ARPA-H: FEDERAL INTEREST AND OUTLOOK

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September 19, 2022

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OVERVIEW OF TODAY'S SESSION

- **Background and Context for ARPA-H:**
  - The ARPA model across the federal government
  - Administration, agency, congressional, and community interest
- **Outstanding challenges to establishing ARPA-H**
- **Preparing to compete for ARPA-H funding**

ARPAS IN THE FEDERAL GOVERNMENT

- DOD's **Defense Advanced Research Projects Agency (DARPA),** founded in 1958
  - Focuses on investing in game-changing technologies and translating fundamental research and early prototypes into new strategic opportunities for national security applications
  - Associated with development of the Internet, GPS, and stealth aircraft

- DOE's **Advanced Research Projects Agency-Energy (ARPA-E)**, founded in 2009
  - Goal: to overcome barriers in the development and deployment of energy technologies
  - To date, ARPA-E has provided close to $3 billion in research and development funding to 1,270 technology projects, which subsequently led to the creation of 109 new energy companies.

- **Homeland Security Advanced Research Projects Agency (HSARPA)**, founded in 2002
- **Intelligence Advanced Research Projects Agency (IARPA)**, founded in 2006
- **Agricultural Advanced Research and Development Authority (AGARDA)**, authorized in 2018
- **Advanced Research Projects Agency – Infrastructure (ARPA-I),** authorized in 2021
- **Advanced Research Projects Agency – Climate (ARPA-C),** proposed in 2021

ARPAS IN THE FEDERAL GOVERNMENT

While each ARPA has a different mission, they all currently share or are likely to share similar attributes, including:

- Funding high-risk, high-reward research (using broad, flexible mechanisms) that translates scientific discoveries and cutting-edge inventions into technological innovations;
- Accelerating transformational technological advances in areas industry alone will not undertake;
- Recruiting world-class talent through designated hiring authority and additional flexibilities;
- Empowering program managers to initiate and run programs of their own creation;
- Bringing in fresh ideas by rotating program managers and other key personnel every three to four years.

WHY ARPA-H AND WHY NOW?

CURRENT BIOMEDICAL RESEARCH ECOSYSTEM

Fundamental Research

- Performed in university, nonprofit, government labs
- Funded mostly by federal government
- Pursues important fundamental questions
- Major progress in discovering molecular and cellular mechanisms underlying health and disease
- Produces knowledge available to all
- Every new FDA approved therapeutic can be traced (in part) to NIH-supported discoveries

Commercial Sector

- Focused largely on research, development, and marketing of specific products to bring highly sophisticated therapies and devices to patients
- Access to significant capital to develop products, provided they can generate sufficient profit
- Currently, more than 8,000 medicines in development, including 1,300 for cancer

Collins, F.S., Schwetz, T.A., Tabak, L.A., Lander, E.S. *Science* **2021**, *373*, 165-167.

GAPS AND OPPORTUNITIES IN THE CURRENT SYSTEM

- Some ideas for biomedical innovations don't fit well into the current ecosystem because:
  - Risk (or perceived risk) is too high
  - Cost is too large
  - Timeframe is too long
  - Focus is too applied for academia
  - Need for complex coordination among multiple parties
  - Near-term market opportunity is too small to justify investment
  - Goal is too broad for one company to do and fund alone
- Interest in bringing the government's bold, fast, ambitious approach to COVID-19 (e.g. rapid development of vaccines, diagnostics, therapies) into other aspects of health and medicine

Collins, F.S., Schwetz, T.A., Tabak, L.A., Lander, E.S. *Science* **2021**, *373*, 165-167.

PRESIDENT BIDEN'S INTEREST IN ARPA-H

- FY 2022 President's Budget Request included $6.5 billion over three years to create ARPA-H within NIH
- ARPA-H would "drive transformational innovation in health research" by:
  - "Tackling bold challenges requiring large scale, sustained, cross-sector coordination
  - Creating new capabilities (e.g., technologies, data resources, disease models)
  - Supporting high-risk exploration that could establish entirely new paradigms
  - Overcoming market failures through critical solutions, including financial incentives"
- Outlines initial focus on cancer, Alzheimer's disease, and diabetes and application of Rapid Acceleration of Diagnostics (RADx) "innovation funnel" model
- Describes flat and nimble organizational structure, autonomy for program managers, and milestone-based contracting mechanisms for funding (e.g. Other Transaction Authority)

https://officeofbudget.od.nih.gov/pdfs/FY21/br/2022%20CJ%20Overview%20Volume%20May%2028_corrections%20Oct%204%20annotated.pdf

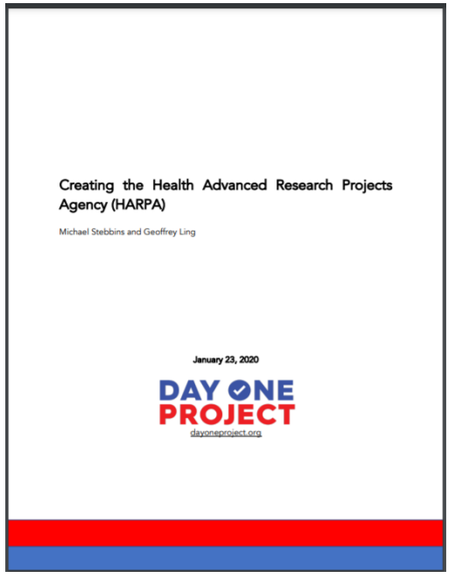
PRESIDENT BIDEN'S INTEREST IN ARPA-H

The Biden Administration's plan for ARPA-H was influenced by the President's strong personal interest in cancer research and proposals from the community dating back to at least 2016.

CANCER MOONSHOT

Congress authorized the creation of NIH's Cancer Moonshot in 2016 as part of the 21st Century Cures Act.

The Suzanne Wright Foundation has been advocating for the creation of a Health Advanced Research Projects Agency (HARPA) since 2017.



The Day One Project included creation of a HARPA among its many science and technology policy proposals for a new Administration in 2020.

CONGRESSIONAL INTEREST

FY 2022 APPROPRIATIONS FOR ARPA-H

The FY 2022 omnibus appropriations package, passed in March 2022, included $1 billion for ARPA-H, available through FY 2024.

- Final appropriated amount lower than levels proposed by both the House ($3 billion) and the Senate ($2.4 billion) in their individual appropriations bills.
- Congress placed $1 billion for ARPA-H within the larger HHS budget but gave HHS Secretary Xavier Becerra transfer authority to move these funds into NIH.
  - Funds were transferred in late April 2022, making ARPA-H officially part of NIH.
  - Secretary Becerra indicated that ARPA-H Director will report to him rather than NIH Director.
- Congressional views towards ARPA-H captured in report language accompanying omnibus:
  - Support for ARPA-H concept in general, but some hesitancy about what exactly ARPA-H will do and how it will work.
  - ARPA-H must be able to develop a unique culture and approach to selecting and funding projects.
  - NIH should review any "duplication or misalignment of programs" once ARPA-H is established and report on any proposed shifts or reorganization to address such issues.

LEGISLATION TO AUTHORIZE ARPA-H

Several proposals are currently under consideration in the House and the Senate to officially authorize the creation of ARPA-H and set direction for the agency.

Bill	Sponsors	Structure	Authorized Funding	Location	Director	Status
S. 3799 (PREVENT Pandemics Act)	Murray (D-WA) Burr (R-NC)	Part of NIH	Such sums as necessary for FY 2023 – FY 2027	Outside DC area	Four-year presidential appointee	Passed out of full committee
H.R. 5585 (ARPA-H Act)	Eshoo (D-CA)	Within HHS	$500 million/year in FY 2023 – FY 2027	Not on any part of NIH campus	Five-year presidential appointee	Passed House

SETTING UP ARPA-H

Initial Planning

NIH AND OSTP – KEY PLAYERS IN INITIAL PLANNING

Larry Tabak, D.D.S., Ph.D.
Acting Director, NIH

Tara Schwetz, Ph.D.
Acting Principal Deputy Director, NIH

NIH AND OSTP LISTENING SESSIONS

- NIH and OSTP hosted 15 public and invite-only listening sessions in summer 2021
- Nearly 250 organizations and over 5,000 participants took part
- Published report summarizing feedback received and FAQs:
  - Scientific directions: disease-agnostic platform technologies (e.g. AI/ML; sensors and wearables; digital health); focus on early detection, diagnostics, and treatment platforms; integrative approaches that emphasize data sharing
  - Process: significant program manager autonomy; streamlined review; milestone-based projects with nontraditional mechanisms (e.g. OTAs)
  - Key elements: emphasis on equity and diversity (research activities and personnel); complement, not compete with NIH; multi-sector partnerships; strong relationships with FDA and CMS

https://www.whitehouse.gov/wp-content/uploads/2021/09/093021-ARPA-H-Listening-Session-Summary_Final.pdf

NIH AND OSTP VISION FOR ARPA-H

Mission:

"To make **pivotal investments in breakthrough technologies** and broadly applicable platforms, capabilities, and resources that have the potential to **transform important areas of medicine and health** and that cannot readily be accomplished through traditional research or commercial activity."

"To **benefit the health of all Americans** by catalyzing health breakthroughs that cannot readily be accomplished through traditional research or commercial activity."

Goals:

- Revolutionize prevention, treatment, and cures in a range of diseases
- Convert use-driven ideas into tangible solutions for patients far more rapidly than previously believed possible
- Make high-risk investments in broadly applicable platforms, capabilities, resources
- Foster breakthroughs across various levels – from the molecular to the societal – and drive them to the point of adoption to serve patients
- Overcome market failures through critical solutions or incentives

https://www.acd.od.nih.gov/documents/presentations/06112021_ARPA-H.pdf

EXAMPLES OF POTENTIAL ARPA-H PROJECTS

Develop mRNA vaccines to prevent most cancers

Create molecular “zip codes” that target drugs only to specific tissues and cell types, to eliminate serious side effects

Holistic interventions to eliminate racial disparities in maternal morbidity/mortality rates and premature births

Highly accurate, inexpensive, non-intrusive, wearable monitors for blood pressure and blood sugar that provide real-time data to patients and providers

https://www.acd.od.nih.gov/documents/presentations/06112021_ARPA-H.pdf

SETTING UP ARPA-H

Where are we now?

CURRENT ARPA-H LEADERSHIP

Adam Russell, D.Phil.
Acting Deputy Director

Renee Wegrzyn, Ph.D.
Inaugural Director
(*start date pending*)

https://dpcpsi.nih.gov/sites/default/files/Day-2-1145AM-ARPA-H-Russell.pdf

HOW WILL ARPA-H WORK?

1. **Program Manager Centric**
   Responsible for programs from proposal to transition

2. **Lean, Nimble Organization**
   Relatively small-sized; limited hierarchy

3. **High Uncertainty-High Return**
   "ARPA hard"; demonstrates possibility; failure is accepted

4. **Time-Bound and Urgent**
   Programs *and* PMs have start and end dates

Mission-Driven
Not requirement- or task-driven

Independent and Autonomous
Top-level support and cover

Active Program Management
Quantitative metrics

Accountability
Technical gates; stage-gating

ARPA·H

Every decision at ARPA-H is informed by the "Heilmeier Questions"

https://dpcpsi.nih.gov/sites/default/files/Day-2-1145AM-ARPA-H-Russell.pdf

HEILMEIER QUESTIONS (ARPA-H'S VERSION)

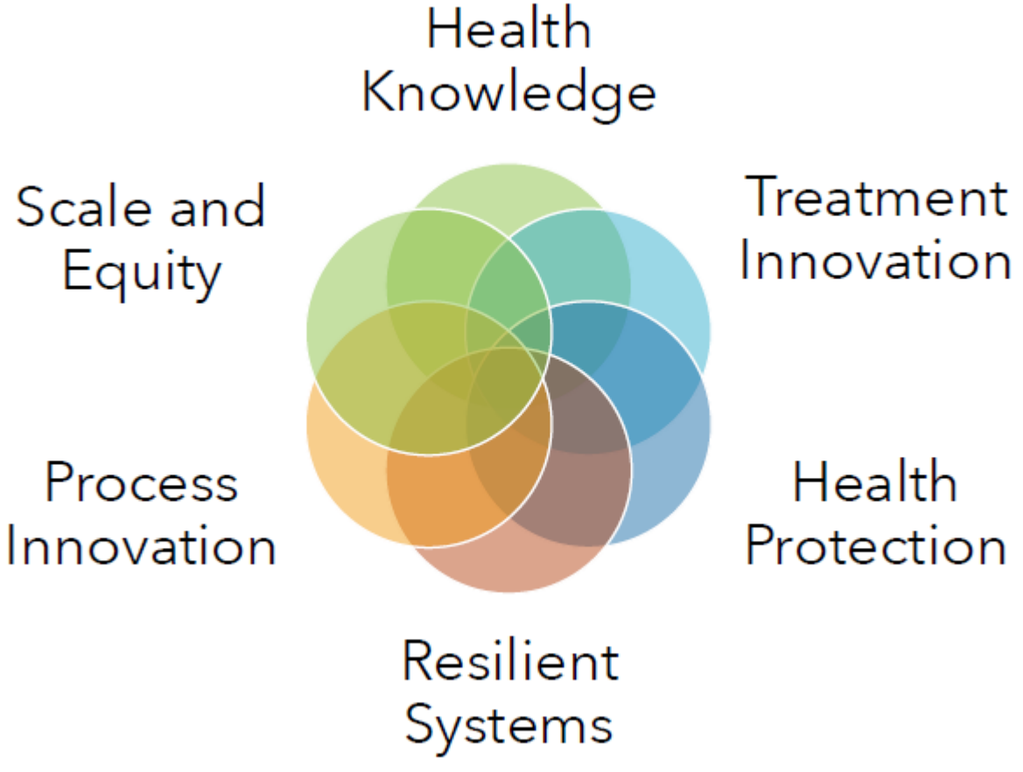
1) What problem are we trying to solve?
2) How does this get done at present? Who does it? What are the limitations of present approaches?
3) What is new about our approach? Why do we think we can be successful at this time?
4) Who cares? If we succeed, what difference will it make? *How can we help ensure outcomes are equitable?**
5) What are the risks?
6) How long will it take?
7) How much will it cost?
8) What are our mid-term and final exams to check for success?

**New for ARPA-H*

https://dpcpsi.nih.gov/sites/default/files/Day-2-1145AM-ARPA-H-Russell.pdf

WHAT WILL ARPA-H FUND?

- Program managers will have significant freedom to develop their own portfolios and pursue the challenges they find most exciting.
- Acting Deputy Director Russell suggested that the gaps between major “levers” within health might be initial points of interest.



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STAKEHOLDER REACTIONS

PERSPECTIVES FROM THE SCIENCE COMMUNITY

- Individual researchers:
  - Excitement about a new potential funding source, especially for riskier projects
  - Concern about ”the rich getting richer” – already well-funded investigators may be better positioned to compete for ARPA-H funding
- Universities and research institutions:
  - Leadership interested in prestige and boost to sponsored research numbers that additional ARPA-H funding could bring
  - Research administrators concerned about logistics of working with a different type of funder (e.g., processing contracts, meeting milestones)
- Scientific societies and advocacy groups:
  - Cautious optimism – interest in potential for ARPA-H to advance biomedical research at large but concerns about competition with other core policy priorities (e.g. growing the NIH base budget)
  - Interest in pushing for discipline- or disease-specific priorities to be included in authorization and planning for ARPA-H (e.g. ALS advocacy)

WHERE WILL ARPA-H HAVE ITS HEADQUARTERS?

★ Locations campaigning to be the home of ARPA-H

CHALLENGES TO CREATING ARPA-H

KEY QUESTIONS AND CHALLENGES FOR ARPA-H

- How do you ensure that ARPA-H can develop the unique culture it needs to be successful?
  - Need to encourage attributes (e.g. risk taking, acceptance of failure, milestone-based approaches) that NIH is traditionally uncomfortable with
- What will the impacts of ARPA-H be on the NIH budget (in FY 2023 and beyond)?
- How do you get buy-in from the biomedical research community?
- How will ARPA-H balance disease-agnostic platform technologies with more clinically oriented projects?
  - Will health care issues, health system design, supply chain challenges, etc. be within scope?
- How quickly can ARPA-H get going and prove its value?

KEY QUESTIONS AND CHALLENGES FOR ARPA-H

What political considerations will impact ARPA-H?

- Is there a vehicle this Congress for ARPA-H authorizing legislation?
- Is authorization legislation needed or wanted given direction from appropriators?
- Where does ARPA-H fit in with other health priorities like pandemic preparedness?
- How does the upcoming retirement of key Senators (Blunt, Burr, Leahy, Shelby) impact future prospects for ARPA-H?
- Will ARPA-H be subject to the same high levels of congressional scrutiny that NIH faces?
- Will President Biden's strong support for ARPA-H be helpful or harmful long-term?

WHAT'S NEXT?

FUTURE PROSPECTS FOR ARPA-H

- Funding for ARPA-H vs. funding for NIH base budget already point of tension in FY 2023 appropriations conversations
  - FY 2023 President's budget request included $4 billion increase for ARPA-H and essentially flat funding for rest of NIH
  - Reps. DeLauro (D-CT) and Cole (R-OK) both unhappy with balance between proposed NIH and ARPA-H funding
- Expect ARPA-H to be discussed as nominee for NIH Director (yet to be named) is considered in the Senate
- Timeline for staff hiring and funding opportunities remains unclear and ambitious:
  - Program manager recruitment should commence soon now that Dr. Wegrzyn has been announced as inaugural Director
  - NIH projected that ARPA-H's first Broad Agency Announcement would be released in fall 2022, with first funding awarded in March 2023

PREPARING TO COMPETE FOR ARPA-H FUNDING

- Evaluate internal teams – what projects, centers, or groups might be well-positioned to compete for ARPA-H funding? How can these partnerships be strengthened now in advance of funding opportunities being released?
- Review existing external partnerships that might be valuable to highlight in a proposal for ARPA-H funding, especially those with industry partners and Minority-Serving Institutions.
- Consider how to re-frame NIH-funded work in the context of ARPA-H, which will require a different lens than the standard NIH process. Work on answering ARPA-H's Heilmeier questions for any projects you would want to propose to the new agency.
- Consult with DARPA-funded colleagues to get their perspectives on best practices in applying for funding. Faculty who have been successful at winning DARPA funding could provide advice, guidance, and/or mentoring to faculty who have not been funded through that agency.
- Be prepared to engage formally with ARPA-H (through workshops, roadshows, etc.) as well as one-on-one with program managers once they are brought on board.
- Look for updates from IHSI and Lewis-Burke as ARPA-H continues to take shape.

THANK YOU!

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