ARPA-H: Combating Global Challenges to Advance the National Interest

As the Department of Health and Human Services sets the wheels in motion to stand up the Advanced Research Projects Agency-Health (ARPA-H), and the House and Senate authorizing committees consider additional direction and authorities for that agency, a pivotal variable is how much flexibility the agency will have to capitalize on big ideas – by inference or in law – that do not directly or initially bear on diseases prevalent in the United States (U.S.).

The authorizing legislation for the Defense Advanced Research Projects Agency (DARPA) and the Advanced Research Projects Agency–Energy (ARPA-E) understandably focus those agencies on national defense capability and energy technologies that directly address U.S. challenges or objectives. Will ARPA-H only consider ideas that directly bear on high burden health threats in the U.S. (as determined by individual, e.g. cancer, or collective, e.g. rare disease, prevalence, or cost), leaving global health threats like emerging infectious diseases or poverty-related neglected diseases (PRNDs) to other agencies or interests?

One could picture this bifurcation arising if policymakers decide that ARPA-H should only address challenges analogous to those other ARPAs have pursued and that global health threats do not fulfil that criterion, or if there is a perception that empowering ARPA-H to look beyond our borders would set the stage for duplication with other federal agencies.

Below we look at each of these potential arguments against empowering ARPA-H to pursue global health-focused breakthroughs.

Achieving High Return Breakthroughs in Health: The Straight Path is Not the Only Path In considering national security or energy advances, a model in which agencies mine for bold ideas that arise directly from immediate or long-terms needs or opportunities in the U.S. has worked well, not only for the U.S., but often for societal good beyond our borders. The research and engineering that went into DARPA's ARPANET set the stage for the worldwide web. ARPA-E's role in the evolution of low cost, high energy batteries has had indispensable applications for U.S. energy and the U.S. economy, while delivering spillover benefits across the globe.

In the case of health, the potential for transformative progress in the interests of our nation does not always begin with a focus on diseases or cross-disease platforms tailored for illnesses prevalent in the U.S. Pursuing big ideas that bear on global health threats can deliver powerful returns to the American people. There are several reasons for this, including:

1) Few diseases respect borders: from SARS-CoV-9 to Ebola to Zika to drug-resistant tuberculosis, destructive, deadly, and costly health threats can enter our nation from anywhere across the globe.

    a) One compelling example of this reality is the emergence of PRNDs in the United States, particularly amongst those living in poverty and for which, therefore, there is little R&D incentive. Once considered diseases affecting only tropical regions of the world, over the past few decades diseases like West Nile virus, Dengue, and Chagas have risen in incidence in the American South because of increasing poverty and substandard living conditions,

changes in the environment, human migration, and globalization. It has been estimated that 3–4 million people in the U.S. Gulf Coast states are affected by at least one PRND.

2) With active-duty military personnel positioned in virtually every country around the world, diseases anywhere pose a threat to American warfighters and their families. Our nation sustains the largest active troop presence overseas of any country across the globe. As of March 2021, there were more than 170,000 active duty military personnel stationed overseas. There are approximately 25,000 Diplomatic and development assistance personnel overseas, not counting the more than 7,000 peace corps volunteers and religious based and other private humanitarian workers. Furthermore, there are those who travel globally for leisure; prior to COVID-19, 93 million Americans traveled abroad each year, and approximately 71% of the US population travels abroad at some time in their lives.

3) Projects that promise transformative medical progress, regardless of the initial focus, can revolutionize the diagnosis, prevention, and treatment of other major diseases. Just one example: Research focused on the rare disease cherubism holds important promise for progress against arthritis and other high prevalence inflammatory conditions.

4) Combating diseases prevalent in low-and middle-income countries (LMICs) is critical to establishing economic progress and stability for these nations, which in turn fosters self-sufficiency and bolsters trade opportunities for developed nations like the U.S.

5) The deadliest and costliest of all health threats – pandemics – can arise anywhere in the world, but are most likely to arise outside the U.S.

The Case for Ensuring ARPA-H's Mission is Broad: Pandemics Unfortunately, there is no way to predict when the next pandemic will occur. There may be no breathing room between COVID-19 and another global infectious disease outbreak. The U.S. should consider the mitigation of pandemic threats an urgent priority and leverage every relevant asset we have, including ARPA-H, to out-innovate them. COVID-19 has taken more than 988,618 lives in the U.S. alone, and our nation has thus far spent more than $3.6 trillion in response to it. An all-out effort to prevent another catastrophic pandemic is clearly called for. ARPA-H is meant to fill a gap in our nation's public and private sector-fueled R&D ecosystem by de-risking the pursuit of big, bold, multi-sector R&D initiatives meant to achieve transformative progress. It is just this kind of enterprise that can deliver breakthroughs that position our nation and the global community to out-smart and out-maneuver the next pandemic. New pandemic threats are emerging more quickly than they ever have. ARPA-H should have the charge and flexibility to tamp them down.

Is Duplication of Effort an Issue? As it stands, The National Institutes of Health (NIH), The Centers for Disease Control and Prevention (CDC), The Biomedical Advanced Research and Development Authority (BARDA), The United States Agency for International Development (USAID), along with several other federal agencies, contribute to progress in the global health arena. Would adding ARPA-H to the mix add value or breed redundancy?

The answer lies in the very reason ARPA-H is such a compelling new initiative: the agency's charge, like that of DARPA and ARPA-E, is to take risks, think big, and fail fast. No other federal agency is tasked with the ability to partner with the private sector to explore bold, risky ideas that could radically transform medical progress itself – the pace of that progress, the number of lives saved, the suffering averted, and the independence and self-sufficiency gained. There is no redundancy between ARPA-H's charge and those of other federal health research agencies, each of which fills another unique and critically vital role in the R&D ecosystem.

Conclusion ARPA-H is an incubator that bets on the longshots, but with the expertise and discipline to achieve big wins. The health and security of the American people cannot be disentangled from that of the world of which we are part. For the reasons detailed above, the benefits ARPA-H can deliver would be

maximized by emphasizing flexibility in the projects the agency considers and diminished by establishing false divides between global R&D progress and U.S. R&D progress.