U.S. Department of Health and Human Services (HHS)
National Institutes of Health (NIH)
Office of the Director (OD)
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

Council of Councils Meeting
January 27–28, 2022

Meeting Minutes

Day 1

I. CALL TO ORDER AND INTRODUCTIONS

James M. Anderson, M.D., Ph.D., Director, DPCPSI, welcomed participants, NIH staff members, and members of the public to the meeting of the Council of Councils. The virtual meeting began at 10:00 a.m. on Thursday, January 27, 2022. The meeting attendees are identified below. Dr. Anderson noted that Ms. Megan O'Boyle, Drs. Paul Kenny and Sachin Kheterpal were unable to attend. He recognized two new members Drs. Karen Johnston and Kent Lloyd. He also acknowledged the retirement of Dr. William T. Riley, former Director of the Office of Behavioral and Social Sciences Research (OBSSR), and welcomed the Acting Director of OBSSR, Dr. Christine Hunter. Dr. Anderson then reviewed the day's agenda.

A. Attendance

1. Council Members

Council Members Present

Chair: James M. Anderson, M.D., Ph.D., Director, DPCPSI
Executive Secretary: Robert W. Eisinger, Ph.D., Senior Scientific Advisor, DPCPSI
Maria L. Acebal, J.D., The Aspen Institute, Washington, DC
Maria Rosario G. Araneta, Ph.D., M.P.H., University of California, San Diego, La Jolla, CA
Kristin Ardlie, Ph.D., Broad Institute of MIT and Harvard, Cambridge, MA
Linda Chang, M.D., FAAN, FANA, FISMRM, University of Maryland School of Medicine, Baltimore, MD
Graham A. Colditz, M.D., Dr.P.H., M.P.H., Washington University School of Medicine in St. Louis, St. Louis, MO
Andrew P. Feinberg, M.D., M.P.H., Johns Hopkins University School of Medicine, Baltimore, MD
Rick Horwitz, Ph.D., Allen Institute for Cell Science, Seattle, WA
Patricia D. Hurn, Ph.D., R.N., University of Michigan, Ann Arbor, MI
Kevin B. Johnson, M.D., M.S., FAAP, FACMI, FIAHSI, FAMIA, Annenberg School for Communication, University of Pennsylvania, Applied Informatics, University of Pennsylvania Health System, Philadelphia, PA
R. Paul Johnson, M.D., Emory University School of Medicine, Atlanta, GA
Karen C. Johnston, M.D., M.Sc., University of Virginia, Charlottesville, VA
Gary A. Koretzky, M.D., Ph.D., Weill Cornell Medical College, New York, NY
Richard D. Krugman, M.D., University of Colorado School of Medicine, Aurora, CO
Jian-Dong Li, M.D., Ph.D., Georgia State University, Atlanta, GA
Kevin C. Kent Lloyd, D.V.M., Ph.D., University of California, Davis, Davis, California

Edith P. Mitchell, M.D., FACP, FCPP, Thomas Jefferson University, Philadelphia, PA
Charles P. Mouton, M.D., M.S., M.B.A., The University of Texas Medical Branch at Galveston, Galveston, TX
Rhonda Robinson-Beale, M.D., UnitedHealth Group, Minneapolis, MN
Susan Sanchez, Ph.D., The University of Georgia, Athens, GA
Jean E. Schaffer, M.D., Joslin Diabetes Center, Harvard Medical School, Boston, MA
Scout, Ph.D., National LGBT Cancer Network, Pawtucket, RI
Anna Maria Siega-Riz, Ph.D., M.S., University of Massachusetts Amherst, Amherst, MA
Russell N. Van Gelder, M.D., Ph.D., University of Washington, Seattle, WA

Council Members Absent

Paul J. Kenny, Ph.D., Icahn School of Medicine at Mount Sinai, New York, NY
Sachin Kheterpal, M.D., M.B.A., University of Michigan Medical School, Ann Arbor, MI
Megan O'Boyle, Phelan-McDermid Syndrome Data Network, Arlington, VA

2. Liaisons

Joseph M. Betz, Ph.D., Acting Director, Office of Dietary Supplements (ODS), DPCPSI
Janine A. Clayton, M.D., Director, Office of Research on Women's Health (ORWH), DPCPSI
Maureen M. Goodenow, Ph.D., Director, Office of AIDS Research, DPCPSI
Susan K. Gregurick, Ph.D., Director, Office of Data Science Strategy (ODSS), DPCPSI
Franziska B. Grieder, D.V.M., Ph.D., Director, Office of Research Infrastructure Programs (ORIP), DPCPSI
Christine M. Hunter, Ph.D., Acting Director, OBSSR, DPCPSI
Christopher J. Lynch, Ph.D., Acting Director, Office of Nutrition Research, DPCPSI
David M. Murray, Ph.D., Director, Office of Disease Prevention (ODP), DPCPSI
Karen L. Parker, Ph.D., M.S.W., Director, Sexual & Gender Minority Research Office (SGMRO), DPCPSI
George M. Santangelo, Ph.D., Director, Office of Portfolio Analysis (OPA), DPCPSI
Marina L. Volkov, Ph.D., Director, Office of Evaluation, Performance, and Reporting, DPCPSI
Elizabeth L. Wilder, Ph.D., Director, Office of Strategic Coordination, DPCPSI
David R. Wilson, Ph.D., Director, Tribal Health Research Office (THRO), DPCPSI

3. *Ex Officio* Member Absent

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

4. Presenters

S. Sonia Arteaga, Ph.D., Program Officer, Environmental influences on Child Health Outcomes (ECHO) Cohorts
Marie A. Bernard, M.D., Chief Officer for Scientific Workforce Diversity, NIH
Joseph M. Betz, Ph.D., Acting Director, ODS, DPCPSI
Arthur L. Castle, Ph.D., Program Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
Mark Caulder, M.S., M.P.H., Biobank Program Director, *All of Us* Research Program
Janine A. Clayton, M.D., FARVO, Director, ORWH, DPCPSI
Anthony S. Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases (NIAID) and Chief Medical Advisor to the President
Joshua A. Gordon, M.D., Ph.D., Director, National Institute of Mental Health (NIMH)
Susan K. Gregurick, Ph.D., Director, ODSS, DPCPSI

Richard J. Hodes, M.D., Director, National Institute on Aging (NIA)
Helene Langevin, M.D., Director, National Center for Complementary and Integrative Health (NCCIH)
David M. Murray, Ph.D., Director, ODP, DPCPSI
Eliseo J. Pérez-Stable, M.D., Director, National Institute on Minority Health and Health Disparities (NIMHD)
George Santangelo, Ph.D., Director, OPA, DPCPSI
Lawrence A. Tabak, D.D.S., Ph.D., Acting Director, NIH
Jennifer Troyer, Ph.D., Program Director, Division of Genome Sciences, National Human Genome Research Institute (NHGRI)
David Wilson, Ph.D., Director, THRO, DPCPSI
Shannon Zenk, Ph.D., M.P.H., R.N., F.A.A.N., Director, National Institute of Nursing Research (NINR)

5. NIH Staff and Guests

In addition to Council members, presenters, and Council liaisons, others in attendance included NIH staff and interested members of the public.

B. Announcements and Updates

Robert W. Eisinger, Ph.D., the executive secretary for the NIH Council of Councils, reviewed the following:

- Council members are Special Government Employees during the days of Council meetings and are therefore subject to the rules of conduct governing federal employees.

- Each Council member submitted a financial disclosure form and conflict-of-interest statement in compliance with federal requirements for membership on advisory councils. The financial disclosures are used to assess real and perceived conflicts of interest, and Council members must recuse themselves from the meeting during discussions of any items for which conflicts were identified.

- Time is allotted for discussion between the Council members and presenters, but time for comments from other meeting attendees is limited. The public may submit comments in writing; instructions are available in the *Federal Register* notice for the meeting, which was published on December 14, 2021.

- Minutes from the September 17, 2021, meeting are posted on the DPCPSI website. The minutes from this meeting also will be posted there.

C. Future Meeting Dates

The next Council meeting is scheduled to be held virtually on May 19–20, 2022.

II. UPDATES FROM THE NIH

Lawrence A. Tabak, D.D.S., Ph.D., the Acting Director of the NIH, provided NIH-wide updates. Under the current continuing resolution, the NIH does not yet have a 2022 budget. The NIH budget has continued to rise steadily in recent years, and the NIH has received numerous emergency supplemental funds and has funded a broad selection of initiatives related to the COVID-19 pandemic. These efforts now are moving toward preparedness for the next potential pandemic. Dr. Tabak also outlined leadership

changes at the NIH, including his current role as Acting Director and Dr. Tara Schwetz as Acting Principal Deputy Director.

Dr. Tabak provided an update on the Advanced Research Projects Agency for Health (ARPA-H), which requires congressional action to proceed. The draft mission is, "To benefit the health of all Americans by catalyzing health breakthroughs that can't be readily accomplished through traditional research or commercial activity." The approach to ARPA-H will leverage strategies pioneered by the Defense Advanced Research Projects Agency that also have been adapted by other agencies. ARPA-H is linked to the NIH to take advantage of the existing knowledge, expertise, and infrastructure, but ARPA-H also must develop its own culture and organization. Innovative and collaborative ideas will be sought, and a diverse group of individuals will be included. All ARPA-H efforts will operate under time urgency, which will require low administrative burden. Dr. Tabak emphasized the need to maintain transparency with all stakeholders and foster ongoing bidirectional engagement. ARPA-H efforts also will need to be allowed to fail early and accept risk as a central precept, and program managers will need to be independent but accountable for reaching goals. The budget has not yet been determined by Congress, but Dr. Tabak assured the Council that the NIH is preparing for each budget possibility. Authorization is needed to begin ARPA-H, and several pathways to authorization have been proposed. A summary report of stakeholder engagement meetings discussing ARPA-H is available through the White House Office of Science and Technology Policy. Dr. Tabak pointed out that the initial engagement sessions form the foundation of the project but will need to continue as ARPA-H develops.

Dr. Tabak explained NIH's diversity, equity, inclusion, and accessibility (DEIA) efforts, continuing the commitment of previous NIH Director Dr. Francis S. Collins. The UNITE Initiative, which includes staff representing every Institute and Center (IC), received 1,100 responses to a request for information (RFI) on how the NIH can advance DEIA and health disparities research. Three themes emerged from these responses: the need to commit to action beyond words; the importance of enhancing existing programs and activities; and the reminder that ending structural racism requires a multifaceted approach and, in some instances, changes to long-standing approaches, practices, and cultural norms. Respondents also pointed out the need to ensure accountability, sustainability, and transparency. Dr. Tabak noted that a small number of respondents denied the existence of issues related to structural racism or other forms of bias, inequitable treatment, or discrimination within the NIH or wider biomedical workforce. He recommended that the NIH engage with these individuals to understand their perspectives and work to help them understand the perspectives of the NIH in this area. The UNITE group also has been holding 90-minute external listening sessions, which have been well attended and fostered robust discussions, demonstrating the high level of interest in DEIA.

Dr. Tabak highlighted the Common Fund initiative Transformative Research to Address Health Disparities and to Advance Health Equity, which has released two funding opportunity announcements (FOAs) to date. The goal of this initiative is to support unusually innovative research projects that, if successful, would have a major impact on developing, disseminating, or implementing innovative and effective interventions that reduce, prevent, or eliminate health disparities and health inequities. Dr. Tabak also reviewed the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) Awards, which support hiring a cohort of individuals devoted to creating cultures of inclusive excellence in the extramural community. The program will include multilevel mentoring and professional development opportunities, but it must be integrated with institution-wide systems that address biases and faculty equity and work-life balance. A Coordination and Evaluation Center will review the program at the faculty and institutional level, and best practices will be shared as evaluations become available.

Dr. Tabak pointed out that gender bias persists in the biomedical research workforce despite some progress and emphasized the need to redress this more aggressively. Additionally, 58 percent of women among academic faculty and staff report experiencing harassment, with rates even more pronounced for

women of color. Barriers throughout the career span cumulatively increase these gender disparities, and this range of issues requires consistent and sustained substantive action. Dr. Tabak highlighted several strategies to mitigate gender bias at the NIH and funded institutions.

The NIH has been working to ensure that funding is awarded exclusively on the merit of the scientific proposal and that review committees are aware of potential gender bias. The Center for Scientific Review (CSR) has been piloting multistage, partial double-blinded review of R01 applications, has formed a working group of their Advisory Council, and has removed individuals who have been accused of sexual harassment from review committees. Reviewer demographic data have been published, and bias awareness training has been provided for reviewers. CSR also provides systems for reporting any concerns about the fairness of a review.

The NIH equates sexual harassment to scientific misconduct and uses similar mechanisms for reporting, investigation, and adjudication. Reporting requirements are in place for extramural investigators who are removed or disciplined in response to concerns about harassment, bullying, retaliation, or hostile working conditions. NIH's definition of a safe work environment now explicitly includes "free of harassment" as a condition of all awards, which gives the NIH the ability to intervene as needed. The NIH has strengthened its policies on preventing and addressing harassment, and it also has centralized the reporting and inquiry process and has included options for anonymous reporting. The NIH policy statement on personal relationships also has been clarified, and information for contractors has been added to the statement.

NIH's intramural program now has guidelines for hiring scientific and clinical directors that include best practices to ensure more diverse hiring, and every search committee for tenure-track, tenure, and senior scientist positions must include a DEIA representative. An NIH Equity Committee has been formed to assess hiring, review resource allocation upon hiring, and identify promotion trends. An NIH Distinguished Scholars Program has been developed to support a group of individuals with a documented dedication to diversity. A recruitment tool has been developed to help identify strong candidates from diverse backgrounds, and Dr. Tabak noted that this tool helps a search committee expand individual committee members' connections to better represent the true pool of applicants. Conferences should include speakers who are men and women, or a justification for a single-gender symposium should be provided. Each conference needs to have a code of conduct, including a clear plan of action to address harassment that occurs at a meeting.

The NIH also has taken steps to address challenges related to family responsibilities, including support for childcare, research continuity and investigator retention efforts in response to qualifying life events or other family responsibilities, and adjustments to appointment status or percent effort in response to unique family circumstance. Dr. Tabak added that a manuscript expanding on NIH's efforts to address gender bias is expected to be published this year.

Discussion Highlights

- When asked about success metrics for NIH's efforts toward greater inclusiveness in the biomedical sciences, Dr. Tabak agreed that both quantitative and qualitative assessments are needed to ensure that progress is occurring and assured the Council that assessments will be conducted. Council members also suggested the need for flexibility given the evolving nature of this concept and requested updates at future Council meetings.
- In response to a question about NIH's pandemic preparedness efforts, Dr. Tabak commented that the COVID-19 pandemic has illuminated the interdependence of each part of the HHS, particularly in regard to emergency response. The future of the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) program is under discussion; industry partners have indicated a desire to maintain connections and readiness for future emergencies. The NIH

also is working to prepare for both future SARS-CoV-2 variants and potentially dangerous pathogens in other viral families. Preparedness efforts will be included in the 2023 budget request.

- When asked about expansion of DEIA projects—such as FIRST—Dr. Tabak commented on the effectiveness of partnerships with industry and foundations related to pandemic response efforts, noting that additional partnerships can expand NIH's capacity to improve inclusiveness and take advantage of renewed interest in this area. Dr. Tabak added that the FIRST program supports cohorts at only a small number of institutions, so new partners could help expand the program. Dr. Anderson proposed providing an update on FIRST at a future Council meeting.
- In response to a question about enforcement of harassment policies at extramural institutions, Dr. Tabak explained that because harassment-free workplaces are required in the terms and conditions of grants, the NIH can engage with the leadership of an institution if harassment is suspected. Although some institutional representatives may try to deflect such investigations, the NIH receives information from many sources and will work closely with institutions to replace individuals while protecting the program and the people within it.
- When asked about implementation research for COVID-19 strategies, Dr. Tabak pointed out that some of the emergency funding has been used to engage underrepresented groups and groups from marginalized communities, particularly in clinical trials and vaccine acceptance. This community-based effort is led by the NIMHD and engages with trusted organizations already working with these communities on other projects. These organizations worked to disseminate information, encourage participation, and answer questions about safety and efficacy. Dr. Tabak noted that the pandemic crystallized the importance and effectiveness of such community-led approaches, which should be used in the future for other kinds of initiatives.
- Council members suggested including speed of response in the metrics for NIH initiatives—such as UNITE and sexual harassment prevention—given the success of the rapid COVID-19 responses. Publicizing these results, in line with NIH's commitment to transparency, would show that the NIH supports these efforts and the significant changes they require. Dr. Tabak pointed out that the UNITE Initiative is publishing data as they become available, including detailed demographics of the NIH workforce and grantee population; granular examination of the demographics as a function of time can be added.

III. THRO UPDATE: DRAFT NIH TRIBAL CONSULTATION POLICY

David Wilson, Ph.D., Director of THRO, reported on the draft NIH Tribal Consultation Policy. Since the United States recognizes American Indian/Alaska Native (AI/AN) tribes as sovereign nations, federal programs and services that benefit AI/AN populations are based on this unique government-to-government relationship. The federal government recognizes 547 tribal nations, each with its own culture, language, government, and history. Tribal consultation is an enhanced form of communication that emphasizes trust, respect, and shared responsibility, as well as open communication in the development of policies, programs, and initiatives. The federal priorities for tribal consultation have been reaffirmed through multiple administrations, including a 2021 Executive memorandum that emphasizes respect for tribal sovereignty and the need for regular, meaningful, and robust consultation with tribal nations.

THRO was established in 2015 and serves as a central hub for coordinating tribal health research and AI/AN capacity building across the NIH, including gathering meaningful input from tribal communities on NIH research policies, programs, and priorities and working to increase engagement and tribal interest in participating in NIH's research activities. THRO ensures that NIH adheres to the NIH Guidance on the Implementation of the HHS Tribal Consultation Policy; however, the NIH Tribal Advisory Committee, which includes tribal leaders across the country, suggested developing a research-specific policy.

Although funding for biomedical research in AI/AN communities has increased in recent years, the need for a standardized approach to gather input from tribal communities, which are diverse, has become even more apparent. Direct input from communities helps ensure that research programs are developed aligned with community needs.

Tribal communities have become engaged in the research consultation process, which involves activities specifically relevant to the needs of each community. For example, the NIH collaborated with the Centers for Disease Control and Prevention (CDC) and the Indian Health Service on a first-of-its-kind consultation on the opioid crisis in tribal communities. Tribal consultations helped provide guidance on the initial COVID-19 priorities of each community, and an upcoming consultation on the National COVID Cohort Collaborative will increase NIH's ability to assist tribal communities assess how the pandemic is progressing in their communities, as well as monitor other health disparities. As a broad range of issues requires support from data-driven research, tribal consultations create opportunities for tribes to provide direct input on how programs are structured and developed, how they support tribal health, and how they can provide meaningful benefit to the AI/AN communities.

The draft NIH Tribal Consultation Policy respects tribal sovereignty and strengthens the nation-to-nation relationship. It also complements the HHS Tribal Consultation Policy while also focusing on NIH-specific issues. This policy will replace the current NIH guidance, which was written in 2014. To develop the policy, Drs. Tabak, Anderson, and Wilson consulted with all of the tribes in each of the 10 HHS regions. Tribal input was compiled with extensive input from NIH's Tribal Advisory Committee, Office of Science Policy, and Office of the General Counsel, as well as IC directors. The policy is close to final approval and will be implemented on March 1, 2022. THRO will continue to support Institutes, Centers, and Offices (ICOs) that hold consultations or receive a request from AI/AN communities to hold consultations on initiatives that have significant importance for tribal communities.

The consultation process begins when the NIH or a tribal community identifies a critical event and requests a consultation. A letter is sent to the tribal leader, then a consultation or series of consultations is held 30 days after receipt of that letter. Tribal communities also requested that THRO develop a webinar to help prepare communities for the discussion that occurs in the consultation, which has been helpful in familiarizing tribal leaders with the biomedical research process. During a consultation, THRO receives written testimony from tribal nations and compiles the input into a report. Dr. Wilson suggested that the increase in AI/AN research efforts would increase the number of yearly tribal consultations, which will help standardize the process so tribes will know what to expect when they request a consultation. The COVID-19 pandemic has made tribal communities more receptive to virtual engagement, which has allowed THRO to engage more communities on a shorter timescale and increase the opportunities for communities that might not normally have been able to participate in a consultation.

Dr. Wilson emphasized that the highest levels of tribal leadership are equivalent to the highest levels of federal government, explaining that tribal leaders provide input and discussion about the key issues during a consultation. The consultation process has allowed ICOs to shape programs that are more effective in achieving their goals and outcomes. He suggested that the Tribal Consultation Policy would increase transparency in ways that tribal communities have requested previously. Tribal consultation should occur early in the research process and continue throughout the research, and a consultation must be the foundation for how programs or policies are developed. Dr. Wilson emphasized that the new NIH policy will increase the inclusion of tribal communities in biomedical research and improve health equity.

<u>Discussion Highlights</u>

- When asked how education and pipeline issues relate to increasing AI/AN representation among NIH-funded scientists, Dr. Wilson explained that listening sessions help THRO engage

communities on a particular topic. These sessions also provide opportunities for tribal community members to share opinions on important strategies, approaches to recognize tribal sovereignty, strategies to increase tribal involvement, and pathways to develop the next generation of AI/AN biomedical researchers.

- In response to a question about consultation with smaller tribal nations, Dr. Wilson explained that THRO often engages tribal consortia, which represent larger geographic areas and include many smaller tribal communities. These consortia often have direct contacts with the communities and areas they represent, which can help engage smaller communities and a broader range of the communities in an area.

IV. *ALL OF US* RESEARCH CONCEPT: *ALL OF US* RESEARCH PROGRAM BIOBANK—A SCALABLE BIOSPECIMEN RESOURCE (VOTE)

Mark Caulder, M.S., M.P.H., Biobank Program Director for the *All of Us* Research Program, presented a concept for continuation of the biobank. The current plan is for the program to solicit applications under a cooperative agreement mechanism, with $35 million in direct costs available for one meritorious application over a 5-year project period. The *All of Us* mission is to accelerate health research to enable individualized prevention, treatment, and care for all. This mission is supported by nurturing long-term partnerships, catalyzing a healthy research ecosystem, and providing access to a large and rich biomedical data set. This program is based on a team culture built around its core values and plans by 2026 to enroll 1 million participants who reflect the diversity of the United States. The program hopes to expand the data available for the 1 million participants to include surveys, health data streams, a whole-genome sequence, environmental data, and physical measures. Ancillary studies will be launched as a core and scalable capability, allowing expansion of the cohort in delivering phenotypic, lifestyle, environmental, and biologic data. The program aims to incorporate participant return of value into data collections (e.g., return of information to participants on genomics and electronic health records [EHRs]) and establish a diverse global community of 10,000 researchers productively using *All of Us* data.

The *All of Us* biobank is responsible for state-of-the-art standardized methods and technologies for biosample collection, processing, handling, management, storage, and distribution, as well as providing all support services needed for biospecimen collection at scale. Core protocols of the *All of Us* Research Program include informed consent, EHRs, authorizations for data sharing, survey data, data from wearable devices, physical measurements, and collection of biospecimens. When developing the biospecimen portion of the protocol, the program aimed to align the types of biospecimens collected with other large cohort programs to maximize the utility of the specimens. The program has enrolled to date more than 447,000 participants from all 50 states. More than 334,000 of these participants have donated biospecimens and 2.3 million primary specimens have been processed to date. Of the participants who have completed all the initial steps of the program's core protocol, more than 80 percent come from groups traditionally underrepresented in biomedical research, with more than 50 percent self-identifying as racial and ethnic minorities. The program supports a network of more than 245 enrollment sites with couriers who pick up the specimens and prepare them for shipment to the biobank.

The biobank served an active role in the program's COVID-19 serology study, which sought to identify individuals with SARS-CoV-2 antibodies in the early weeks of the pandemic in the United States. Nine of the 24,079 *All of Us* participants included in the study—all of whom had a biospecimen collected between January 2 and March 18, 2020—were seropositive for SARS-CoV-2, with seven positive samples collected before the first confirmed cases in their states of residence. This contributed to growing evidence of low-level SARS-CoV-2 circulation in the United States earlier than previously reported.

Mr. Caulder described the *All of Us* genomics pipeline and return of information. The goal is to allow researchers access to the data through the launch of the *All of Us* Researcher Workbench Control-Tier in

2022. The biobank has generated workflows capable of accommodating numerous genomics partners and their requirements at scale. The biobank has shipped 220,000 DNA samples for whole-genome sequencing and 260,000 DNA samples for microarray genotyping. About 175,000 participants have confirmed their willingness to receive genetic return of results, and about 100,000 have been notified of their genomics reports. Of these, 68,000 have completed the requisite genetics informing loops, and about 67,000 have viewed their genetic ancestry or any trait reports. The return-of-results pipeline will further expand to include health-related and pharmacogenetic results in the future. The biobank is committed to research participant confidentiality, adhering to the commitments made to tribes and AI/AN peoples, outlined in the *All of Us* Research Program Tribal Consultation Final Report; maintaining high-quality, robust, flexible, and secure information systems; providing security and back-up systems and a plan for disaster recovery; and performing all activities with rigorous quality control and quality assurance programs. Mr. Caulder noted that several issues arise when considering how best to scale up the *All of Us* biobank. One consideration involves the sheer number of biospecimens needing to be stored at the biobank. The current biospecimen collection protocols allow the collection of seven blood tubes, a urine tube, and a saliva tube from each participant. These samples subsequently are processed into 30 secondary aliquots per participant. This scheme multiplied out to roughly 33 million tubes stored at the biobank based on the primary collections alone. Specimens arriving at the biobank are accessioned, processed, aliquoted, and stored within 16 hours. The biobank has about 65,000 square feet of dedicated *All of Us* space and utilizes automation at all levels of the sample workflow to achieve a sample throughput rate of roughly 1,200 participants per day. The biobank has a sister site in Jacksonville, Florida, that is used to store roughly a quarter of participants' specimens as a primary off-site location to aid with disaster mitigation.

While the biobank has met the current needs and requirements of the program, programmatic activities over the next 5 years are planned to ensure continued support and achievement of milestones. Long-term goals for the biobank include supporting partner expansion; fully implementing the biospecimen access process for researchers; supporting the development, validation, and evaluation of novel bioassays in various pilot studies; helping plan for and implement programmatic reassessment of participants, including biospecimens; enhancing the withdrawal process for AI/AN participants to allow inter-tribal blessing ceremonies before sample destruction; supporting the biospecimen collection requirements for pediatric enrollment; and the Nutrition for Precision Health ancillary study.

Discussion Highlights

- The discussants, Drs. Kristin Ardlie and Graham A. Colditz, provided their comments. Dr. Ardlie expressed her support for continued funding for the biobank. She noted 4,000 missing genomic sequencing samples in the presentation and asked whether the program was aiming to improve their sequencing protocols. She also asked for clarification regarding biospecimen-related reassessments of the longitudinal cohort, noting that these efforts would be incredibly valuable, but would expand significantly the number of samples housed in the collections. Dr. Ardlie asked if the biobank specimen-processing protocols were open access, which would be helpful in supporting global biobanks. She also asked about the nature of the ancillary studies described for future directions for the biobank, about usage policies associated with the biobank, and about plans for single-cell analysis of the biobank samples.
- Dr. Colditz asked about plans related to the disaster mitigation scheme for the biobank, noting that the current site in Jacksonville, Florida, might be prone to weather-related challenges.
- Mr. Caulder replied that the program aims to be innovative, iterative, and open in terms of process development and future directions. Single-cell sequencing was considered during the conception of the biobank; however, the initial biospecimen collection process was oriented around samples that align well with broad-based, rather than in-depth, research. The program now

is considering integrating single-cell analysis and other novel techniques. The program also has preliminary plans regarding how to use the specimens more efficiently at the *All of Us* scale and how to prepare the database for researchers to mine.

- In response to a question about the long-term vision for the biobank, Mr. Caulder explained that the program aims to be flexible in terms of the number and volume of stored biosamples. Long-term planning includes ensuring that specimens are used, which includes having an access process to enable broader access to the biospecimens in support of advancing science.
- When asked about plans to require that biospecimens acquired during funded research be included automatically in the *All of Us* biobank, Mr. Caulder explained that the program is looking into ways in which they can harness the value of the biobank and expand what it does. Some of these efforts would occur via potential ancillary studies that could ask narrower questions regarding significantly annotated data and biospecimens. Mr. Caulder noted that he will work with both NIH and outside agencies to discuss and share information related to the biobank efforts. The overall goal is to be as open and transparent as possible.
- When asked about linking with other organizations to identify individuals with rare diseases, Mr. Caulder explained that they currently have a large EHR data stream, and that some information could be gleaned from that source or from the whole-genome sequencing. The goal for *All of Us* is to be indicative of the general population, rather than a collection of rare diseases. However, the program is looking actively to partner with other organizations that might be interested in the data.
- In response to a question about collaborations with the National Cancer Institute (NCI) Cancer Centers, Mr. Caulder answered that he is not aware of current specific collaborations with these Centers. *All of Us* and NCI representatives meet regularly and could discuss potential collaborations with the Cancer Centers.

Vote

A motion to approve the *All of Us* Research Program biobank research concept was forwarded and seconded. The motion passed with no abstentions.

V. COMMON FUND FINAL REPORT: NIH COLLABORATORY—HEALTH CARE SYSTEMS RESEARCH COLLABORATORY

Richard J. Hodes, M.D., Director of NIA, provided an overview of the Health Care Systems Research Collaboratory, which was launched in 2012 with the mission to strengthen the national capacity to implement cost-effective, large-scale research studies that engage health care delivery organizations as research partners. The Collaboratory embedded pragmatic clinical trials to bridge research into clinical care. Studies were designed with input from health system stakeholders, and data were collected through EHRs in health care settings. The outcomes were defined based on considerations important to the decision-makers for health care systems, and the interventions were incorporated into routine clinical workflow. These projects also focused on diverse, representative study populations.

The program was organized through the Collaboratory Coordinating Center; demonstration projects were carried out through the ICs. Oversight was provided by a steering committee, as well as an NIH project officer and IC representatives. The Coordinating Center also supported the knowledge repository and several working groups. The working groups—which focus on biostatistics and study design, EHRs, health care systems interactions, patient-centered outcomes, and ethics and regulatory issues—are critical to the operation of the Collaboratory. Each provides expertise across trials, resources for the community, and an administrative framework for the program.

Five requests for applications (RFAs) for milestone-driven awards were issued over the years, each with a UG3/UH3 configuration—which involves a planning year (UG3) followed by evaluation, then a 4-year implementation phase (UH3) if the planning phase is successful. Each funded project included at least three partnering health systems, and these health systems covered most of the country, with 1,100 clinical sites and more than 900,000 participants. Twenty-one projects—90 percent to date—have moved from the UG3 planning year to the full UH3 implementation phase successfully, and nine projects have been completed.

The Collaboratory supports several widely used resources—such as the Living Textbook—which compiles lessons learned about all the dimensions of pragmatic trials and has been accessed by 76,000 users. The Collaboratory also supports popular grand rounds, presentations, and social media accounts, as well as weekly webinars on a wide range of research topics. Additionally, the Collaboratory has published guidance documents and journal articles. All these resources reflect how the Collaboratory and its efforts will remain a focus for research and researchers in this area after the end of Common Fund support.

Helene Langevin, M.D., Director of NCCIH, explained that the path forward for the Collaboratory is a transition from its beginnings as a Common Fund–initiated program, which included centralized operational support for its pragmatic trial demonstration projects, provided by a coordinating center and its core working groups. In 2017, individual ICs joined the Common Fund in providing co-funding for demonstration projects and the Coordinating Center. In 2019, the NIH Helping to End Addiction Long-term℠ (HEAL℠) initiative began providing some funding for the Coordinating Center and demonstration project. Beginning in 2022, the program is now funded entirely by the NIH HEAL Initiative and individual ICs.

The Health Care Systems Research Collaboratory is well recognized in the research community. However, other collaboratories have been created since its inception. The program's upcoming 10-year anniversary offers an opportunity for rebranding to the NIH Pragmatic Trials Collaboratory, reflecting the broad scope of the type of studies funded by this initiative. Pragmatic trials are defined as large-scale trials conducted in the real world that provide evidence for adoption of an intervention in clinical practice. A large group of NIH ICs and Offices (ICOs), have agreed to continue funding the Collaboratory. These supporting ICOs reconsidered areas of focus, added an emphasis on the study of interventions that have evidence for efficacy, but may not be implemented optimally in current health care systems, and an increased focus on how research can help clarify and overcome implementation barriers. A focus on addressing health disparities in health care systems also has been added.

The continuation plan for this Collaboratory includes recompetition using a request for applications (RFA) for the Coordinating Center, a U24 cooperative agreement funding mechanism for 6 years to match the RFA timing for the Coordinating Center and establishing a memorandum of understanding with each of the participating ICOs. The pragmatic or implementation trials RFA was issued in October 2021 with receipt dates in December 2021 and June 2022. These will be fully powered effectiveness trials conducted in at least three health care systems, with a maximum of $1 million per year in direct costs. Most applications funded to date enrolled more than 1,000 participants, and at least two trials enrolled more than 100,000 participants. Dr. Langevin noted that the Collaboratory has transitioned successfully from Common Fund to ICO support, more than 90 percent of projects have transitioned to UH3 clinical trials, and the Collaboratory's demonstration projects have had unparalleled impact on clinical knowledge and practice.

No discussion points were raised.

VI. ODP UPDATE: NEW ODP STRATEGIC PLAN PRIORITY ADDRESSING HEALTH EQUITY

David M. Murray, Ph.D., Director of ODP, presented on a change to the ODP strategic plan. The current plan has six strategic priorities: (1) analysis of the NIH prevention research portfolio; (2) identifying research gaps; (3) improving the research methods used in prevention research supported by the NIH; (4) promoting collaborative research; (5) supporting and managing the Tobacco Regulatory Science Program; and (6) communicating about the work to interested audiences. Previously, three crosscutting themes were used across these priorities: leading causes and risk factors for premature morbidity and mortality; health disparities; and dissemination and implementation research. ODP has chosen to increase the profile of its health disparities activities by changing this from a crosscutting theme to the seventh strategic priority: to promote and coordinate prevention research that addresses health disparities. The first objective under the new priority is to coordinate an NIH-wide effort and develop FOAs, as well as develop and test new interventions and strategies to disseminate existing interventions that address the leading risk factors for death and disability in populations experiencing health disparities. The second objective is to assess the NIH prevention research portfolio related to health disparities to identify research, infrastructure, and training gaps and develop strategies to address those gaps. The third objective is to serve as a resource on health disparities-related prevention research to ICs developing FOAs, convening workshops, and conducting other activities.

ODP decided to increase its emphasis on health disparities in response to the results of its analysis of the NIH prevention research portfolio. The analysis showed that prevention research is about 20 percent of the overall NIH portfolio. Only 3.6 percent of NIH prevention research includes randomized interventions to address a leading risk factor for death or disability in populations that experience health disparities. These risk factors account for 74 percent of the variability in county-level life expectancy, and the associations between socioeconomic status and life expectancy, or race and ethnicity and life expectancy, are largely mediated through these risk factors. Dr. Murray emphasized that social and structural determinants of health are significant contributors to these risk factors. A new team at ODP has been established to support this strategic priority, in line with the dedicated support teams for each of the other six strategic priorities. As the priority evolves, the team will increase in number. ODP already has surveyed leadership and ICOs about partnering to develop and test new interventions and to develop and test new strategies to disseminate existing interventions that address the leading risk factors for death and disability in health disparities populations. This initiative, driven by ICOs and coordinated by ODP, is being planned with the participation of 24 ICOs. Each is interested in various risk factors and related preventive services, as well as specific health disparities populations. ODP asked the ICOs to identify relevant activities already planned or underway and organized four working groups that reflect shared interests: (1) cardiometabolic; (2) alcohol, tobacco, and other drugs; (3) cancer; and (4) and mental health. The cardiometabolic group has begun meeting, and the other groups will organize in the upcoming months. The working groups are encouraged to consider broadly how they can address the leading risk factors for death and disability, as well as the relevant health disparities populations, in their areas of focus. Each group will develop FOAs to support research in these areas, which are anticipated beginning late this fiscal year, with the first awards planned to be made in fall 2023.

Discussion Highlights

- Dr. Murray clarified that the leading risk factors do not encompass all important risk factors. The most common factors are not independent from other risk factors (e.g., physical, sexual, and emotional abuse) so the working groups have been encouraged to consider factors beyond the top 10 and consider broadly about ways to reduce health disparities.

- When asked how ODP plans to integrate the groups when the topics overlap, Dr. Murray explained that the initiative includes a group of advisors from each participating ICO that meets regularly to plan activities and receive progress updates. When working group initiatives seem similar, the advisory group will work to unify these efforts. Additionally, ODP staff co-chair each of the working groups and can identify and encourage such linkage.
- In response to a question about what might be lost by changing health disparities from a crosscutting theme to a strategic priority, Dr. Murray clarified that this change will increase the focus on health disparities. Previously, each strategic priority team was asked to address the crosscutting themes in their activities; the new team will be able to now focus on health disparities exclusively and collaborate with the other strategic priority teams to increase their efforts in this area. The remaining crosscutting themes will continue to be areas of focus in all seven priorities.

VII. COMMON FUND CONCEPT CLEARANCE: COMMUNITY PARTNERSHIPS TO ADVANCE SCIENCE FOR SOCIETY (VOTE)

Janine A. Clayton, M.D., FARVO, Director of ORWH, introduced the concept clearance for the Community Partnerships to Advance Science for Society (ComPASS) program. She emphasized that community-engaged science has emerged as a core principle for evidence-based approaches to address the complex issues that affect the health of marginalized populations. An understanding of the burden of poor health, education, or other social outcomes is necessary to improve the quality and outcomes of health promotion activities, disease prevention initiatives, and research studies. By building community trust through a collaborative framework, researchers can gain a more nuanced understanding of health issues in affected communities and increase the relevance of science questions examined for the affected individuals.

Shannon Zenk, Ph.D., M.P.H., R.N., F.A.A.N., Director of NINR, explained that ComPASS reflects the efforts of subject matter experts from multiple NIH ICOs, in addition to the NIH Common Fund, and it is responsive to the community and other external stakeholders. Dr. Collins was the first NIH director to commit to ending structural racism at the NIH. The UNITE initiative's Committee N proposed a new Common Fund program to marshal resources for research on health disparities, minority health, and health equity. The two proposed program goals are to (1) facilitate and implement a cross-IC framework for health equity structural intervention research, and (2) catalyze, deploy, and evaluate community-driven health equity structural interventions that leverage multisector partnerships to reduce health disparities.

Dr. Zenk emphasized that health disparities are pervasive, persistent, and seemingly intractable. Researchers must examine the upstream structural drivers of these disparities. Structural factors can include such sectors as housing, transportation, education, business, the food system, and law enforcement. Limited NIH research to date has focused on health equity or structural interventions, and even less research has examined specific impacts on health disparities or health equity. ComPASS will utilize a solution-oriented complementary set of disease-agnostic initiatives designed to advance health equity through community-driven structural interventions. Structural interventions benefit from partnerships among diverse stakeholders across sectors, including community organizations, businesses, federal agencies, and local and state governments. This investment will advance future health equity research across ICOs by cultivating community trust and partnerships, building research capacity across all partners, enhancing competitiveness for future IC funding, and providing proof-of-concept to spur implementation projects by other partners. The program's focus is consistent with the NIH-wide commitment to end structural racism.

In fall 2021, the Common Fund held eight listening sessions with stakeholders, including community organizations, faith-based organizations, nonprofits, and tribal communities. More than 2,100 individuals registered for the sessions, and more than 500 individuals attended. The sessions reinforced the importance of building and maintaining strong partnerships and establishing trust with communities. The challenge of avoiding health equity research tourism was noted, as well as the importance of fostering mutually beneficial relationships among communities, research organization partners, and other stakeholders. Research capacity–building needs for communities were discussed, and participants noted the importance of innovative public–private partnerships, as well as collaborations between the NIH and other federal agencies, to develop multidisciplinary and multisector partnerships for research on structural interventions. Local-level data and return on investment data also are needed. Dr. Zenk noted that many examples of structural health equity interventions have been identified, and the specific intervention targets in ComPASS will be driven by community priorities. The program partnerships (e.g., with federal agencies) will facilitate rigorous planned experiments of policies and programs as they germinate and are being planned.

Joshua A. Gordon, M.D., Ph.D., Director of NIMH, outlined the proposed ComPASS initiatives. The core of the overall structure comprises a series of community organizations that are conducting structural intervention research in partnership with various stakeholders and are governed by a local Health Equity Research Assembly (HERA). These efforts are coordinated by a national coordinating center, which is guided by a national HERA. The Health Equity Research Hub will bring together community organizations and partnerships to assist with training, research support, and other responsibilities.

The health equity structural interventions will involve multiple partners (e.g., community organizations, academic and other research organizations, public health departments, state and local government, and community members). The partnership will be tasked with developing a local HERA to govern and plan research activities and interpret results. Each intervention will undergo three phases of support. The first phase will focus on providing time to form partnerships, develop scientific questions, plan interventions, and identify outcomes. The second phase will focus on implementing the structural intervention in the community and measuring the outcomes. The third phase will focus on disseminating best practices (e.g., tool kits, publications, and multimedia products).

A coordination center will be formed at the beginning of the project to assist with overall coordination, identification of Common Data Elements, definition of health outcomes, development of capacity building, development of training curricula and programs, establishment of a repository of health equity structural interventions, creation of infrastructure for data sharing, and creation of infrastructure for dissemination and outreach. The coordination center also will develop its own national HERA, which will be composed of interdisciplinary subject-matter experts, representatives of federal agencies and other national partners, policymakers, community organizations, private-sector organizations, and health care organizations. The HERA will partner with the coordination center in governance and facilitation of research and will assist community organizations in identifying local partners. Multiple health equity research hubs will be formed to organize small groups of projects into a collaborative model that will support each project's research, support local training and capacity building, ensure that the collaborations between the community organizations and their partners are conducted efficiently, and ensure that best practices are shared across hubs. The initiative will support the development of 5 hubs to support 25 individual projects.

Dr. Zenk highlighted ComPASS deliverables, which include improved health outcomes (e.g., structural interventions, mechanisms for social determinants of health), capacity building and training (e.g., competitiveness for IC-funded research, diversity and inclusion) a health equity research framework (e.g., common data measures, shared framework, cross-hub cohort, multisector research assemblies), and

dissemination and implementation (e.g., intervention repository, innovative models, training curricula and resources, new knowledge).

Eliseo J. Pérez-Stable, M.D., the Director of the NIMHD, provided additional comments on the program. He noted that NIH IC directors have expressed broad and enthusiastic support for the initiative. He underscored the importance of engaging with communities and fostering transformational change. Several projects for COVID-19 research (e.g., Rapid Acceleration of Diagnostics [RADx] Underserved Populations [RADx-UP], NIH Community Engagement Alliance [CEAL] Against COVID-19 Disparities) have provided information that can inform this transformative effort. The fact that ComPASS proposes starting with funding community organizations is transformative. Dr. Pérez-Stable also noted the value of multisector partnerships.

Discussion Highlights

- The discussants, Drs. Maria Rosario G. Araneta and Rick Horwitz, provided their comments. Dr. Araneta expressed support for the concept, which she noted is ambitious, necessary, and urgent. She underscored the importance of carefully considering appropriate community organizations beyond partnerships that already are established and highlighted the need for study sections to review applications in a nontraditional way. In response to Dr. Araneta's question about study sections, Dr. Pérez-Stable noted that details regarding review still are being discussed. He noted that the team will identify clear criteria, and the process will be as fair and transparent as possible and will address the unique aspects of the program. He added that the RADx-UP and CEAL initiatives have provided valuable insight in this area. Dr. Anderson noted that the program will be classified as other transactions (OT)—not as grants or contracts—which enables greater flexibility in designating a tailored review process.
- Dr. Araneta asked whether the 25 community organizations would be selected based on local health quality equity indices. Additionally, Dr. Araneta asked how the research hubs will be categorized (e.g., geography, intervention type). She also inquired about engagement with the private sector to promote sustainability. She noted that the effects of interventions can take years to measure and suggested coordination with the *All of Us* Research Program. Dr. Gordon explained that the study will take place over the 5 years of the implementation phase of the project. Longer-term assessments would be dependent on the project and migration of the project infrastructure.
- Dr. Horwitz expressed support for the concept, commenting that health equity is an essential goal and that community engagement is often overlooked. He noted the need to consider approaches to maximize the initiative's success. Dr. Horwitz noted that discussion of the budget breakdown would be appropriate. He also asked how the research hubs and applicant organizations will be selected. He emphasized that ComPASS could raise political and philosophical challenges.
- In response to Dr. Horwitz's question about how the research hubs and applicant organizations will be selected, Dr. Gordon stated that the team will play an active role in determining which hubs are necessary to support the projects. The hubs will be matched to partnerships as appropriate. Dr. Pérez-Stable explained that the applications will be assessed for their quality and responsiveness to the FOA. He emphasized the importance of rigor, science, and standardized measurement. He also noted the program will engage awardees throughout the project.
- Council members noted that assessment of productivity will be crucial and asked whether new partnerships would be included to replace any that are unable to complete the full award period. Dr. Anderson explained that the OT mechanism allows the incorporation of new partners as needed throughout the process.

- Council members suggested considering approaches to streamline the review process and expand candidate pools, for which the OT mechanism is well suited.
- When asked whether communities defined by other traits, such as gender identity, could submit proposals, Dr. Clayton responded that the award is open to all communities. Dr. Gordon added that a goal of ComPASS is to develop intellectual infrastructure in community-driven organizations, and the hubs will provide training opportunities for preparing traditional NIH grant applications.

Vote

A motion to approve the ComPASS concept was forwarded and seconded. The motion passed with three abstentions.

VIII. ODSS CONCEPT: EARLY STAGE AND ESTABLISHED BIOMEDICAL DATA REPOSITORIES AND KNOWLEDGEBASES (VOTE)

Susan K. Gregurick, Ph.D., Director of ODSS, presented a concept clearance to continue an initial pilot for support of investigator-initiated biomedical data repositories and knowledge bases as data resources. The program goals are to fill a scientific need or gap, employ and promote good and efficient data management and dissemination, engage the research community to contribute and use data, and govern to address data life cycle and preservation. The pilot has involved several NIH Institutes and a goal to support desired characteristics of data repositories which include both FAIR (Findable, Accessible, Interoperable, and Reusable) and TRUST (Transparency, Responsibility, User focus, Sustainability and Technology) Data Principles.

The pilot fulfills the need for a consistent NIH program to fund repositories as resources; the funds are distributed through a U24 mechanism, and reviews are conducted through the CSR Special Emphasis Panels. To date, 30 applications have been reviewed, of which 7 have been funded. Applicants must address scientific significance; demonstrate community use and engagement; address quality of data, services, and efficiency of efficacy of operations; and document and implement governance processes. Additional requirements include a Project Management Plan, Resource Sharing Plan, and Resource Sustainability Plan. Resources supported though this program have included for example UniProt, BioPortal, and the International Committee on Taxonomy of Viruses.

Changes to the pilot will include an explicit pathway for investigators to submit applications for early-stage resources at a reduced budget. Dr. Gregurick noted that "early stage" is defined as initial development of a data repository or knowledge base with potential for an increase in usage and adoption in the community; "established" refers to high-value data resources that are near or at optimal research community penetration and are critical research resources as demonstrated by their usage, utility, and impact. The reissue would involve inclusion of a domain-specific mission, adoption of best practices, requirements for open metrics, and alignment of support with the stage of the repository of database. The program will lower barriers for data sharing, reduce or eliminate siloes, allow discovery and use of data, optimize efficiency of operations and costs, and disentangle data resources from research projects.

Other efforts—both international and within other federal agencies—support a similar data resource model. The Global Biodata Coalition is soliciting applications for global, core biodata resources. The U.S. Department of Energy Public Resources (PuRe) program also aligns to common themes of long-term sustainability and stewardship. This effort is part of a larger initiative to support a modern biomedical research and NIH data ecosystem; this effort involves strengthening existing NIH data and repositories, supporting data types that might not have a home, and establishing a Data Repository and Knowledgebase Ecosystem.

Discussion Highlights

- The discussants, Drs. Ardlie and Kevin Johnson, provided their comments. Dr. Ardlie pointed out that such knowledge bases help improve data accessibility for the entire research community. She commented that support for early-stage resources is critical, as is the need for advice from the NIH on sustainability to support data resources beyond 5 years. She also emphasized that the community should develop metrics for measuring performance, including those that are comparable across resources.
- Dr. Johnson stated that the concept is appropriate in scope, and its reissue will be valuable. He commented that the U24 mechanism could provide opportunities to explore data labeling regarding data utility, as well as data equity and bias, and suggested adding language on those issues. He also wondered whether the research community could play a role both in developing metrics and moving toward sustainability.
- Dr. Gregurick reiterated the importance of support for early-stage resources, noting that this concept has resonated with the working group. Metrics also have been an important topic of discussion. Dr. Gregurick agreed with Dr. Johnson's suggestion for data labeling, noting that this concept could be incorporated into future FOAs. She also agreed that sustainability is an important topic for future conversations within the research community, and the topic will be explored in the next phase of the pilot.

Vote

A motion to approve the Early Stage and Established Biomedical Data Repositories and Knowledgebases concept was forwarded and seconded. The motion passed with no abstentions.

IX. ODS STRATEGIC PLAN FOR 2022–2026

Joseph M. Betz, Ph.D., the Acting Director of ODS, introduced the ODS strategic plan for 2022 to 2026. The ODS was established to strengthen the knowledge and understanding of dietary supplements by exploring the potential role of dietary supplements as a significant part of the efforts of the United States to improve health care, as well as promoting scientific studies of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions. The ODS conducts and coordinates scientific research within the NIH related to dietary supplements and to the extent to which dietary supplements can limit or reduce the risk of diseases; collects and compiles the results of scientific research related to dietary supplements. The ODS Director serves as the principal advisor to the Secretary and Assistant Secretary for Health; provides advice to the Director of the NIH, the Director of the CDC, and the Commissioner of Foods and Drugs on issues relating to dietary supplements; compiles a database of scientific research on dietary supplements and individual nutrients; and coordinates NIH funding related to dietary supplements.

The ODS Strategic Plan for 2022-2026 was developed using a planning process that included priority setting and program planning by ODS staff with critical input from key stakeholders, the public, and NIH leadership. ODS staff began this process by conducting NIH-wide program reviews, logic modeling, and priority setting, which was used to prepare an initial draft with input from the Federal Working Group on Dietary Supplements. Constituent reviewer groups, including academic researchers, trade associations, and medical societies, provided input on the initial draft document. Public comments will be obtained in response to an RFI on the draft Plan. The final version of the plan will be developed with NIH leadership. Logic models were used to illustrate the responses, activities, and desired outcome and proved to be effective tools for program planning, implementation, management, evaluation, and reporting. Priorities in the plan were developed by identifying key issues, then determining existing knowledge on the nature of the public health issue, nutrient intake levels, measurement availability and reliability, and evidence of

health impacts. ODS staff determined how the Office can address these issues by responding to knowledge gaps, coordinating activities across the NIH, and translating research results for external stakeholders.

The goals of the new strategic plan are to: (1) expand the scientific knowledge base on dietary supplements by stimulating and supporting a full range of biomedical research and developing and contributing to collaborative initiatives, workshops, meetings, and conferences; (2) enhance the dietary supplement research workforce through training and career development; (3) foster development and dissemination of research resources and tools to enhance the quality of dietary supplement research; (4) translate dietary supplement research findings into useful information for consumers, health professionals, researchers, and policymakers; and (5) coordinate and support the development of collaborative initiatives to address gaps in dietary supplement research. Dr. Betz commented that ODS always has engaged in such coordination and plans to add additional structure to these activities.

The first new initiative in the new strategic plan is to establish the NIH Dietary Supplement Research Coordinating Committee (DSRCC) to increase NIH-wide information exchange, communication, collaboration, and coordination on dietary supplements and total dietary intake research and training activities. The DSRCC will provide input on scientific gaps in dietary supplement research and emerging and crosscutting research areas; platforms for collaborative initiatives across NIH and the federal government; dietary supplement programmatic and policy issues; and activities that affect ODS or to which ODS can contribute and coordinate within the NIH and the external dietary supplement research community.

The second new initiative is to increase activities to address diversity and health equity through investigation, communication, and workforce development activities. ODS aims to facilitate, coordinate, and support research that develops a better understanding of nutrient-based health disparities. ODS also plans to support development of a diverse new generation of dietary supplements researchers through training and outreach programs to enhance representation in the workforce.

ODS will expand the coordination, development, and dissemination of analytical methods that can be used to discriminate between plant species, provide descriptions of the chemical constituents associated with biological activities of interest, and advance efforts at ingredient and product standardization. ODS also will collaborate with partners to standardize reporting in federal databases of ingredients in natural supplements. Additionally, ODS has been working with NCCIH to establish an NIH-wide Resilience and Health Research Program. ODS also will develop concepts for future NIH Consortium for Advancing Research on Botanical and Other Natural Products (CARBON) Program initiatives, including convening an expert panel to consider critical gaps and needs in research on chemically complex botanical and other natural products.

Discussion Highlights

- When asked to expand on the concept of resilience. Dr. Betz explained that because ODS is not allowed to work with products intended to treat, mitigate, or prevent disease, i.e., drugs, dietary supplements naturally relate to a focus on health maintenance and wellness. A key factor in this is the body's ability to withstand stress and recover from psychological or physical stressors. ODS established an NIH-wide resilience working group and identified several ICs supported grants studying resilience. This working group is coordinating these efforts and developing a common vocabulary and NIH definition of resilience.
- In response to a question about supplements for protective effects against COVID-19, Dr. Betz explained that no dietary supplements have been shown to be effective against COVID-19 disease. Although it has been speculated that Vitamin D may have protective effects against this

disease, no causality has been established. Other supplements are currently being studied, including herbs traditionally used to supplement the immune system. To date, there has not been any evidence that the use of those herbs for COVID-19 or other conditions has been confirmed. ODS has developed a fact sheet entitled, "Dietary Supplements in the Time of COVID-19," which is available on its website (https://ods.od.nih.gov/factsheets/DietarySupplementsInTheTimeOfCOVID19-Consumer/).

- When asked about drug interactions, Dr. Betz explained that ODS and NCCIH have co-funded several highly meritorious grants submitted in response to RFAs focused on herb–drug interactions.
- In response to a question about providing information to the public on supplement equivalence, Dr. Betz explained that too many combinations of ingredients are possible and too many products are on the market to evaluate individually. He noted that ODS provides tools that allow manufacturers, regulators, and researchers to evaluate materials and follow good manufacturing practice. ODS also encourages researchers in this field of research to follow a product integrity process originally developed by NCCIH.
- Dr. Betz commented that about $55 billion is spent on dietary supplements each year in the United States, and more than 50 percent of consumers use dietary supplements.
- In response to a question about recording use of dietary supplements in EHRs, Dr. Betz noted that hospital systems use different EHR platforms, and some forms do not have fields for dietary supplements. Some hospitals have added to EHR records a dietary supplement option to their list of drugs a person is using. ODS is working with stakeholders to add that option and ensure EHRs can be coordinated. ODS also recommends on its fact sheets that people talk to their health care providers about supplements that they use. ODS provides tools for consumers to capture the supplements they are taking to show to their physicians. Dr. Betz noted that EHRs need to be able to communicate with other systems to ensure that information on a patient's dietary supplements is available to other health care providers.

X. ADJOURNMENT FOR THE DAY

Dr. Anderson adjourned the meeting at 4:13 p.m. on January 27, 2022.

Day 2

I. REVIEW OF GRANT APPLICATIONS

This portion of the meeting was closed to the public, in accordance with the provisions set forth in Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix).[1] Members were instructed to exit the meeting if they deemed that their participation in the deliberation of any matter before the Council would represent a real or perceived conflict of interest. Members were asked to sign a conflict-of-interest/confidentiality certification to this effect. The *en bloc* vote for concurrence with the initial review recommendations was affirmed by all Council members present. During the closed session, the Council concurred with the

[1] For the record, it is noted that members absented themselves from the meeting when the Council discussed applications (a) from their respective institutions or (b) in which a conflict of interest may have occurred. This procedure applied only to applications that were discussed individually, not to *en bloc* actions.

review of 452 ORIP applications with requested first-year direct costs of $327,989,423. No Common Fund applications were reviewed.

II. CALL TO ORDER

Dr. Anderson welcomed participants, NIH staff members, and members of the public to the second day of the meeting and reviewed the day's agenda. The virtual meeting began at 11:15 a.m. on Friday, January 28, 2022.

III. OPA UPDATE: THE INTEGRATED *iSearch* SUITE OF TOOLS: DELIVERING POWERFUL ANALYTICS TO NIH STAFF AND THE PUBLIC

George Santangelo, Ph.D., Director of OPA, provided an update on OPA's *iSearch* tools. One objective in the current strategic plan is to develop and disseminate metrics and standards. OPA's mission— supporting data-driven decision making— requires development of new analytical tools, including those that leverage advances in artificial intelligence and machine learning (AI/ML). The overarching goal is to catalyze attempts to better understand the scientific enterprise and learn how to accelerate progress. The *iSearch* tool (version 2.0), a comprehensive AI/ML-based portfolio analysis platform, has been available within the NIH since 2019. It is being reimagined as *iSearch* 3.0 for NIH and other HHS users, as well as Analytics 1.0 for use by the public. The *iSearch* Analytics will allow external users to access and analyze publicly available data.

The vision of *iSearch* is to provide an intuitive user-centric platform for analytics that must be streamlined to integrate key functions currently available across a range of OPA AI/ML advances and tools into one toolkit that delivers comprehensive portfolio analysis for a wide range of users. *iSearch* must be configurable and provide flexible views and visualizations that allow a wide range of interrogations and analytic activities. The platform also will be scalable and capable of accommodating high demand.

As part of the development process, OPA has been collecting user feedback and conducting market research using leading-edge, industry standard methodology. OPA is leveraging this information to identify other tools and functionalities that are available to users, then integrating the best features of existing tools with new features required by users. The integration of many tools is complex, especially because OPA is adding features and value using internally developed AI/ML.

New *iSearch* will include three features with transformative functionality. The first is a reimagined AI/ML-based topic cluster visualization that will provide a better view of the desired portfolio and will enhance the user's ability to explore research topics and allow more sophisticated searching, filtering, and faceting. Another new feature is person disambiguation, using an AI/ML approach that includes many features from author/ publication entries and NIH applicant records to accurately link scientists to their research outputs. This disambiguation solution performs better than human curation and will be particularly useful when authors with similar names conduct research in similar fields. The third new feature is an expansion of the literature beyond PubMed to initially include preprints and later also to incorporate articles from CrossRef.

Dr. Santangelo reviewed the requirements gathering and design process, which begins with feedback from both internal stakeholders and those in the scientific community. The design process starts with discovery and research; this information is then synthesized and developed into a design strategy. Next is placement and layout design which is critical for making the tool as intuitive as possible and providing functionality as straightforwardly and obviously as possible. Finally, the tool is executed and validated in an iterative process. In the requirements gathering phase, existing relevant tools are analyzed; users are

surveyed to identify their needs, motivations, and expectations; and a subset of users are then interviewed to identify issues with functionality and areas for improvement.

OPA found that users within the NIH care most about search processes, ease of use, integration with other tools, and visualization. For the public tool, OPA released an RFI on how to meet the analytical needs of prospective public users. Most of the respondents to this RFI were from academia, one of the core groups this tool will serve, and many agreed to be contacted for follow-up interviews. OPA has been conducting interviews and user testing with staff from NIH and other government agencies and will continue these processes with public RFI respondents.

Dr. Santangelo pointed out the importance of ensuring that the new tool avoids the weaknesses of existing tools, including paywalls, complex querying, and poor visualization. *iSearch* already incorporates flexibility and filtering, which will be expanded and improved to provide a tool that is flexible, integrated, and easy to use and that returns results quickly with informative visualizations and reliable, high-quality data. Some potential users may be lay members of the public who are scientifically literate and interested in this kind of information, others may be practicing scientists who are exploring a less familiar area, and some users may be members of the metascience community conducting analytics—OPA's goal is to serve all of these groups.

When the requirements-gathering stage is complete, OPA will build, test, and continue the process to update the tool and test it again. Dr. Santangelo emphasized that this will be an iterative feedback loop culminating in the final development and building of the tool. Workstreams in progress include gathering user feedback and implementing a cloud-based, reliable, scalable tool that incorporates leading-edge technology. OPA has a well-elaborated communication plan and defined milestones, and core build functions already have begun. The execution phase will begin soon in anticipation of a beta launch in the summer. OPA hopes that this tool will become a sophisticated yet intuitive platform for analytics.

Discussion Highlights

- In response to a question about collaborations within the NIH, Dr. Santangelo clarified that the core mission of OPA is to improve data-driven decision making across NIH, so OPA works closely with stakeholders and decision makers in the NIH community and consults regularly with NIH staff and members of the public interested in analytical pursuit.
- Dr. Santangelo confirmed the wide range of resources, including FAQs and tutorials, that will be available for the public tool.
- When asked about the possibility of including user-defined metadata in the *iSearch* visualization, Dr. Santangelo commented that OPA is interested in the function, but it is difficult to conduct at scale and not planned for the initial release. Once the tool is in use, OPA can determine how to deliver that type of functionality.
- Council members suggested potential partnerships, such as the Association of American Medical Colleges, U.S. Preventive Services Task Force, and Cochrane Library. Dr. Santangelo noted that the RFI is the only external engagement to date, but OPA can review responses to determine if any of those potential collaborators have submitted feedback.
- In response to a question about the expanded search function, Dr. Santangelo clarified that some organizations do not provide open access to all content, but the tool will at least gather all data from relevant preprint servers that provide full access. Currently, only NIH-funded research is linked through the person disambiguation feature, but over time this feature can be updated to include linkages to research funded by other agencies.

- Dr. Santangelo pointed out that OPA will seek beta testers to use the tool, answer specific questions, and provide feedback about their experiences.

IV. COMMON FUND FINAL REPORT: HUMAN HEREDITY AND HEALTH IN AFRICA

Jennifer Troyer, Ph.D., Program Director of the Division of Genome Sciences at NHGRI, presented a final report on the Human Heredity and Health in Africa (H3Africa) program. The program's goal was to facilitate an African-based research approach to the study of genomic and environmental determinants of common diseases, with the goal of improving the health of African populations. At the start of the project, most genomics research was performed in a small portion of the world's population, and the need for more global genomic efforts was recognized. To achieve this outcome, capacity development (e.g., human and research infrastructure) and collaborative networks were needed.

The H3Africa program was considered transformative, crosscutting, and unique. The first RFAs were released in 2010, and the first awards were made in 2011. Several additional RFAs were released subsequently. The program was renewed in 2016 and will end in August 2022. The program, and several of the funded projects, underwent pilot and scale-up phases. Dr. Troyer noted that the COVID-19 pandemic has led to challenges and delays within the program, and no-cost extensions likely will be needed. The first H3Africa Consortium–wide paper was published in 2013. Goals outlined in the paper include: (1) developing infrastructure and culture for collaboration, data sharing, sample sharing, and release; and (2) building capacity, interest, and funding for biomedical and genomics research in Africa.

The RFAs included calls for biomedical research projects; ethical, legal, and social implications research projects; collaborative centers research; biorepositories, an informatics network; a bioinformatics training program; and a coordinating center. Projects were clustered into topic areas (e.g., mental health, complex disease, genetic disease, infectious disease, microbiome). These clusters have fostered new collaborations among investigators.

The H3Africa Consortium—which includes primary sites, laboratory sites, collection sites, and analysis sites—spans the African continent. The Steering Committee is composed of principal investigators and funders. Working groups have been established to consider such topics as ethics and community engagement, data and biospecimen sharing, education, and coordinated training. Other working groups are focused on specific disease areas. The working groups report back to the Steering Committee. An Independent Expert Committee meets with the consortium and provides advice.

Working group outcomes have included a variety of policies and guidelines), as well as research tools and products. Fifty-one projects have been funded, and about 50,000 samples have been analyzed using the H3Africa Genotyping Chip. Project outcomes have included phenotype data (e.g., demographic, anthropometric, disease and health), genomic data (e.g., sequence, genotyping array, epigenetic, transcriptomic), microbiome sequence data (e.g., patient, nonhuman), and qualitative data (e.g., focus groups, surveys, workshops). Nearly 700 papers have been published through the consortium. One study, published in October 2020, focused on filling gaps in African genomes across the continent. This work was generated from the Genome Analysis Working Group. The data associated with this work are among the most highly requested.

Data resources available through the consortium include H3ABioNet, which provides computing and network infrastructure; data management support; data analysis tools and workflows; and data storage, submission, and access. Repositories have been established for the western, eastern, and southern regions of the continent. Additionally, several new or enhanced graduate degree programs in bioinformatics have been established across the continent; these programs have supported hundreds of graduate students,

postdoctoral associates, and young investigators trained within H3Africa research projects. Thousands of individuals have been trained through the Introduction to Bioinformatics Training distance-learning class. Other courses, workshops, and webinars are operated throughout the consortium. Materials are available through the H3Africa website and YouTube channel.

The existing infrastructure allowed investigators across the consortium to respond quickly to the COVID-19 pandemic. Dr. Troyer briefly highlighted notable efforts in this area. Christian Happi, Ph.D., sequenced the first African SARS-CoV-2 genome, and Tulio de Oliveira, Ph.D., was responsible for identification and characterization of the Omicron SARS-CoV-2 variant. The consortium's biorepositories serve as primary sites for sample storage and were instrumental in establishing testing protocols early in the COVID-19 pandemic, and community engagement and health care workers played a critical role in providing information on masks and vaccines.

H3Africa investigators are pursuing new international collaborations with several entities including ClinGen, the Human Pangenome Reference Consortium, and the Global Alliance for Genomics and Health. Members also are seeking funding opportunities through the NIH and other federal agencies. The topic of genomics in Africa continues to attract broad support, reflecting the success of H3Africa's efforts during the past decade. The African Society of Human Genetics will provide a network for ongoing and future interactions among investigators.

Discussion Highlights

- Dr. Troyer explained that H3Africa will not continue as its own consortium, but its components will be incorporated into other entities as appropriate. The Cardiovascular Disease Working Group has received support through NHGRI to study polygenic risk scores in diverse populations, and several consortium members are involved in DS-I Africa, others will be involved in the Wellcome Trust-supported African Population Cohort Consortium. Additionally, many of the investigators are supported through R01 funding.
- Dr. Troyer noted that many unique genomic findings have been informative for specific disease processes, such as developmental disorders and cardiometabolic diseases.

V. COMMON FUND FINAL REPORT: METABOLOMICS

Arthur L. Castle, Ph.D., a Program Director in the Division of Diabetes, Endocrinology, and Metabolic Diseases at NIDDK, summarized the past decade of the Common Fund Metabolomics Program. He noted that the Common Fund Metabolomics Program was established to meet increasing demand for this technology in the absence of sufficiently trained investigators and resources for analyzing and sharing the data.

The program was established in two phases. Phase I was implemented from 2012 to 2017 and involved increasing the national capacity for performing metabolomics. Six regional centers were funded to support more than 2,000 services and pilot and feasibility studies. Training and mentorship were provided to researchers in the field through 83 collaborative supplements to ongoing research project grants across the United States. Other training, technology, and career development initiatives were subsequently awarded. The Metabolomics Workbench—the National Metabolomics Data Repository that provides analysis tools and access to metabolite standards, protocols, tutorials, and training—was established at the University of California, San Diego (UCSD) to promote data sharing. More than 800 publications have been linked to the Phase I centers, and more than 350 publications have been associated with Phase I awards. Dr. Castle highlighted the increasing number of NIH grants awards and publications that mention metabolomics since the program was implemented in 2012. Phase II was implemented from 2018 to 2022 and addressed limitations of the technology. Seven tool development projects were funded across the

United States with compound identification cores established at 5 research institutions. The UCSD data repository was improved to support researchers in the field. A coordination center was established at the University of Florida to coordinate efforts and promote best practices.

Dr. Castle described several challenges associated with improving metabolomic data analysis and interpretation tools. Spectral data are analyzed statistically to separate signal from noise, and potential compounds are identified; this information is then used to model metabolic pathways and networks. He provided the example of a software package for pathway analysis called Mummichog, which was developed in 2013. This package uses statistical analysis to map unknown biological networks without having to identify all metabolites in a biological sample. Researchers at Jackson Labs and Scripps were funded to improve this software, including expanding visual analytics and integrating this software with other general analysis tools. The original Mummichog publication now has more than 500 citations, and the new site at Jackson Labs has completed more than 6,000 user jobs. Dr. Castle cited the Automated Data Analysis Pipeline (ADAP) as another example of improvements to the metabolomic analysis pathway. ADAP is a suite of computational algorithms and associated graphical user interfaces for preprocessing raw untargeted spectrometric metabolomics data to acquire optimal spectral peak information. The ADAP suite was expanded, enabling the mining and analysis of massive amounts of raw spectral data within the repository. ADAP data processing is presently being used at the National Institute of Environmental Health Sciences' Human Health Exposure Analysis Resource (HHEAR) Initiative, the Common Fund's Nutrition for Precision Health Program, and the NHLBI Coronary Artery Risk Development in Young Adults (CARDIA) Study.

Compound identification relies on authenticated standards and presently it is not possible to create unique standards for the infinite number of possible metabolites. To address this challenge, experimental and computational identification is based on both experimental and in silico data. Dr. Oliver Fiehn's group at the West Coast Metabolomics Core at the University of California, Davis is using a hybrid strategy—matching experimental standard libraries with data from *in silico* liquid chromatography–mass spectrometry (LC-MS) modeling—to improve confidence in compound identification. This approach has reduced the compound false discovery rate by 50 percent and currently outperforms dozens of other algorithms. The Pacific Northwest Advanced Compound Identification Core has developed the *in silico* chemical library engine (ISiCLE), an experimentation and quantum chemistry workflow for machine learning–based prediction of chemical properties for identification, and Data Extraction for Integrated Multidimensional Spectrometry (DEIMoS), a Python application programming interface and command-line tool for high-dimensional mass spectrometry data analysis workflows.

Dr. Castle described data sharing efforts enabled by the Metabolomics Workbench, which was established in 2014 and expanded in 2018. The repository contains 75,000 samples deposited from more than 2,000 studies, in which 32,000 known metabolites and 3.5 million unknown chemical features have been detected. The database comprises 134 different species, 133 different biological conditions, and 151 different tissue and sample types and contains 25 terabytes of raw spectral data for developing and improving metabolomic technologies. The Metabolomics Workbench also provides dozens of tools in a cloud workspace, with links to other relevant resources and analysis tool databases.

Several working groups were formed to promote best practices in metabolomics. In total, 17 supplements in Advancing Compound Identification and Promoting Software Development were awarded in fiscal years 2019 - 2021 to support collaboration and best practices.

Dr. Castle summarized the accomplishments of the Metabolomics Common Fund Program during the past 10 years. The program has provided access and training to hundreds of investigators in many fields and has helped support a community of collaborating researchers. A repository has been established to enable data sharing and analyses via cloud computing. Metabolomics software standards and guidelines

have been developed, and specific tools have been produced for each stage of the analysis pipeline. Compound identification has been enabled with experimental and *in silico* data. Future directions for the consortium include supporting large NIH-funded projects that are dependent on metabolomics data, improving the integration of controlled-access metabolomics data, and expanding the use of *in silico* compound identification techniques.

Discussion Highlights

- When asked about the prospects for metabolomics at the single-cell level and about the most significant scientific (rather than technical) outcome of these efforts, Dr. Castle answered that the technology for single-cell metabolomics is being developed presently and that he expects this field to become more popular in the future. Dr. Castle listed associations between particular metabolites and Type 1 diabetes and between several microbiome-associated metabolites and heart disease as among several outstanding discoveries that have emerged from the field of metabolomics.
- In response to a question about the sustainability of these efforts, Dr. Castle noted that funding for the cores has decreased steadily since they were established and that the cores have remained financially sustainable because of service fees. He noted that compound identification and tool development efforts will require ongoing support, but that this can be accomplished by research mechanism funding from NIH and other sources. The question of funding large repositories, like the Metabolomics Workbench, is a broader question that NIH needs to address.

VII. COVID-19 UPDATE

Anthony S. Fauci, M.D., Director of NIAID and Chief Medical Advisor to the President, outlined the current knowledge on SARS-CoV-2 and COVID-19, a historic pandemic at a level that has not been seen for more than 100 years. Globally, more than 360 million cases and 6 million deaths have been recorded. Dr. Fauci noted that this is an underestimate because of the lack of proper reporting in many countries. The United States has had some of the worst morbidity and mortality outcomes of any country in the world, with more than 70 million recorded cases and almost 900,000 deaths to date. The current surge, related to the Omicron variant, is the fifth globally. SARS-CoV-2 is a beta-coronavirus with the same subgenus as certain bat coronaviruses, from which it likely arose. It is an RNA virus with a large genome and four structural proteins, the most important of which is the S protein, which has a receptor-binding domain that binds to the ACE2 receptor. The ACE2 receptor is found in many places in the body, but predominately in the upper airway, lungs, gastrointestinal tract, and several endothelial cells. Transmission of this virus occurs by exposure to infectious respiratory fluids in small droplets, and aerosol particles are critical to transmission, because particles are deposited on the mucus membranes of the mouth, nose, and eyes. He noted that initially substantial transmission was thought to occur through fomites (e.g., surface transmission); however, overwhelming evidence indicates this is extremely uncommon. The greatest risk is in enclosed spaces with poor ventilation, particularly with prolonged indoor exposure and during such activities as exercise and singing. One unusual aspect of COVID-19 is that at least 30-40 percent of people infected never develop any symptoms. He commented that about 60 percent of transmissions occur from an asymptomatic person—someone who is in the pre-symptomatic stage or will never develop symptoms. With this degree of asymptomatic transmission, contact tracing and source control become extremely difficult.

Dr. Fauci described the clinical course of COVID-19. For those who become symptomatic, the clinical presentation is similar to a flu-like syndrome. Novel aspects include the loss of smell and taste, which often precedes the onset of symptoms, but sometimes can linger for a considerable period of time after. For those who have symptoms, at least 80 percent are mild to moderate, not resulting in the need for special medical attention or hospitalization. However, 15 to 20 percent of those individuals with

symptoms have severe or critical disease that requires hospitalization, with a case fatality rate that ranges from 2.3 percent to about 20 percent in those who require mechanical ventilation. He noted that the patterns of risk of disease have been consistent; with older adults at higher risk for severe outcomes and the risk increases incrementally with older age, particularly for those older than 85 years. People of any age with certain underlying conditions are at much higher risk for severe outcomes, including death. While severe COVID-19 manifestations are dominated by acute respiratory distress syndrome, effects in multiple organ systems can occur, including neurological manifestations, cardiac dysfunction, acute kidney injury, and certain pathogenic processes (e.g., hypercoagulability with microthrombi in small vessels and hyperinflammation) often leading to the need to dampen the immunologic and inflammatory response late in the course of disease. In addition, multisystem inflammatory syndrome has occurred in many children.

Dr. Fauci commented that patients also continue to experience effects after acute infection subsides. Some patients may have easily explained residual organ system dysfunction, such as people who have compromised pulmonary function after considerable time on a ventilator. However, a significant number of people (ranging from 10 percent to 40 percent) upon recovery from an acute episode of SARS-CoV-2 infection or COVID-19, develop signs and symptoms that last anywhere from weeks to months. These manifestations are not currently explainable by readily apparent pathogenic processes. These symptoms include post-exertional extreme fatigue, muscle aches, lightheadedness, temperature dysregulation, sleep disorders, and the inability to focus or concentrate, which is often referred to as “brain fog.”

Dr. Fauci outlined medical management strategies for those infected with SARS-CoV-2. For a large majority of people who become infected, specific medical attention is not required, and symptoms can be controlled with anti-inflammatory agents. End-organ support can be provided for those who have acute respiratory distress syndrome and need intubation and mechanical ventilation, as well as some that might need dialysis and cardiovascular sustentation. Antivirals and immunomodulators also can be used. He explained that the treatment strategy for COVID-19 often involves targeting the virus or moderating an aberrant host response. During the last 2 years, progress has been made in drugs that target the virus. Remdesivir has been approved by the FDA for treatment of other diseases and now is available as an outpatient treatment for COVID-19 patients. Paxlovid, a Pfizer protease inhibitor, has been shown to have about a 90 percent likelihood of preventing hospitalization or death if given in the first 3 to 5 days, and molnupiravir is 30 percent effective against COVID-19 disease. He noted that an aberrant immune response can be moderated with monoclonal antibodies or with such commonly used drugs as dexamethasone.

Dr. Fauci emphasized the great success in the rapid development of highly effective and safe vaccines against COVID-19 less than a year from the realization of the genetic sequence of SARS-CoV-2. Three separate virus platforms are currently in use in the United States Government development platform: mRNA, an adenovector, and a recombinant protein with adjuvant. The Pfizer-BioNTech mRNA vaccine has received full FDA approval; Moderna, an mRNA vaccine, and Johnson & Johnson, a human Ad26 vector, have received emergency use authorizations (EUAs), and several other vaccine candidates have pending EUA applications. These vaccines have a striking 94 percent to 95 percent efficacy in clinical trials, with even more encouraging effectiveness in real-world settings, which Dr. Fauci pointed out is extremely unusual. In the United States, unvaccinated people have 13 times greater risk of testing positive for SARS-CoV-2 and 68 times greater risk of dying from COVID-19 than vaccinated people. However, immunity wanes even with highly effective vaccines, so booster shots now are recommended for up-to-date, optimal protection. Boosters have been shown to markedly increase antibody titers against multiple variants. Clinical studies have indicated that booster shots reconstitute diminished protection against symptomatic infection—particularly against severe disease and death.

Although CDC now recommends boosters to everyone eligible, the emergence of multiple variants has challenged the containment effort. The currently surging variant, Omicron, has a large number of mutations, including 30 in the spike protein and more than 12 in the receptor binding domain, which allows Omicron to evade the protection afforded by the immune response to COVID-19 vaccines and prior infection. Dr. Fauci noted that Omicron now is the dominant variant in the United States. Transmissibility of the Omicron variant is much higher than other variants, although severity of the disease seems to be lower than both the Delta and Beta variants. Some preclinical studies suggest that the Omicron variant may be less inherently pathogenic, but this variant clearly evades immunity. He commented that a booster has been an important component of refreshing protection. Immunological memory, in the form of memory B cells and CD8 + and CD4+ T-cells, cross-recognizes variants from Alpha to Omicron, so although antibody levels decline, protection from severe disease persists by those mechanisms. However, two of the main monoclonal antibodies are no longer useful against the Omicron variant; two others are effective against Omicron or can be used for pre-exposure prophylaxis. He noted that small-molecule antivirals also are effective against the Omicron variant; thus, useful therapies still exist.

Dr. Fauci commented on the future of COVID-19 strategies, noting the urgent need for a universal coronavirus vaccine. During the past 20 years, three major outbreaks of coronavirus diseases—severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19—have occurred, and five major variants of SARS-CoV-2 have emerged to date. Innovative approaches are needed to induce broad and durable protection against known and unknown coronaviruses, necessitating a pan-coronavirus vaccine. He proposed that a pan-SARS-CoV-2 vaccine should be the first priority, which would include protection against all possible variants with the next step could be a vaccine against all beta coronaviruses. He noted that NIH and NIAID have invested more than $3 billion in strategies related to the COVID-19 pandemic with $1.4 billion of that funding dedicated to COVID-19 vaccine research. Most recently, four academic awards, totaling close to $45 million, have been made for the specific purpose of developing vaccines against multiple types of coronaviruses. Additionally, NIH has launched the Antiviral Program for Pandemics which is aimed at the development and discovery of new antivirals based on the strategy used to develop antivirals for HIV, which involves describing the replication cycle and identifying vulnerable targets.

Dr. Fauci pointed out that SARS-CoV-2 probably cannot be eradicated now, and elimination probably is also too aspirational a goal. He hoped for a level of control in which the underlying immunity in the population—whether developed through vaccination and boosting or infection—along with other mitigation methods, would allow SARS-CoV-2 infection and spread in the community to reach levels similar to other viruses currently accepted as standard—such as para-flu, RSV, and influenza—which do not disrupt society as extensively as SARS-CoV-2 has. Dr. Fauci expressed his belief that continuing vaccination and boosting—as well as increasing the supply of antivirals, access to testing, and adherence to public health measures—will allow the United States to approach a more normal state in 2022.

Discussion Highlights

- In response to a question about potential reservoirs in pets, Dr. Fauci acknowledged that the virus readily infects animals, including deer and rodents. Although this is an NIH-wide issue, a well-justified project in this area could be considered for potential funding by the Common Fund.
- Dr. Fauci confirmed that studies have shown that SARS-CoV-2 does not seem to possess mechanisms for integration into the host genome.
- Although individual genetic risk and resilience factors in hosts have not been identified, Dr. Fauci pointed out that social determinants of health cause significant discrepancies in outcomes, including greater risk of severe outcomes for some individuals.

- Dr. Fauci commented that definitively identifying the zoonotic origin of SARS-CoV-2 is difficult; however, evidence is increasing that the virus originated in bats and moved into an intermediate host before infecting a human, likely at the Wuhan Wet Market.
- Dr. Fauci invited continued discussion about how to use DPCPSI's abilities in developing flexible programs to rapidly address unexpected research situations.
- When asked about countering negative communication about the COVID-19 vaccines, Dr. Fauci agreed that the amount of disinformation has been a significant challenge in increasing vaccination rates. Vaccination is a public health and scientific issue, and the groups of people refusing vaccination based on political ideology are extremely damaging to the overall effort to contain SARS-CoV-2. Recommended strategies, including broadly publicizing correct information, do not seem to have a substantial effect on the intense divisiveness fueled by this misinformation. Dr. Anderson referred Council members to the Surgeon General's November 2021 advisory on misinformation and its effect on public health.
- In response to a question about the safety of eating in a restaurant during the Omicron surge, Dr. Fauci explained that the threat of SARS-CoV-2 transmission through fomites on inanimate objects, e.g., plates or napkins, is either nonexistent or very low. Since the virus is aerosolized, no study can accurately determine how long it remains in air; however, the time period is entirely dependent on the degree of ventilation. He commented that aerosolized SARS-CoV-2 could dissipate within seconds to a minute in a well-ventilated indoor space, but a poorly ventilated space could require several minutes for dissipation. Dr. Fauci cautioned that these data require further confirmation.
- When asked about the possibility of a prophylactic treatment, similar to pre-exposure prophylaxis (PrEP) for HIV, Dr. Fauci explained that the antibody Evusheld (AstraZeneca) has been shown to be effective when used as pre-exposure prophylaxis in people at very high risk, such as heavily immunosuppressed patients in whom the vaccine is not expected to work. Theoretically this could be used for those who are vaccine-resistant; however, there also are risks with an infusion of monoclonal antibodies.

VIII. ECHO CONCEPT: PEDIATRIC COHORTS PROGRAM RENEWAL (VOTE)

S. Sonia Arteaga, Ph.D., Program Officer for the ECHO Cohorts, introduced the concept clearance for the renewal of the ECHO Pediatric Cohorts Program, a nationwide consortium that investigates the roles of a broad range of early exposures, among diverse populations. The purpose of the renewal is to extend and expand the ECHO cohort, already one of the largest investments that NIH has made for research on child health. The ECHO cohort renewal will be from 2023 to 2029, using the cooperative agreement mechanism. The funding is contingent upon congressional appropriation. The 7-year funding period is anticipated to support 50 awards for cohort study sites and one award each for a coordinating center, a data science center, a measurement core, and a laboratory core. The program initially was established in 2016 with funding for seven years. It is a nationwide observational study of five common pediatric outcomes that have major public health impact including: 1) prenatal, perinatal, and postnatal stages; (2) upper and lower airway; (3) obesity; (4) neurodevelopment; and (5) positive health. The ECHO program has integrated data from a consortium of 72 longitudinal maternal–child studies into a single large cohort study—the ECHO cohort. The cohort is a highly diverse population of more than 50,000 children (and their family members) located in 33 states, Washington, D.C., and Puerto Rico. ECHO emphasizes multidisciplinary science and the capacity for pioneering innovative methods and technologies and is an unprecedented resource for the child health and development research community.

The program office established three strategic goals: (1) enabling high-impact research; (2) facilitating the establishment of ECHO as a national resource; and (3) diversifying the scientific workforce. ECHO

investigators have published more than 800 publications in leading journals in the fields of pediatrics, obstetrics, epidemiology, and environmental health. ECHO publications have a median impact factor of 5, and for collaborative publications, a median relative citation ratio close to the 90th percentile. Dr. Arteaga provided two examples of collaborative research studies that highlight the innovation of the science and how the research can inform programs, practices, and policies. One study was the first to show disparities in asthma incidence rates across the United States by racial and ethnic population in early childhood. This study is important because it may lead to the development of potential solutions addressing health disparities. Another ECHO study found that ultrafine particles late in pregnancy is associated with development of asthma in the first years of life. This finding is novel and has the potential to inform the regulation of ultrafine particles smaller than 0.1 micron, which are not currently regulated by the Environmental Protection Agency.

The second study presented by Dr. Arteaga demonstrated the ability of ECHO to quickly pivot to address the COVID-19 pandemic. COVID-19-specific questionnaires for children and pregnant women were developed and then made publicly available through NIH resources. Several time-sensitive COVID-19 projects were funded. One study focused on social inequalities in response to the pandemic and the impact on child positive health outcomes. The study addressed the impact of COVID-19–related hardships and acute stress, the influence of that stress on child well-being, and the role for social support in promoting and protecting child well-being amid such hardships. The study used two samples of cross-sectional data collected between May 2020 and May 2021. It included almost 1,000 participants across 19 states from 11 cohorts. This study demonstrated that for children ages 2 to 12 years, COVID-19–related family hardships contributed to both caregiver and child stress, thus negatively affecting child life satisfaction. Practical considerations resulting from this study included the use of federal and state agencies to develop and expand interventions that targeted hardships (e.g., COVID-19 stimulus benefits) and developing interventions that target both negative and positive psychological functioning (e.g., mindfulness interventions). In the second part of the study, the authors determined that social connections and family engagement can promote children's life satisfaction even in the presence of COVID-19–associated stress. Practical considerations resulting from this study included nonmedical referrals from health professionals, recommendations for participation in community clubs and activities, and the possibility of using childcare wellness visits to foster family engagement strategies. This study identified promotive and protective factors of positive psychological well-being in children during a time of universal distress.

ECHO also has established a National Data and Biospecimen Resource. This repository currently has more than 97,000 participants and includes data from more than 59,000 children, 27,000 of whom are in active follow-up. Participants are diverse in terms of race, ethnicity, age, socioeconomic status, and geography. The repository will be available to the community through the nearly anonymized, controlled-access public-use data set at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development's Data and Specimen Hub, as well as on a data enclave in a secure cloud environment hosted by ECHO's Data Analysis Center. The associated biorepository has more than 42,000 biospecimens, including blood, hair, and urine.

To support the development of a diverse scientific workforce, ECHO has established the Opportunities and Infrastructure Fund (OIF) Awards to support early-stage investigators. Several awardees have subsequently received R01 awards. Fifty-one awards have been made with many of the awardees from diverse backgrounds. The OIF program promotes diversity through supporting a diverse community of early-stage investigators pursuing innovative research, including geospatial work, artificial intelligence, machine learning, new technologies, positive health, and health disparities. To further promote diversity, ECHO has funded research supplements for 15 predoctoral and postdoctoral researchers focusing on a range of topics, including disparities and equity.

Dr. Arteaga described the future of the program. ECHO aims to leverage existing cohort infrastructure and extend and expand the cohort. The 40,000 current ECHO children and their families will continue to be followed, with the goal of expanding to include 20,000 additional women recruited during pregnancy and their partners. Using an approach informed by a 2021 workshop attended by international experts, the expansion will include a preconception pilot of 10,000 couples at moderate-to-high probability of subsequent pregnancies, with the high likelihood that this study will result in 3,000 births. By recruiting ECHO participants during the interpregnancy period, preconception data can be obtained and logistical challenges overcome. The extension and expansion of the ECHO cohort will lead to a large, diverse cohort from preconception through adolescence. Potential new and expanded scientific opportunities include further understanding of health disparities and health equity, which is consistent with NIH-wide priorities for DEIA, and examining the early origins of disparities, which widen from childhood onwards. Social determinants of health also will be assessed, including how they relate to maternal stress in pregnancy and how they interact with biology and influence health outcomes. Other opportunities will include examining natural experiments or health crises—an extension of the response to the COVID-19 pandemic—and investigating health effects of novel chemicals. Dr. Arteaga noted that the average American is exposed to at least 30,000 pounds of chemicals, the vast majority of which are unknown, and that children and pregnant women are particularly susceptible to their effects. Health trajectories will be studied, and early critical periods for primary prevention will be identified. Aspects of resilience and reversibility will be examined (e.g., puberty as a sensitive time period). Biological pathways—such as epigenetics, metabolomics, and exposomics—will be incorporated into these studies, which also will include preconception exposures to novel chemicals, lifestyle factors, and substance use. Present ECHO themes will continue and intensify. All applicants will be asked to include plans to promote DEIA. The program will focus on recruitment and retention of diverse participants, diversification of the scientific workforce, and scientific questions that address health disparities and equity. ECHO also will continue to emphasize a team science approach, as well as solution-oriented research that informs programs, policies, and practices.

ECHO is engaged with more than 90 stakeholder organizations that help develop research questions and disseminate findings. An active NIH-wide group consists of more than 25 ICOs to help guide the program and provide valuable input. The next phase of ECHO closely aligns with the NIH strategic plan. This phase will include several components, including cohort study sites that will recruit new pregnancies and have a preconception pilot; study sites that will follow existing ECHO children and their families; a data science center to enrich research infrastructure and data science to facilitate broader sharing of data and resources with the scientific community; a coordinating center to implement effective coordination and project management across the ECHO study; a measurement core to enable efficient processes to incorporate new and revised measures to advance ECHO science; and a laboratory core to collect, process, and preserve biospecimens in the repository and to manage biospecimen assays.

In summary, the ECHO program has made great progress in its first phase, as demonstrated by its high-impact research, establishment of a national research resource, and development of the next generation of the scientific workforce. In the next phase, ECHO will build on its success to extend and expand solution-oriented research on early origins of common childhood conditions with high public health significance. With this renewed investment, ECHO research will continue to inform programs, policies, and practices to enhance the health of children for generations to come.

Discussion Highlights

- The discussants, Drs. Richard D. Krugman and Anna Maria Siega-Riz, provided their comments. Both enthusiastically supported renewal.

- Dr. Arteaga confirmed that ECHO participants are asked about histories of physical, sexual, and emotional abuse, and current manuscripts being prepared assess the relationship between maternal trauma and childhood outcomes.
- When asked about expanding to other diverse communities where excess child and maternal mortality occurs, Dr. Arteaga noted the significant emphasis on health equity and health disparities in the next phase of this program. ECHO will continue to follow its current cohort and emphasize retaining a diverse sample population. Community-engaged strategies are being promoted for recruitment of the 20,000 new pregnancies.
- In response to a question about collaborations with other Common Fund programs, Dr. Arteaga emphasized the importance of complementing and synergizing with the activities of other cohort programs without duplicating their efforts. ECHO and *All of Us* share materials despite the current lack of a pediatric program in *All of Us.* Dr. Arteaga's team has discussed with the leaders of the ComPASS program how best to engage diverse populations.

Vote

A motion to approve the ECHO Pediatric Cohorts Program Renewal was forwarded and seconded. The motion passed with no abstentions.

IX. NIH-WIDE STRATEGIC PLAN FOR DEIA

Marie A. Bernard, M.D., the NIH Chief Officer for Scientific Workforce Diversity, presented the *NIH-Wide Strategic Plan for DEIA*. In 2021, Congress directed the NIH to develop a strategic plan with long- and short-term goals to identify and address racial, ethnic, and gender disparities at the NIH and identify and address barriers in access to NIH funding for investigators researching health disparities. The working group developing and implementing the plan is composed of a broad range of NIH-wide representatives and integrates input from relevant stakeholders. The Strategic Plan also will be responsive to relevant executive orders. Of particular note, Executive Order 14035, *DEIA in the Federal Workforce,* issued June 25, 2021, launched a whole-of-government initiative to cultivate a federal workforce that draws from the full diversity of the nation and advances equitable employment opportunities.

The *Government-Wide Strategic Plan to Advance DEIA in the Federal Workforce* was released on November 23, 2021. It delineates key steps agencies can take to strengthen DEIA in their workforce policies, practices, and culture and charges HHS with developing an agency-wide plan by March 23, 2022. The NIH DEIA Strategic Plan is being developed by co-leads Dr. Bernard, the director of the Office of Human Resources, and the acting director of the Office of Equity, Diversity, and Inclusion, with management from DPCPSI, and a team aim of 80+ NIH staff. They aim to develop the plan by early summer. The government-wide plan provides vision and mission statements; establishes five operating principles to advance and sustain DEIA within agencies; further outlines the DEIA priorities expressed in the executive order; details strategies for advancing DEIA; provides an example maturity model to support growth; outlines steps to create a comprehensive framework to address workplace harassment; and explains next steps for advancing DEIA.

The NIH process is in the third of five phases, currently conducting an ICO data call to update the inventory of NIH DEIA activities gathered earlier in the process. The working group developing the plan includes representatives from all ICs and from many OD and DPCPSI Offices. Members also have been surveyed to ensure good representation from across relevant NIH committees and affinity groups.

The plan is designed to have a broad scope, communicate aspirational goals for the entire NIH that are achievable, articulate NIH definitions of DEIA, provide example accomplishments, convey goals for the

next 5 years, include broad goals and specific priority activities, provide accountability, and include input from internal and external stakeholders. The plan articulates NIH's vision for strengthening DEIA and captures activities that the NIH workforce will undertake to meet the vision of the strategic plan. It also is harmonized to the *NIH-Wide Strategic Plan* framework, with NIH's DEIA priorities organized around accomplishments, needs, opportunities, and challenges.

The plan's vision statement is "to embrace, integrate, and strengthen DEIA across all NIH activities to achieve the NIH mission." The DEIA Strategic Plan has three objectives. The first is to implement organizational practices to center and prioritize DEIA in the workforce, which includes both the NIH workforce and the workforce at institutions supported by NIH funding. The second objective is to grow and sustain DEIA through structural and cultural change, which will be executed through stewardship, partnerships and engagements, accountability and confidence, and management and operations. The third objective is to advance DEIA through both the workforce and health research.

Currently, the working group is communicating with ICOs to gather an inventory of activities, status, accomplishments, and other components that align with and will inform the strategic plan, and additional information will be obtained from the UNITE Initiative.

Discussion Highlights

- In response to a question about the overlap between the congressional mandate and the executive order, Dr. Bernard clarified that the congressional mandate was issued in December 2020, and one of the objectives specifically addresses that overlap. Other Council members encouraged Dr. Bernard to take the opportunity to press all stakeholders toward greater diversity in how they think about both research applications and the workforce.
- When asked whether the NIH can set the standard for this effort across agencies, Dr. Bernard explained that regular meetings are held with other agencies, and informal conversations also occur. The activities of the UNITE Initiative have made progress in terms of racial and ethnic equity. In other areas, NIH's progress is similar to that of other agencies.
- In response to a question about whether NIH grantees will be included in the plan, Dr. Bernard responded that the effort includes both internal and external DEIA. She suggested that DEIA improvements within ICO programs across the NIH will influence the kind of efforts the NIH supports in the future. She added that this Council can hold the group accountable for the results of the plan.
- When asked about inclusion of sexual and gender minorities in the plan, Dr. Bernard explained that Dr. Karen Parker, the director of SGMRO, is a leader in the development of the plan, and other SGMRO representatives are participating in the writing process. She anticipated that external individuals and organizations that support various formats of DEIA activities would submit robust feedback to the RFI to help expand the plan.
- Dr. Bernard agreed that success metrics are important. She acknowledged that clear definitions of each plan component are needed, but she pointed out that the plan is currently in development.

X. CLOSING REMARKS

Dr. Anderson thanked the Council members and speakers for their contributions at this meeting. He reminded the members that the next Council meeting is scheduled for May 19–20, 2022, and also will be virtual.

XI. ADJOURNMENT

Dr. Anderson adjourned the meeting at 3:03 p.m. on January 28, 2022.

XII. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing summary minutes are accurate and complete.

James M. Anderson -S Digitally signed by James M. Anderson -S
Date: 2022.03.07 19:05:21 -05'00'

James M. Anderson, M.D., Ph.D.
Chair, NIH Council of Councils
Director, DPCPSI, OD, NIH

Date

Robert W. Eisinger -S Digitally signed by Robert W. Eisinger -S
Date: 2022.03.07 20:52:38 -05'00'

Robert W. Eisinger, Ph.D.
Executive Secretary, NIH Council of Councils
Senior Scientific Advisor, DPCPSI, OD, NIH

Date