The Global Health Technologies Coalition (GHTC) is pleased to submit updated feedback on the draft 21st Century Cures 2.0 legislation. GHTC is a coalition of 38 nonprofit organizations, academic institutions, and aligned businesses advancing policies to accelerate the creation of new drugs, vaccines, diagnostics, and other tools that bring healthy lives within reach for all people. We are eager to share the perspective of our coalition on the bill's authorization of the Advanced Research Projects Agency for Health (ARPA-H), a new entity we believe has tremendous potential to develop breakthrough health technologies and platform technologies "focused on solving practical problems that advance equity," as stated in the initial factsheet on ARPA-H shared with the discussion draft of Cures 2.0.

In particular, GHTC believes there is a strong case for ARPA-H to focus on poverty-related and neglected diseases (PRNDs), such as HIV/AIDS, tuberculosis, malaria, neglected tropical diseases, and antimicrobial resistance—a health area "ripe for major transformation with the right support and collaboration," as described by Representatives DeGette and Upton in their vision for the entity. If the goal for ARPA-H is to produce transformative innovation where there otherwise would be none, few areas offer as much potential for R&D impact as PRNDs, for three main reasons:

First, as afflictions associated with conditions of poverty globally, including in the United States, **PRNDs offer little commercial incentive for the private sector to develop medical products to diagnose, treat, or prevent them. This market failure has led to historic under investment relative to the societal burden that these diseases produce.** In 2016, the global private pharmaceutical sector spent approximately $159.9 billion on R&D for health *overall*, but only $511 million—less than one-third of one percent—on R&D for neglected diseases.[i] In contrast, the private sector is investing heavily in R&D on treatments for cancer and Alzheimer's disease. According to the Congressional Budget Office, in 2018, there were more than twice as many ongoing clinical trials for cancer and nervous system disorders (such as Alzheimer's) than the next three biggest disease classes combined.[ii] While more resources are needed for R&D in many health areas that affect American and global health, leveraging the unique capabilities of the proposed ARPA-H model for PRNDs creates an opportunity to make a major impact in eliminating or even completely eradicating some diseases that are unlikely to be a focus of other stakeholders because, as the draft bill states, "the relevant industries by themselves are not likely to undertake [them] because of technical, financial, or other uncertainty."

Second, even though past US investments from different R&D agencies have produced laudable scientific advances against some PRNDs, **a considerable number of high-impact innovation gaps remain**: the world still awaits a vaccine and cure for HIV/AIDS, a single-dose cure for the deadliest form of malaria, shorter tuberculosis treatment regimens, better diagnostics for neglected tropical diseases, highly effective vaccines for tuberculosis and malaria, and many other innovations that could transform global health. Defeating these global health challenges remains a lofty goal, but as with COVID-19 in the United States, the right mix of resources and ingenuity—including through game-changing initiatives like ARPA-H—could create bridges to a healthier future for all.

Third, if the goal of ARPA-H, like DARPA, is to foster transformative, sector-defining breakthroughs, then policymakers should note that **investments in infectious disease research have historically paid dividends across the health R&D landscape**. For instance, investments in HIV/AIDS research led to the immunological breakthroughs critical to understanding the pathogenesis of COVID-19. Research on malaria has produced anti-malarial drugs that are being evaluated as promising anti-cancer treatments.[iii]

And a one-hundred-year-old tuberculosis vaccine is now being evaluated for its potential therapeutic and protective effects against Type 1 Diabetes, Alzheimer's, and other diseases.[iv] In short, investments in infectious disease research have historically nourished a rich soil of scientific knowledge from which innovations for other disease areas have blossomed. It is clear that investing in PRND R&D closer to the level of need through support from ARPA-H would yield a harvest of health advancements across the entire landscape of pressing needs.

Related to the entity's structure, GHTC supports an ARPA-H framework that closely mirrors that of the Defense Advanced Research Projects Agency (DARPA). This framework should include policies that would give APRA-H program managers maximum flexibility in how they distribute funding—enabling them to place high-risk, high-reward bets with strategic partners. For instance, if freed from the burdens of the typical NIH funding process, ARPA-H program managers could more easily collaborate with product development partnerships (PDPs)—partnerships that combine expertise, resources, and funding from the public, philanthropic, and private sectors to create products that address specific public health goals. With flexible funding capacities, ARPA-H program managers could leverage PDPs and other aligned partners as a powerful tool for solving the most difficult public health challenges.

We understand that designing and authorizing ARPA-H in the final Cures 2.0 legislation will require a thoughtful negotiation between congressional oversight and the flexibility necessary to foster innovation, as well as a thoughtful balance among many competing disease priorities rising to the fore based on public health need, scientific neglect, ripeness for breakthroughs, and other factors. We believe that a focus on PRNDs—an area of historic market failures—holds the greatest potential for ARPA-H's societal impact and that flexible funding capacities designed to foster partnership are essential for its success, and would support minor edits to the draft legislation to those ends. We stand ready to work with you on the design and authorization of this exciting initiative. Please do not hesitate to contact Emily Conron, the US policy officer for GHTC, at econron@ghtcoalition.org if you have questions or requests for additional information.

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