing across the country.
    - This transformation will use digital technologies and data to support a responsive, resilient public health system that facilitates timely bidirectional flow of the right information among diverse stakeholders to promote preparedness and support real-time, evidence-based decision making.
    - Maximize the use of existing standards when exchanging public health data, and actively integrate public health experts in the standards development, implementation, and maintenance processes.
    - Improve access to and use of data to inform public health action by establishing new—and enhancing existing—relationships and streamlining data exchange processes.

Conclusion

To catalyze the ecosystem, the leaders of ARPA-H will need to embrace and promote data standards and other interoperability methods across basic research, applied research, clinical care, and community living, supporting the efforts of lead agencies, such as the ONC and CMS. Such an approach will support an efficient health innovation pipeline, as it creates the preconditions for new approaches for unmet health needs. This infrastructure will permit tools such as artificial intelligence to realize their enormous potential to improve health, without reinforcing existing systemic biases. The result? *Better, life¬saving and health-improving interventions delivered to people and their communities at the pace of science.*

The proposed framework, authorities, and recommendations for ARPA-H can revitalize innovation to improve health for all people across the nation. In the process, ARPA-H can catalyze the transformation of the health ecosystem toward a system that identifies important research gaps, aligns data and resources across organizations in a collaborative way, and measures and rewards performance in improving health outcomes and reducing disparities. This strategy will prepare the federal government to proactively drive wellness and rapidly address public health emergencies and chronic and emerging health challenges. As a result, our nation will be more healthy, secure, and resilient, and will retain its leadership on the global stage.

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    BARDA, "to further advance research, development, and manufacturing of medical countermeasures" at 47 U.S.C. §247d-7e(a)(3),(6),(c)(4)-(5)

    NIH, "to be exercised in the conduct of "high impact cutting-edge research that fosters scientific creativity and increases fundamental biological understanding leading to the prevention, diagnosis or treatment of diseases and disorders, or research urgently required to respond to a public health threat" at 42 U.S.C. §282(n)(1)(C)

    National Heart, Lung and Blood Institute, "as may be necessary in the conduct of the Director's functions, with any public agency, or with any person, firm, association, corporation, or educational institutions…" at 42 U.S.C. §285b-3

    National Center for Advancing Translational Sciences, "to enter into other transactions to fund projects in connection with the functions of the Cures Acceleration Network" at 42 U.S.C. §287a(b)(3)(C)

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