

DEADLIEST CANCERS COALITION

July 16, 2021

The Honorable Diana DeGette
U.S. House of Representatives
Washington, DC 20515

The Honorable Fred Upton
U.S. House of Representatives
Washington, DC 20515

Dear Representatives DeGette and Upton:

On behalf of the undersigned members of the Deadliest Cancers Coalition, a collaboration of national non-profit organizations and industry focused on addressing issues related to our nation's most lethal cancers, we are writing to respond to your request for stakeholder input on the development of a new Advanced Research Projects Agency for Health (ARPA-H).

Overall, we enthusiastically support the creation of ARPA-H as it has the potential to provide a vital bridge between the lack of tools and resources currently available to deadliest cancer patients and the improved survival rates that are so desperately needed. The deadliest cancers (aka, recalcitrant cancers) exemplify the need for such a program as these are the cancers with the lowest survival rates. It is important to note that these cancers are distinguished by extraordinarily low survival rates, not by incidence. While many of the deadliest cancers are also considered rare, some (e.g., lung cancer) are not. Similarly, many rare cancers have high survival rates and therefore are not recalcitrant. There is overlap between rare and deadly, but they are not synonymous.

Deadliest or recalcitrant cancers are defined by the Recalcitrant Cancer Research Act, which was enacted in 2012, as those with a five-year survival rate below 50 percent and include brain, esophageal, liver, lung, ovarian, pancreatic, and stomach cancers, as well as mesothelioma. While the NCI has taken critical steps in implementing this legislation and has made progress on developing new approaches and resources for some cancers, including pancreatic adenocarcinoma, small-cell lung cancer and glioblastoma, there is still much work that needs to be done for these and the other recalcitrant cancers. We welcome the potential that ARPA-H has in spurring new and innovative approaches in prevention, early detection, and treatment of these cancers for which answers have been elusive.

In calling for the creation of ARPA-H, President Biden has cited the success of the Defense Advanced Research Projects Agency (DARPA) and expressed his belief that ARPA-H should be similar. Please provide specific details on which aspects of DARPA ARPA-H should replicate and why this would lead to similar success.

While the NIH process is critical in developing new tools for the deadliest cancers and other diseases, it traditionally favors incremental, hypothesis-driven research. As the Office of

Science & Technology Policy noted in their ARPA-H concept paper, NIH proposals are typically “curiosity-driven”. We are particularly intrigued by the DARPA approach to focus on “use-driven” research that is directed at solving a practical problem. We believe that approaching medical issues from both ends of the spectrum – curiosity-driven and use-driven – will speed progress toward developing the tools our patients desperately need.

We also support using the DARPA principle of embracing failure in a newly created ARPA-H. The hallmark of this program should be a focus on bold projects that would be transformative to patient care. While NIH paylines tend to necessitate a focus on funding projects that are likely to succeed, it is critical that ARPA-H embrace true innovation and out-of-the-box thinking. Risk-taking should therefore be a fundamental principle in determining areas of focus and funded-projects. In that regard, we agree with the statement made by White House Office of Science and Technology Policy (OSTP) Director Dr. Eric Lander, NIH Director Francis Collins and others that “ARPA-H should expect that a sizable fraction of its efforts will fail; if not, the organization is being too risk-averse. The best approach is to fail early in the process, by addressing key risks upfront.”¹

To ensure it has the biggest impact, on what activities or areas should ARPA-H focus? What activities or areas should ARPA-H avoid?

We were pleased to note that both in your concept paper and in President Biden’s budget, the stated purpose of ARPA-H is to focus on bold projects that would be transformative to patient care. We strongly believe that this focus on fundamentally changing patient outcomes is critical to ARPA-H’s success and encourage you to hold fast to this principle as you are developing the legislative language authorizing the program. While we understand that “quick hits” would be helpful in demonstrating the potential success of a new ARPA-H, we urge you to focus instead on projects that aim to enable clear change in disease from that which is recalcitrant to manageable and curable.

Currently, there are few tools available to patients diagnosed with one of the deadliest cancers. The discussion between physicians and deadliest cancers patients are typically focused on end-of-life instead of exploring treatment options that will provide the best quality and extension of life. Deadliest cancers exemplify areas where medical practice would be dramatically changed through the technologies and platforms that could be developed under ARPA-H. For these reasons, we ask that you ensure that ARPA-H focuses on the hardest problems and areas where medical practice will be dramatically changed, including the deadliest cancers, as you develop authorizing language. Specifically, we urge you to ensure that the principles that ARPA-H uses to prioritize funding decisions incorporates a definition of “need” that includes mortality rates and areas where tools are particularly lacking instead of solely focusing on incidence.

¹ <https://www.whitehouse.gov/ostp/news-updates/2021/06/22/science-magazine-arpa-h-accelerating-biomedical-breakthroughs/> Accessed July 9, 2021.

Some assert ARPA-H's ability to operate independently and transparently will be essential to its success. Do you agree? If so, what is the best way to design ARPA-H in order to accomplish this?

The Deadliest Cancers Coalition steadfastly supports the critical research funded through the NIH in establishing a basic understanding of the deadliest cancers. This work and their approach of funding the best science – wherever that science leads – is essential in our fight to reduce cancer mortality.

Our hope is that ARPA-H is authorized in such a way to speed cures in a different fashion – by focusing on specific problems that have eluded us to date. To achieve these goals, ARPA-H will need to be able to make funding decisions independent of NIH's current processes and culture.

Some examples of the types of projects we believe should be funded through ARPA-H are:

- Tumor penetration – For some of the deadliest cancers, the issue is not just our ability to target cancer cells, but also to penetrate the protective barrier that exists around some tumors (e.g., the pancreatic cancer stroma and the blood-brain barrier). Creating molecular 'zip codes' that target a drug or gene therapy vector to any specific tissue and cell type, is intriguing, but this is an issue that may impede success – at least for the deadliest cancers.
- Early Detection Tools – Including Liquid Biopsy, Imaging and Companion Diagnostics – One of the hallmarks of a deadliest cancer is that time is rarely on the patient's side. Treatment decisions must be made quickly and are often made with little information. Easily accessible and effective liquid biopsy, high-quality imaging and molecular profiling are examples of tools that are currently lacking but would be enormously helpful in increasing mortality for those diagnosed with one of the deadliest cancers.
- Leverage the power of patient experience through technology - The rise of Real World Evidence as a potential source of data in prospective FDA-regulated clinical trials is also creating new opportunities for remote monitoring of patients through the use of wearable and other mobile technology. ARPA-H, based on experience from technology innovation from DARPA, could propel this field forward through a focused initiative on producing affordable, regulatory-grade, standardized patient- and caregiver-reported (symptom, sign, function) assessment tools. Validation and adoption of patient-reported outcomes measures would significantly improve the patient-centeredness of drug development and also help reveal clinical benefit in addition to survival.

Given ARPA-H's lofty goals and the diverse patient population it aims to serve, transparency in making funding decisions will also be critical. Patient advocates and researchers need to be able to understand the rationale that is being used. Further, and perhaps most important, we must also have transparency into projects that have failed so that we can learn from them.

What is the best way to ensure ARPA-H has a mission, culture, organizational leadership, mode of operation, expectations, and success metrics that are different than the status quo?

Fundamentally, ARPA-H must adopt a culture and operational processes that are distinct from NIH and which are driven by an urgency to improve patient outcomes. The agency must be empowered to, and embrace, collaborations with any and all stakeholders that can advance

breakthroughs for patients including other federal agencies and public-private partnerships with industry. Further, the agency should have full transactional authority, as well as the ability to conduct all phases of research, product development and regulatory approval.

As noted above, the Deadliest Cancers Coalition believes that transparency must be a hallmark of ARPA-H, particularly with respect to the selection criteria and decision-making process for its broad strategic investment goals and selection of individual research projects. Further, we feel strongly that identification of unmet needs within disease areas should be conducted through a formal multi-stakeholder process that includes patient advocacy groups focused on that particular disease. Cancer is not one disease. Stakeholders representing all aspects of the cancer community should be involved in the stakeholder process.

What is the appropriate funding level for ARPA-H? How do we ensure ARPA-H funding does not come at the expense of traditional funding for the National Institutes of Health?

We believe that funding for ARPA-H must be both sufficiently substantial and sustainable over time to truly transform the biomedical ecosystem. In addition, ARPA-H funding should neither subtract from existing NIH funding nor prevent robust, annual increases—no less than the rate of biomedical inflation—for the NCI and other core NIH research programs.

We greatly appreciate your leadership on this issue and the opportunity to provide input on the formation of ARPA-H. We look forward to working with you as you develop legislative language authorizing the program. Please contact Megan Gordon Don, Executive Director, at mgdon@mgdstrategies.com or 202.246.8095 with any questions or to set up a meeting.

Sincerely,

American Association for the Study of Liver Diseases
American Gastroenterological Association
Asbestos Disease Awareness Organization
Blue Faery: The Adrienne Wilson Liver Cancer Association
Cholangiocarcinoma Foundation
Debbie's Dream Foundation: Curing Stomach Cancer
Digestive Disease National Coalition
Esophageal Cancer Action Network
Global Liver Institute

GO₂ Foundation for Lung Cancer
Hepatitis B Foundation
Mesothelioma Applied Research Foundation
National Brain Tumor Society
National Pancreas Foundation
Ovarian Cancer Research Alliance
Pancreatic Cancer Action Network
TargetCancer Foundation