White House Office of Science and Technology Policy
U.S. Department of Health and Human Services National Institutes of Health
ARPA-H Listening Sessions

Listening Session 3: Advocates for Research on Eye Disease and Visual Impairment, Deafness and Communication Disorders, Dental and Craniofacial Disorders, and Autoimmune Disorders of the Salivary Glands
July 26, 2021

The third of 10 listening sessions to gather feedback on the proposed Advanced Research Projects Agency for Health (ARPA-H) program was held virtually on July 26, 2021. Advocates for research on eye disease and visual impairment, deafness and communication disorders, dental and craniofacial disorders, and autoimmune disorders of the salivary glands shared their opinions. The National Institutes of Health (NIH) is working closely with the White House Office of Science and Technology Policy (OSTP) to establish ARPA-H to focus on ambitious and innovative projects that will shape the future of health and medicine for all Americans.

Participants

White House Office of Science and Technology Policy (OSTP)

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National Institutes of Health (NIH)

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Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director
Michael F. Chiang, M.D., Director, National Eye Institute (NEI)
Rena D'Souza, D.D.S., M.S., Ph.D., Director, National Institute of Dental and Craniofacial Research (NIDCR)
Debara L. Tucci, M.D., M.S., M.B.A, Director, National Institute on Deafness and Other Communication Disorders (NIDCD)

Invited Stakeholders

James C. Denneny III, M.D., Executive Vice President and CEO, American Academy of Otolaryngology−Head and Neck Surgeons, Alexandria, VA
Christopher H. Fox, D.M.D., D.M.Sc., Chief Executive Officer, American Association for Dental, Oral, and Craniofacial Research (AADOCR), Alexandria, VA
Katherine M. Hammitt, M.A., Vice President, Medical and Scientific Affairs, Sjögren's Syndrome Foundation, Reston, VA
Barbara Kelley, Executive Director, Hearing Loss Association of America, Rockville, MD
Stephen D. McLeod, M.D., American Academy of Ophthalmology, San Francisco, CA, Editor-in-Chief, *Ophthalmology*; Theresa M. and Wayne M. Caygill, M.D., Distinguished Professor and Chair, Department of Ophthalmology, University of California, San Francisco, CA
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Jamie L. Perry, Ph.D., Board of Directors, American Cleft Palate–Craniofacial Association (ACPA), Chapel Hill, NC; Editor-in-Chief, *The Cleft Palate-Craniofacial Journal,* Greenville, NC
Jeffrey Regan, M.A., Director of Government Affairs and Public Policy, American Speech-Language-Hearing Association, Rockville, MD
Benjamin Yerxa, Ph.D., Chief Executive Officer, Foundation Fighting Blindness, Columbia, MD

Meeting Summary

Welcome and Opening Remarks

Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, National Institutes of Health (NIH)
Francis S. Collins, M.D., Ph.D., Director, NIH
Max G. Bronstein, M.P.P., Assistant Director for Health Innovation, White House Office of Science and Technology Policy (OSTP)
Michael F. Chiang, M.D., Director, National Eye Institute (NEI)
Debara L. Tucci, M.D., M.S., M.B.A, Director, National Institute on Deafness and Other Communication Disorders (NIDCD)
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Dr. Tabak welcomed attendees and provided logistical information for the Q&A session that would occur at the end of the session. If approved, the Advanced Research Projects Agency for Health (ARPA-H) will be a new division within NIH, with a radically different culture and organization. The new agency will be designed to foster bold ideas that are largely use-driven and to conduct research that solves practical problems. The resulting platforms, capabilities, and resources will apply across many diseases and conditions. ARPA-H will also have a distinct focus on equity to ensure diversity in funding recipients and in the patient populations that will benefit from its breakthroughs.

Dr. Collins welcomed participants and attendees to the third of 10 listening sessions to gather feedback on the proposed ARPA-H. NIH is working closely with OSTP on ARPA-H, which is a high priority for the Biden administration. ARPA-H is designed to catalyze ambitious ideas and approaches that will shape the future of health and medicine for all Americans. The new agency, which will follow the Defense Advanced Research Projects Agency (DARPA) model, will focus on high-risk, high-reward projects and will be guided by visionary project managers. ARPA-H will recruit researchers who might otherwise not apply to NIH for support, and its projects will be driven by clearly defined milestones. OSTP and NIH wish to gather opinions from stakeholders, who will play a critical role in the establishment and success of ARPA-H. The 10 listening sessions will focus on specific research areas and will involve NIH Institute and Center (IC) directors who represent those areas.

Mr. Bronstein said that ARPA-H aims to fill gaps in the biomedical research ecosystem to which NIH supplies vital infrastructure. Advancing new ideas to improve human health and biomedical science will require a novel approach. The ARPA model has taken shape as the Advanced Research Projects Agency–Energy (ARPA-E), Intelligence Advanced Research Projects Agency (IARPA), and DARPA; these examples show that the model works. It is now time to deploy the model for innovation in health.

Dr. Chiang said that the development of the COVID-19 vaccines provides a good example of the type of innovation that can happen when a public health threat mobilizes researchers to work together. Hopefully, ARPA-H can bring this same level of focus to

vision disease. As many as 7 million Americans live with blindness or uncorrectable low vision, and 164 million Americans wear glasses. Sight is how we experience the world, and vision affects our ability to work, get an education, and avoid accidents. ARPA-H can advance vision research by using artificial intelligence (AI) to solve real-world problems, such as improved screening for diabetic eye disease, or to accelerate the use and adoption of and improve access to advanced ocular imaging.

Dr. Tucci said that ARPA-H would provide an unprecedented opportunity to fund high-risk, high-reward research to spur discoveries and accelerate treatments. Advanced, targeted drug- and cell-based therapies to treat sensory and communication disorders might include in utero gene therapy research for hereditary hearing loss. Advances in regenerative medicine could lead to functional restoration of damaged inner ear sensory cells and recovery of hearing imbalances. Machine learning could be used to improve hearing aids, cochlear implants, and other devices. Chronic ear infections in children and deficits in taste and smell are two important conditions that would benefit from innovative research. An improved understanding of the mechanisms for olfactory system neuron regeneration and stem cell therapies for neurological diseases are needed. Further development of assistive devices and brain–computer interfaces could help restore communication abilities for people who have lost the ability to speak. Investments are needed to spur competition and drive down costs to make these types of devices affordable and accessible to all.

Dr. D'Souza said that ARPA-H has the potential to create a new era of research that improves health for all. NIDCR intends to use the program to challenge the status quo, aim for the extraordinary, and deliver the scientific and clinical evidence necessary to improve dental, oral, and craniofacial health. Because of oral health's importance in overall health, the World Health Organization recently recommended including oral health care in universal health coverage. Craniofacial disorders constitute half of all inherited disorders, and cleft palate occurs in 1 of 700 live births. Untreated decay is the most common reason that children miss school and require emergency department visits. There are many conditions and disorders across the lifespan where advanced data science could be used to identify common risk factors and reduce the inequities and disparities in access to oral health care. Opportunities abound for transformative research that could change the prevention, diagnosis, and treatment of oral health conditions that pose major national and international public health threats.

Comments from Invited Stakeholders

Stephen D. McLeod, M.D., American Academy of Ophthalmology, San Francisco, CA, Editor-in-Chief, Ophthalmology; Theresa M. and Wayne M. Caygill, MD, Distinguished Professor and Chair, Department of Ophthalmology, University of California, San Francisco, CA

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Katherine M. Hammitt, M.A., Vice President, Medical and Scientific Affairs, Sjögren's Syndrome Foundation, Reston, VA

Dr. McLeod said that the American Academy of Ophthalmology is supportive of serious initiatives that search for solutions to large, intractable public health problems. Patients rank vision loss as one of their greatest fears; from a societal perspective, the cost of caring for vision disorders is enormous. Irreversible causes of blindness, such as macular degeneration, diabetic retinopathy, and glaucoma, take a high social toll and remain ripe for innovative treatments. Although ophthalmology has experienced many recent advances for treating macular degeneration, diabetes, and gene therapy, the pathway to new therapies has relied on the convergence of high-risk, costly, and complex multidisciplinary research methods. Funding multidisciplinary groups with a single purpose can be especially powerful for translational science. The top therapeutic challenges lie at the intersection of cellular and molecular biology, biochemistry, neuroscience, engineering, and surgical implementation. The dynamic and collaborative ophthalmology community will benefit from the formation and funding of ARPA-H. The right initial targets will balance risk, cost, complexity, and impact. NIH will be a good home for ARPA-H, because NEI has been an organizing force for collaboration and coordination within the ophthalmology community.

Dr. McMahon suggested several topics that could be used to create ARPA-H projects. Collaborative groups from academia, industry, and NIH could join efforts to extend current technologies and AI to develop solutions for patients with visual impairments. ARPA-H researchers could use optical coherence tomography to study human eye biomarkers for the detection, diagnosis, and monitoring of neurodegenerative diseases and the effectiveness of treatments for these conditions. Vision screening for children and adults, especially in underserved areas, could be enhanced using technology and partnerships between academia, industry, and NIH. ARPA-H could also help meet the need for minority providers in the health care professions.

Dr. Yerxa said that the Foundation Fighting Blindness fully supports the development of ARPA-H, because funding translational science would complement the work done in NIH's basic science programs. Cross-cutting, translational projects in neuroprotection and regeneration would have a significant impact beyond retinal disease, extending to other types of brain research. Dr. Yerxa suggested that, like salamanders, humans should be able to regrow their eyes. Whole eye transplants should be possible. Affordable and

accessible gene therapy manufacturing, testing, and storage libraries are current gaps in the field. The speed and cost of genetic testing is lacking and a source of disparity. Many useful and useable products are currently too hard, expensive, and time-consuming to produce, which also makes them inaccessible. To ensure future success, new project funding should be time- and milestone-based, focus on applied work rather than hypotheses, and include a high level of accountability. Many methods have been used to accelerate high-priority projects, and the Foundation Fighting Blindness has found funding early-to-late translational projects to be a successful model. New legislation that could complement ARPA-H has been drafted. H.R.3437, the LOANS for Biomedical Research Act, would require the Secretary of Health and Human Services to guarantee "BioBonds" to provide funding for loans to eligible biomedical companies and universities to carry out clinical trials approved by the Food and Drug Administration (FDA) and for other purposes.

Dr. Denneny said that ARPA-H projects would ideally have an impact across broad populations, increase access and quality of life, and have a positive effect on interrelated problems or unrelated diseases. This goal is well-matched with the treatment of subclassifications within the broader context of hearing and balance disorders. Effective AI, nerve repair, and hair cell regeneration projects could assist with the development of a common platform and better devices for hearing aid technology. Nerve protection projects could help prevent damage from noise, medications, and chemicals. Projects that address immune-related diseases and multisystem issues would affect multiple head and neck conditions, including sinusitis, asthma, hearing loss, balance disorder, dermatitis, Sjögren's syndrome, and head and neck cancers, among others. Current gaps include the lack of a comprehensive and coordinated approach to research and development projects, low rates for the sharing of key resources, and prohibitive FDA policies. Commercialization challenges are centered on long grant timelines, peer review delays, and product liability concerns. Successes have occurred when industry and government teams have worked together from the earliest stages of project design and development. Clinical data registries have been successful for building resources, increasing communication, and reducing conflicts of interest. Subject matter experts are excellent leaders for creating efficiency and speed from initial idea to project completion. Beyond addressing hearing and balance disorders, funded projects would reach patients with Alzheimer's disease, dementia, and peripheral and cranial nerve deficits.

Mr. Regan expressed support for ARPA-H on behalf of audiologists and speech language pathologists. Two priority areas for ARPA-H—Alzheimer's disease and amyotrophic lateral sclerosis (ALS)—significantly affect effective communication. A growing body of literature suggested that adults with disabilities face poorer health and medical outcomes and greater challenges accessing health care, locating medical providers, and receiving high-quality routine care. This is particularly true for people with communication disorders and speech, language, and voice disabilities, who often forego medical care due to the high cost and low availability of services. There are large disparities in care between minority and non-minority patients with communication disorders, due to unrecognized clinical needs, systemic racism in the health care system, and provider bias. Providers often lack skills and the appropriate attitude for communicating with people living with communication disorders, and this deficit negatively affects health outcomes. Most health systems are poorly equipped to serve people with hearing loss. Individuals

with communication disorders must provide input into all research projects to make those projects useful and effective. ARPA-H can help people with communication disorders by creating use-driven research models that solve practical problems and develop solutions with multiple applications, developing ways to better disseminate and implement research findings, expanding the research workforce with scientists and researchers from diverse and underrepresented populations, and coordinating collaboration with diverse public and private stakeholders.

Ms. Kelley said that the Hearing Loss Association of America strongly supports the development of ARPA-H to help treat and mitigate hearing loss, a major disrupter to life. Hearing testing in people age 50 and over should be mandatory. Novel research funding could come from non-NIH departments that benefit from medical research. For example, if cochlear implants help reduce the cost of education, then joint research funding would come from the Department of Education. Funding for hearing loss co-morbidities, such as depression and dementia, could also contribute to hearing loss research. Video conferencing platforms could be used to collect informative data on hearing loss. Patient involvement, or including people who live with hearing loss daily, is a critical part of all stages of translational science. The hope is that ARPA-H research will truly benefit people with hearing loss. Industry and academic collaboration is key to the success of ARPA-H. The interface between commercial and academic research is sometimes hampered on the academic side by individualistic IRBs, onerous contracting procedures, licensing and patenting policies, and conflict-of-interest policies. Companies hesitate to conduct multisite trials when each site has these different nuances.

Dr. Perry said that cleft palate is the most common birth defect in the United States. Its resulting hyper-nasal speech leads to a continued need for speech therapy, multiple surgeries (with related negative consequences and sequelae), an increased burden of care, and increased health care costs. Transformative research to accelerate advances in this field is needed to reverse the stagnant rate of birth defects. Care for children with cleft palate currently creates a burden of limited access, because interdisciplinary care teams are unavailable in rural areas. Conducting research to address this gap would fill an unmet need. Creativity beyond the provision of telehealth services is needed, as are solutions for addressing equity of care. ACPA's broad goals include advancing research that transforms how patients with cleft palate are treated, including the development of presurgical planning tools to improve surgical outcomes and the reduction of barriers to receiving comprehensive care.

Dr. Fox said that AADOCR was enthusiastic about the proposal to create ARPA-H, especially if it had the ability to address several intractable problems in dental, oral, and craniofacial research. There are 5 specific research areas that could benefit from inclusion in ARPA-H. The biologic mechanisms, genetic pathways, and environmental input for cleft palate and gene-based therapies for treating cleft palate need further study. Early detection and treatments for oral cancer and oropharyngeal cancer, especially those caused by human papillomavirus, are especially important for children and young adults. Dental caries and periodontal disease are a public health problem, especially in the context of the health disparities that surround these conditions. Bold and innovative approaches are needed to disrupt these diseases, using deeper knowledge of biologic pathways, environmental and societal influences, and social determinants of health. A

systems biology approach with multiple omics technologies, bioinformatics, and data acquisition and analyses has only just begun to be used in the study of oral diseases. Applying AI and machine learning to electronic health records could reveal a deeper understanding of the relationship between oral disease and other diseases. Studying mucosal defenses, including physical barriers and secretions from associated glands, and developing molecular maps of mucosal tissue would increase our understanding of these systems and help fight diseases like COVID-19 and AIDS. Finally, disruptive advancement is needed in the design and fabrication of new and smart dental materials.

Ms. Hammitt said that the Sjögren's Syndrome Foundation was excited about the potential for ARPA-H to transform research for diseases like Sjögren's. The concept of using cross-cutting themes to study disease and the "what, why, and how" approach—rather than looking at single diseases with outdated scientific definitions—is awe-inspiring. COVID-19 has illuminated intriguing areas that are ripe for investigation across many disease fronts, and the Sjögren's Syndrome Foundation would like to see mRNA vaccines investigated for the treatment of autoimmune disease. Further advancement is also needed of the increased recognition of dysautonomia and the role it plays in many diseases, including Sjögren's, by causing fatigue, depression, and oral and ocular dryness. "Brain fog" is another major problem with long-term COVID-19 that also occurs in autoimmune and other diseases where multiple diverse pathophysiological pathways involve the brain; the nervous, endocrine, and immune systems all converge. Perhaps ARPA-H could also help speed the development of gene therapy and gene transfer to determine how to safely regenerate damaged glands. In Sjögren's, damaged and dysfunctional salivary, lacrimal, and other glands lead to a major burden on quality of life. Wearable devices could be used to record symptoms and disease repercussions to improve clinical management and clinical trial success. Biomarkers and the microbiome are emerging fields that affect many chronic conditions and diseases, including Sjögren's.

Discussion

- *When it comes to priority setting, how would ARPA-H assess and decide on the many unmet needs in health care today? Which problems will ARPA-H work on first?* Dr. Schwetz said that ARPA-H's priority setting will be informed by multiple sources, including stakeholders in academia, patient advocacy groups, and industry. The prioritization process is still being developed. Like DARPA, ideas will primarily be generated through the program managers.

- *Many federal agencies are involved in research and development for science. How will ARPA-H prevent silos from forming and ensure that the best ideas from the federal government are brought forward?* Dr. Schwetz said that ARPA-H will coordinate with all NIH Institutes and Centers (ICs) and a variety of agencies across HHS, DARPA, ARPA-E, and others in an interagency working group. This working group will help establish clear mechanisms for cooperation across the federal government, because this communication and cooperation is a critical part of the effort. Dr. Tabak said that a similar small group of IC directors will consider these concerns as they relate to NIH. A high-level interagency committee

of leaders may be formed after ARPA-H is launched.

- *How can dentists become a more integral part of the medical community via ARPA-H's efforts to help patients, including those with complex medical issues?* Mr. Bronstein said that dentists are frontline responders for many patients, especially in parts of the country where access to specialists is limited. He asked whether dentists could play a larger role in collaborating with ARPA-H. Dr. D'Souza said that this multifaceted issue would require a multi-pronged approach. The structural barriers are obvious. Creating integrated health records that allow any health care provider to see a patient's entire chart is an important way to prevent and diagnose conditions and would be an opportunity for ARPA-H. There are also social determinants of health and structural barriers in society that need to be addressed. Dr. D'Souza said that she was not sure whether prevention would be a theme for ARPA-H, but she hopes that it will be considered. Using technology wisely to reach populations that have difficulty accessing care would be a useful theme. There are also many molecular mechanisms that are shared between dental care and multiple diseases and conditions.

- *Who will lead ARPA-H and how will they be appointed?* Dr. Schwetz said that the appointment process is still being considered. It may be a presidential appointment or an appointment by the HHS Secretary, which is similar to the way that NIH IC directors are chosen. The first person chosen will create the culture for the organization and set the stage for the next several years. The culture of ARPA-H will be a critical part of its mission. The new director is likely to be a thoughtful and bold leader with experience in industry, academia, and elsewhere and will promote an innovative environment. They will be a well-rounded expert and inspiring leader who also empowers others to lead.

- *How important and transformative would it be to develop a portable ocular imaging device?* Dr. Chiang said that imaging technologies have transformed how physicians provide eye care. These devices are usually located in doctor offices, but the care model has begun to shift to the home. The technologies can be made into home devices, but manufacturers are reluctant to build the devices without a market in place—a chicken-and-egg situation.

Closing

Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, NIH

Dr. Tabak thanked participants and attendees for their interest in ARPA-H. ARPA-H is a work in progress, and OSTP and NIH will be hosting additional listening sessions to continue gathering information to help guide its establishment. Dr. Tabak invited attendees to send comments and questions to the ARPA-H comment box (ARPAHcomments@nih.gov) and to visit the ARPA-H webpage.