The 168th meeting of the National Advisory Environmental Health Sciences Council convened as a hybrid meeting on February 21 and 22, 2023. Open session convened at 11:00 am and ended at 2:45 pm February 21. A closed session took place from 3:00 pm to 4:06 pm February 21. Open session began at 11:00 am and adjourned at 4:01 pm on February 22. Dr. Rick Woychik, Director, NIEHS, presided as chair.

(Personnel listed in italics below attended in person.)

**Participating Council Members**

Yulia Iossifova Carroll, MD, PhD (*ex officio*)
Suzanne Fitzpatrick, PhD (*ex officio*)
Andrew Geller, PhD (*ex officio*)
Lynn Goldman, MD, MPH
Irva Hertz-Picciotto, PhD
Andrij Holian, PhD
Jani Ingram, PhD
Terrance Kavanagh, PhD
Gary Miller, PhD
Patricia Nez Henderson, MD, MPH (*ad hoc*)
Trevor Penning, PhD
Marla Pérez-Lugo, PhD
Karen Vasquez, PhD

**NIEHS Staff**

Kathy Ahlmark
Trevor Archer, PhD
David Balshaw, PhD
Linda Bass, PhD
Sharon Beard
Abee Boyles, PhD
Danielle Carlin, PhD
Toccara Chamberlain
Jennifer Collins
Gwen Collman, PhD
Yuxia Cui, PhD
OPEN SESSION
The meeting was open to the public on February 21, 2023 from 11:00 a.m. to 2:45 p.m. and on February 22, 2023 from 11:00 a.m. to 4:01 p.m. In accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the meeting was closed to the public on February 21, 2023 from 3:00 p.m. to 4:00 p.m. for consideration of grant applications. Notice of the meeting was published in the Federal Register. Dr. Rick Woychik presided as Chair.

I. Call To Order and Opening Remarks, Review of Confidentiality and Conflict of Interest
NIEHS and NTP Director Rick Woychik, Ph.D., welcomed attendees and called the meeting to order. He read the Government in the Sunshine Act. Acting DERT Director David Balshaw, Ph.D., asked Council members in the room and present on the Zoom call to introduce themselves. Council member Philip Bourne, PhD, was unable to attend. Members of the NIEHS senior leadership team in the room and dialed in via Zoom introduced themselves. Dr. Balshaw went over some of the logistics for the hybrid meeting, and read the conflict of interest statement.

II. Consideration of September 2022 Meeting Minutes
Approval of the September 2022 meeting minutes was moved by Dr. Hertz-Picciotto and seconded by Dr. Penning. Council voted to approve the minutes, with all in favor.
III. Report of the Director, NIEHS

Dr. Woychik briefed Council on Institute developments since the September 2022 Council meeting.

He began by recognizing the departing Council members, for whom this would be their last meeting: Drs. Goldman, Kavanagh, and Pérez-Lugo.

He turned to budgetary matters. “Overall, it’s a good message,” he remarked. He reported that the FY2022-2023 budget was finalized in December 2022, with $40 million dedicated to research on the health effects of climate change. The overall allocation totaled slightly over $1 billion.

Dr. Woychik summarized NIEHS interactions with the White House, the Senate, and the House of Representatives. The main focus of efforts since September 2022 has been meetings with several members of Congress to help them understand the new NIH-wide effort on the health effects of climate change. He said that overall it was a very engaging set of interactions, with the message that the strategy is NIH-wide and not confined to any single institute having been very well received. He also mentioned several of the new leaders in Congress resulting from the recent mid-term election.

Dr. Woychik described progress on the development process for the 2024-2028 NIEHS Strategic Plan. The initial phase will continue through the spring, including a virtual Open Space Technology meeting scheduled for April 11, 12, and 14. The analysis and draft phase will run from June through February 2024, with finalization and publication scheduled from April – June 2024. He also reported on progress on the existing strategic plan, including details in four of the six emerging scientific priority areas: the exposome, precision environmental health (PEH), climate change and health (CCH), and environmental justice and health disparities.

He summarized the 2022 activities related to exposomics, including five virtual workshops and a summit held September 14-16, which resulted in a final report documenting 64 issues identified by the community that cover the full landscape of exposomics. The workshop series identified five themes and ten high priority areas to operationalize exposomics. Follow-up activities will include a special issue of the journal Exposome and a research concept, “Global Exposome Research Coordination to Accelerate Precision Environmental Health.”

Regarding PEH, Dr. Woychik reported on efforts to address the individual variability associated with responses to environmental exposures by integrating data from genetics, epigenetics, environment, and omics. He discussed the International Common Disease Alliance (ICDA), and emphasized that the environmental health sciences
community needs to engage with the ICDA to include environmental exposure and epigenetics into efforts to phenotype the cohorts in the ICDA. He mentioned interactions with the All of Us program, including the development of ancillary study recommendations. He noted that the Personalized Environment and Genes Study (PEGS) in the NIEHS Intramural Division follows the aims of PEH. He provided an overview of the PEGS study.

He described recent activities related to CCH, including the coalescing of NIH leaders from several ICs as an executive committee. The leaders have re-energized the NIH Working Group, and Gwen Collman is providing coordination across the NIH. He discussed the CCH strategic framework formulated by the working group, comprised of four major priority areas of science. There were four initiatives begun in FY2022 with funds from all seven NIH initiative partners, prior to the new Congressional allocation:

- Research Coordinating Center (RCC) for the Climate Change and Health Community of Practice
- Research Opportunity Announcement Alliance for Community Engagement – Climate and Health (ACE-CH)
- Notice of Special Interest: Climate Change and Health
- Notices of Special Interest: Innovative Technology and Research on Climate Change and Human Health

He provided details on the RCC, which is intended to catalyze transdisciplinary efforts and build a community of practice in CCH, including the timeline associated with the RCC funding announcement. With the ACE-CH, 16 proposals have been received and four awards have been made, establishing four ACE-CH hubs. Dr. Woychik also described the 2022-2023 NIH Climate and Health Scholars Program, which is designed to attract scientists actively working in CCH to share knowledge and help build CCH science capacity within NIH. He mentioned another important new initiative funded by HHS, an NIH data project called Climate Change and Patient-Centered Health Outcomes, which is designed to create a resource that researchers can use to identify and reduce the health effects associated with environmental or climate-related events and improve patient and population health outcomes. There is also a new program called the Intramural Targeted Climate Change and Health Program, an intramural funding initiative to support climate-related research activities.

Dr. Woychik reported several developments in environmental justice and health disparities, including the establishment of the EHD/EJ faculty, which includes more than 70 NIEHS employees. Part of the faculty’s activities is to interface with community partners. Dr. Woychik and Deputy Director Dr. Trevor Archer are working together with community partners to plan community forums. He provided examples of those interactions, including engaging with central North Carolina communities, to work with
environmental justice communities “in our backyard” such as a Western Electric site in Burlington. He noted that Dr. Archer has been named interim Acting Scientific Director of the Division of Translational Toxicology.

Dr. Woychik discussed several instances of NIEHS working collaboratively with other NIH ICs, such as NINDS, and NCI, and NHGRI. He noted that Dr. Renee Wegrzyn has been appointed to be the director of ARPA-H. He concluded his presentation by noting the new NIH Data Management and Sharing Policy, which took effect January 25, 2023.

Dr. Miller asked whether the environment is being considered in ARPA-H. Dr. Woychik replied that it absolutely is, citing a presentation given to IC directors recently by the new director. He said there is much interest. Dr. Miller asked if there is a timeline for when ARPA-H will be launching its initiatives. Dr. Woychik said that he would report on that in the June Council meeting. The agency is currently staffing up, including an official with expertise in exposomics. He noted that the agency is going to be capable of moving very quickly.

Dr. Hertz-Picciotto asked Dr. Woychik to elaborate on the NCI collaboration. He said he had recently met with Dr. Ned Sharpless, the NCI director, and they had discussed the importance of the environment. Dr. Sharpless was very agreeable that programs need to be developed. Dr. Michelle Heacock is currently working with Dr. Ron Johnson from NCI in an NIEHS-NCI Cancer and the Environment Working Group, which meets monthly to develop specific strategies. Also, there was a recent workshop, with another scheduled for June, to discuss integrating environmental exposures with both institutes’ work on cancer. Dr. Heacock added that there is a link online for information about the February workshop, and that there will be more information soon about the planned June workshop. Dr. Woychik provided information about recent developments with the environment and neuroscience.

Dr. Penning provided an update on the Intercenter working group on climate change and human health. He said there are now up to 20 centers involved, with over 140 people who have joined. He asked Dr. Woychik how the grants from the added $40 million in funding will be reviewed. Dr. Woychik said that is currently under consideration, but the details cannot yet be revealed. Dr. Penning urged that a special emphasis panel be used to review the grants, rather than ordinary study sections.

Dr. Geller asked about how grants from the Alliance for Community Engagement program would be channeled to HBCUs and their communities, and inquired about the point of contact for the North Carolina EJ initiative. Dr. Collman said the Alliance builds on the platform for the CEAL program, the NIH Community Engagement Alliance Against COVID-19 Disparities. Sharon Beard mentioned that Dr. Geller could communicate directly with her regarding the North Carolina effort.
IV. Report of the Acting Director, DERT

Acting DERT Director Dr. David Balshaw briefed Council on DERT activities and accomplishments since the September 2022 Council meeting.

He recognized the retirements of Dr. Pat Mastin and Dr. Bill Suk, and thanked them for their many years of service to NIEHS. Other recent staff departures included Helena Kennedy, Tina Powell, Demia Wright, and Sara Amolegbe. New hires have included Gary Wright, Jr. in the Worker Education and Training Branch. Dr. Michelle Heacock has stepped into the role of Acting Chief of the Hazardous Substances Research Branch, Director of the Superfund Research Program, and has become a member of DERT leadership.

Dr. Balshaw introduced the annual statutory requirement for the council to approve delegated authorities—actions delegated to DERT staff that require no follow-up action with Council. The current list is:

1. Change of institution
2. Change of PI
3. Continuation of Grant with Interim PI
4. Extension Without Funds
5. Extension With Funds

There is also an update to the Special Council Review Policy, which has changed from greater than $1 million direct cost to greater than $2 million total cost, to comply with NIH policy.

Dr. Kavanagh moved to approve the authorities; Dr. Miller seconded. Council voted approval.

Dr. Balshaw provided an overview of the FY2022 DERT budget. There were 1,298 applications reviewed. The payline was at 10%, with success rates of 15.4% for R01s and 16.5% for RPGs. RPGs ($280 million for 596 competing and non-competing grants) were 71% of the total $394.6 million in extramural grants. Of the RPGs, 160 ($72 million) were competing and 436 ($208 million) were non-competing. The average award was $450,000). In non-RPG grants, $39.2 million funded Centers, $23.2 million funded Training, $20.6 million funded SBIR/STTR, and a total of $32.2 million funded other grant mechanisms. The Superfund budget for FY2022 was $77.9 million.

Dr. Balshaw noted that DERT has been working hard to fund grants earlier, and depicted data supporting the trend.

He said that $24.3 million has been set aside for FY2023 RFAs, and listed the RFA titles. In addition, $1.1 million has been set aside for NIEHS co-funded initiatives.
There has been progress toward the goal of increasing Diversity Supplement investments, with more funding invested in 2022 than any other year.

Dr. Balshaw provided a timeline and summary of DERT meetings since the last Council meeting, as well as a list of upcoming meetings through the next Council meeting in June.

He presented information on new guidance regarding randomized clinical trials and proposed changes to RPG peer review criteria. The new framework will reorganize the current five scored review criteria into three factors:

- Factor 1: Importance of the Research
- Factor 2: Feasibility & Rigor
- Factor 3: Expertise & Resources

The overall impact score (1-9) is to be based on Factors 1-3 and additional review criteria.

Dr. Balshaw discussed the initial recommendations of the UNITE-E implementation committee on anti-bias training in peer review, which included bias training, a reporting mechanism for bias, and the promotion of a culture shift in review panels.

He concluded his presentation by briefly referring to two significant, recent Guide notices. The first notes that NIH encourages the use of the ARRIVE essential 10 checklist in all publications reporting on the results of vertebrate animals and cephalopod research. The second was an RFI on re-envisioning U.S. postdoctoral research training and career progression within the biomedical research enterprise.

Dr. Hertz-Picciotto asked about the success rate in the ONES program. Dr. Balshaw replied that the success rate for ONES applications has historically been "pretty good." Dr. Christie Drew added that she would provide more information to Dr. Hertz-Picciotto soon. Dr. Balshaw said that K99 is not directly comparable to ONES. However, within the recent evaluation of the program, the rate of conversion from R00 to R01 was very high. Almost all ONES investigators have received a subsequent R01 from NIEHS.

Dr. Penning asked whether the new R01 review criteria would affect the biosketches. Dr. Alfonso Latoni replied that there did not appear to be any change to the biosketch. Dr. Penning said that it could bias the review score. Dr. Balshaw asked Dr. Latoni to comment on anonymized review. He said the NIEHS does not use that.

Dr. Penning asked about the RFI for postdocs. He noted that his institution had just gone through an update of its stipend levels for NIH postdocs. He wondered where the supplementary funds would come from. Thus, as the issue moves forward, some budget monitoring will be required, he said. Dr. Balshaw said that was exactly the kind
of feedback being sought. Dr. Miller added that budgetary constraints would potentially squeeze out junior faculty, as salaries are increased. He also asked about R35s, and whether their use is freeing up R01 slots. Dr. Balshaw replied that anecdotally, there have been some cases where it has created opportunities. There has not been a formal evaluation yet. He said the first cohort of RIVER investigators is arriving at the time for renewals, so it will be time to evaluate the program.

V. Gut Microbial Composition is Altered Prior to Seroconversion in HIV Patients

NIEHS Scientific Director Dr. Darryl Zeldin introduced the meeting’s DIR speaker, Dr. Shyamal Peddada, Deputy Chief of the Biostatistics and Computational Biology Branch and Senior Investigator.

Dr. Peddada posed two questions:

- Are some people more likely to develop an infectious disease than others?
- For example, suppose two people are exposed to an infection such as HIV. Is one more likely to become sick (seroconvert) than the other? Why?

For this project, he and his collaborators accessed biospecimens, specifically stool and blood samples, from the Multicenter AIDS Cohort Study (MACS), which was a prospective study of men having sex with men (MSM) in the 1980s, in Pittsburgh, Baltimore, Chicago, and Los Angeles, none of whom were HIV-positive at that point.

At baseline, there were 265 men, of whom 156 remained HIV-, i.e., they did not seroconvert. 109 seroconverted after approximately 6 months. Of that group, 32 developed AIDS within 5 years, while 31 developed AIDS within 5-10 years. 46 developed AIDS after 10 years.

Dr. Peddada and his collaborator’s explored the influence of the internal environment—the microbiome—on the development of AIDS in the HIV+ patients. They discovered changes in the abundance of various microbial species occurred before seroconversion and the timing of the development of AIDS.

Dr. Zeldin asked whether the microbiome could be manipulated to reduce the likelihood of seroconversion. Dr. Peddada replied that that such approaches are possible.

Dr. Hertz-Picciotto asked whether similar trends are seen in other diseases. Dr. Peddada said that they are, and cited the association of Prevotella with obesity as an example.

Dr. Penning asked Dr. Peddada to elaborate on the statistical methods used for compositional analysis. Dr. Peddada discussed how compositional analysis had been
used in the study he had presented, as well as generally. He said that such methods had become more accepted.

Dr. Woychik said that data suggests that the genetic background of an individual can also influence the composition of the microbiome. Dr. Peddada agreed. In that case, Dr. Woychik asked, could that be the driving force in seroconversion, with the microbiome being simply a reflection of a genetic combination that is actually the driver of seroconversion? Dr. Peddada acknowledged that that was possible. Dr. Woychik asked if there had been any questions about the diets of the individuals, and whether diet could be an operative variable in this case. Dr. Peddada said yes, because the precursor is many exposures, including the diet. He added that the data on diet was not rich in the original study.

VI. Supporting Science through Innovation, Collaboration, and Inclusion

J’Ingrid Mathis, Associate Director for Management and Executive Officer from the NIEHS Office of Management (OM), joined NIEHS in July 2022. She presented to the council about her background, experience, and her current role, and provided an overview of her office’s responsibilities, vision, and priorities.

The Associate Director for Management has a wide variety of duties, including workforce management, financial management, scientific support, space & facilities, clinical program services, the library, sustainability efforts, supplies & logistics, travel administration, contracts, safety & security, ethics, the childcare center, accessibility needs, and coordination with federal, state, and county governments.

The Office of Management’s mission is to provide infrastructure and administrative services to advance NIEHS science. Critical services include:

- Budget formulation, execution, and management
- Acquisitions management
- Ethics
- Campus operations and security
- Health, safety, and environmental stewardship
- Travel review and approval
- Administrative facilitation and coordination

OM currently has 170 staff members, with a $3.1 million budget. Ms. Mathis pointed out that her role at NIEHS is unique among her NIH counterparts, as NIEHS is the only NIH IC with its own campus remote from Bethesda.

OM supports DERT and the grants process, with 40% of its budget staff supporting grants.
• OM’s Financial Management Branch sets aside funds for Requests for Applications
• OM certifies funds availability to support decisions made by NAEHS Council
• OM creates funding plans to support execution of grants
• OM participates in development of updated web-based functionalities to improve tracking of grants from budget formulation through execution
• OM tracks execution of grants daily

OM’s vision is highly efficient, effective, and integrated administrative and operational services through innovation, collaboration, and inclusion that enable NIEHS to advance its scientific mission. The vision is achieved by initiatives encompassing the workforce, workplace, and processes.

Dr. Hertz-Picciotto congratulated Ms. Mathis on NIEHS’s Net Zero recognition. Ms. Mathis described some of the subsequent efforts in that arena. Dr. Woychik suggested that she arrange a tour of the very energy-efficient NIEHS warehouse.

Dr. Geller asked Ms. Mathis to elaborate on the WELL Health-Safety Rating. She explained that it is an international certification for facility operations and management, with several criteria, including management of air and water quality, provision of health services to employees, cleaning and sanitation protocols, and more. NIEHS is currently the only federal agency with the certification.

CLOSED SESSION

This portion of the meeting was closed to the public in accordance with the determination that it concerned matters exempt from mandatory disclosures under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended.

REVIEW OF APPLICATIONS

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions and recommendations. Members absented themselves from the meeting during the discussion of, and voting on, applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. The Council considered and recommended 440 applications requesting $235,871,892 in total costs. For the record, it is noted that secondary applications were also considered en bloc.
OPEN SESSION

The meeting was open to the public from 11:00 am – 4:01 pm February 22, 2023.

VII. Environmental Health and Older Adults: Research Priorities of the National Institute on Aging

Dr. Richard Hodes, Director of the National Institute on Aging (NIA), briefed the Council on the institute’s research priorities related to environmental health and older adults.

He provided an overview of the NIA’s mission, organizational structure, and budget, including funding for Alzheimer’s Disease/Alzheimer’s Disease-Related Dementias (AD/ADRD) research. NIA has supported AD/ADRD research at various institutes across NIH, including NIEHS. “We are anxious and interested in increasing the already rich collaborations between our two institutes,” he said.

Dr. Hodes presented the NIA health disparities framework, which includes efforts to increase recruitment of diverse participants in clinical trials.

Addressing the NIA’s research priorities in environmental health, he noted that environmental exposures shape health outcomes of older adults. NIA research examines how the timing, duration, and intensity of diverse exposures over the life course impact later life health and well-being. NIA recognizes that more research is needed to capture how the comprehensive set of exposures, i.e., the exposome, affects risk and resilience associated with age-related diseases and conditions, including AD/ADRD.

NIA issued a Notice of Special Interest (NOSI) in June 2022 to support the development of research infrastructure for exposome studies in AD/ADRD, building the foundation for new centers for exposome studies. The NOSI allowed for rapid funding of rigorous exposome-related infrastructure within FY2022. NIA, NIEHS, and NINDS participated in the NOSI, with a total of 13 applications funded. NIA has also invited applications for a Research Coordinating Center on the Exposome and Alzheimer's Disease AD/ADRD. Dr. Hodes related several environmental research concepts on AD/ADRD that were recently approved by the NIA council.

Dr. Hodes described NIA-NIEHS joint initiatives. The NIEHS/NIA Telomere Research Network is dedicated to facilitating collaboration among basic telomere biologists, population and exposure researchers, and other scientists to advance interdisciplinary research on telomeres as sentinels of environmental exposure, psychosocial stress, and disease susceptibility. The group will hold its annual meeting at NIEHS March 30-31, 2023. As part of NIA participation in the Trans-NIH Climate Change & Health Initiative, NIA is taking part in three NIEHS NOSIs related to CCH. NIA is hosting Dr.
Zhen Cong as a 2023 NIH Climate Change and Health Scholar. NIA is providing co-funding to the NIEHS TaRGET II program, a research consortium to examine the role of environmental exposures on epigenomic signatures in target tissues using mouse models. NIA is also participating along with NIEHS and NINDS in PAR-22-048, Clinical Relevance of the Linkage between Environmental Toxicant Exposures and Alzheimer’s Disease and Related Dementias. Several funded studies are ongoing.

Dr. Hodes described several recent, relevant scientific advances, previewed a variety of upcoming events, and related many ways to stay informed and connected on issues associated with aging and the environment.

Dr. Miller asked how much of ADRD is related to cerebrovascular infarcts. Dr. Hodes said that in studies of the pathology in individuals diagnosed with dementia, a large portion have mixed pathologies, among which vascular pathologies are extremely common, and become more common with age. He discussed several past studies of age-related cognitive decline and cognitive impairment. He said that going forward it will be important to look at the role of preventive factors related to vascular lesions.

Dr. Penning asked whether NIA has projections on the impact of community event diseases on the aging population. Dr. Hodes said that recent studies have looked at relevant factors and census projections in a number of different age groups, and extrapolated from there. New data has shown that the incidence of AD may be slowing or plateauing correlating with elements such as education. The plateau may be being reversed by increases in obesity and untreated hypertension as risk factors for dementia, as well as COVID, which may accelerate cognitive decline in individuals diagnosed with AD. Also, the onset of AD may have increased due to COVID exposure. He added that the increased number of people at advanced age is likely to overwhelm any advantages from preventive factors, leading to a net increase in incidence. Settings are also important to determine outcomes. People living in close proximity settings such as nursing homes have been shown to be particularly vulnerable.

Dr. Miller and Dr. Hodes exchanged remarks about the Research Coordinating Center. Dr. Hodes said it would be a tragedy to miss the opportunity to be able to measure some of the biologic implications and reflections of environmental exposures.

Dr. Woychik asked Dr. Hodes about the state of the science related to caloric restriction and expanding lifespan, and whether there is any application to Alzheimer's. Dr. Hodes said that the earliest research in that area was in rodent models, but more recently there has been research in macaques and humans, also encompassing intermittent fasting. He described several of the recent studies.

Dr. Geller asked whether NIA is part of the HHS UNITE effort on structural racism. Dr. Hodes replied that it is involved. Dr. Geller asked Dr. Hodes whether racial disparities
are a focus of the increased Alzheimer’s funding. Dr. Hodes said that they are, and noted that the relative risk of AD in African-Americans is about twice that of Caucasian non-Hispanics. He cited the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) longitudinal study in Baltimore as an example of collaborative research in that area, looking at the role of socioeconomic status, racial and ethnic elements, and other factors.

Dr. Hertz-Picciotto mentioned her recent research on wildfires and vulnerable populations, including the aging population. She added that heat stress is another area for research in older people. Dr. Hodes said that such studies are important, particularly when looking at longitudinal effects of exposures.

VIII. Global Exposome Research Coordination to Accelerate Precision Environmental Health Concept

Dr. Yuxia Cui from the Exposure, Response, and Technology Branch briefed the Council on the proposed program called Global Exposome Research Coordination to Accelerate Precision Environmental Health.

She defined the exposome as the totality of exposures to which an individual is subjected from conception to death. The exposome brings the domains together: ecosystems, lifestyle, social, and physical-chemical.

Dr. Cui described the many exposome-related initiatives around the world between 2005 and 2022, as the paradigm has emerged and flourished.

She related details from the Accelerating Precision Environmental Health: Demonstrating the Value of the Exposome series of workshops held in 2022, which culminated in the Exposomics Summit. The workshop series concentrated in five areas and identified ten priority topics:

- What to measure?
  - What should we measure in population studies?
  - Use animal & in vitro models to prioritize measurements
- How to measure?
  - Standardize and scale up exposome measurements
  - Map the exposome
- Share and harmonize
  - Harmonize data across studies (both epi and basic biology)
  - Create and sustain interoperable data repositories
- Integrate, analyze, & interpret
  - Use AI/ML to integrate diverse & high dimensional data (omics,…)
  - Incorporate social, chemical, & biological knowledge into interpretation
• Translate & impact
  o Address health disparities and improve public health
  o Advance individualized intervention & prevention

Overall, the intent was to operationalize exposomics. The summit meeting showed that there are needs for guiding principles for conducting exposomics, for a cultural change in methods, data, and resource sharing, and for education, communication, and training in exposomics.

The overall goal of the proposed program is to develop a commonly agreed upon framework for exposomics, promote best practices in data collection and sharing, and build a global exposome research community of diversity and inclusion to foster national and international collaborations. Dr Cui presented the fundamental questions to be addressed, the activities expected, and activities involved in working with the European “Global Coordination of Exposome Research” and other partners. Relevant efforts will be NIEHS-led, NIH-wide, and will also encompass other national and international efforts. The expected outcomes will be:

• A tangible framework for exposomics
• Standardized/harmonized methodologies
• Methods and resources sharing
• Proposals and new ideas for future research
• Increased capacity in exposomics as a community
• Gaps and unmet needs to advance precision health

The program team multi-disciplinary, with domain-specific and with complementary expertise, will be highly collaborative, and will have the vision and ability to work with international partners. The support mechanism for the program will be a U24 cooperative agreement, with significant staff involvement.

Dr. Penning was the first Council discussant. He said it would be very important to be able to operationalize exposome research and develop a community of practice. As the field expands, it will be a challenge to determine how to share data. He emphasized that it will be exceptionally important that the FAIR principles are followed. “You have my support as a Council member to move forward with this initiative,” he said. He noted that the domains to be integrated will be vast, with common language being particularly challenging. Standards will be fundamental to bringing the field forward. One of the most important domains needing to be normalized is electronic health records. He cited the OHDSI health data network as a program working to tackle the issue and produce a natural language algorithm. He expressed the need to operationalize how to take into account social determinants of health. Another challenge will be to integrate the domains once data has been collected in them. Until a framework is established, it will
be challenging to do exposome-wide association studies. There will be a need to ensure that the various institutes taking on the initiative will work together effectively. He recommended establishing proof of principle to show that the effort will be worthwhile to actually push the envelope in improving public health. He said the key to success will be the adoption of the best practices established. He felt that overall the proposed program is quite timely, and brings together the many different features of all of the recent exposomics activities.

Dr. Hertz-Picciotto was the second Council discussant. She said it was exciting to hear so many big, new ideas. She noted that the concept proposal is the first tangible fruit of the many workshop activities. She agreed that developing standards for the field is critical, and the proposal puts that in concrete terms. She felt that there was space to be filled in between the proposal's vision and activities in terms of strategies, governing structure, and how to facilitate such a wide-ranging activity—what are the first steps? How to prioritize what to do? She agreed that Dr. Penning’s idea of beginning with a single model system may be helpful. She felt that it would be useful to address the global issues from the outset. She approved of idea of including round-robin activities for laboratories.

Dr. Penning added that he did in fact “absolutely support” the global initiative. However, the time window involved in realizing the U24 program could be used to consider how to effectively operationalize exposomics research.

Dr. Geller said that he very much supports the effort, having participated in the summer 2022 workshops. He commented that many of his EPA colleagues have resisted the idea of the exposome because of the need for a proof of concept. He described some of the elements that will need to be included, such as the need to quantify cumulative effects across domains. He felt there would be a place for the SRP to be involved. He asked Dr. Miller to elaborate on the global exposomics efforts

Dr. Miller replied that there have been several efforts on the European side toward harmonization. One of the European infrastructure grants related to exposomics is called EIRENE, with 20 institutions including Columbia University involved. He said that it would be good from a credibility standpoint for there to be an NIH-level entity. He said the proposed structure would be helpful for interactions with European institutions. There are currently many connections, but they are informal. He added comments about the importance of harmonization.

Dr. Hodes agreed that it will be critically important to determine what to measure and to prioritize. He wondered if the European efforts would shed light on that. Dr. Miller replied that the European work is contributing a great deal of geospatial information, along with biobank samples. The combination of the two can help provide phenotypic
information. He said there is the possibility of coming up with “top ten” lists of approaches to use to set some priorities.

Dr. Geller discussed the need to define a fundamental set of environmental exposures and social determinants of health for cumulative impact laws being enacted. He cited a New Jersey law that has defined 26 indicators of environmental exposures and social determinants to determine disproportionality and disparate exposures. Such laws will be used to make decisions about permits and other regulatory issues.

In terms of what to measure, Dr. Penning recommended geospatial analysis, biobank data, and electronic health records (EHRs). Combining those three things together would allow determination of proof of principle. Dr. Woychik asked Dr. Penning to elaborate on EHRs in terms of the types of questions physicians ask their patients. Dr. Penning replied that while it is true that physicians are becoming busier and busier, perhaps patients could be asked to fill out surveys with some of the types of questions needed. Dr. Goldman added that most EHRs do not have a standardized place to record the information. She said that EHRs are just not set up to capture social determinants or environmental determinants of health.

Dr. Balshaw called for a motion to approve the concept. Dr. Hertz-Picciotto so moved; Dr. Kavanagh seconded the motion. Council voted to approve the concept.

IX. Reporting Back Environmental Health and Non-Genomic Research Results Concept

Liam O’Fallon from the Population Health Branch presented the concept developed in partnership with the NIH Office of Science Policy (OSP) and the All of Us Program. The program will be a collaboration between OSP, All of Us, and NHGRI.

The Report Back of Research Results (RBRR) effort has evolved and matured since the first council discussion in February 2022. Mr. O’Fallon said that RBRR is critical to:

- Build trust
- Demonstrate respect
- Increase transparency
- Foster engagement in research
- Strengthen science & environmental health literacy
- Increase community empowerment

The concept is designed to support multidisciplinary projects that identify, develop, and adapt, as well as test strategies for responsibly reporting back environmental health and non-genomic research results to study participants and/or key partners, grounded in a bioethics framework. It will:
• Advance the science of report-back
• Inform best practices/guidelines for effective report-back
• Develop new RBRR tools & approaches or adapt and test extant ones
• Improve understanding of how people use data

Mr. O’Fallon said that the recommendations for RBRR include dedicated guidance, expertise, and resources, clarified guidelines, expanded training and capacity building, and resources for implementation. Research is needed:

• To keep improving report-back methods
• On best practices for researchers giving participants access to resources to do something
• On best practices for focusing report-back on actionability
• For how people use report-back to modify their behavior

The concept will support multidisciplinary research that will address at least two of the following three topics: health equity, communications approaches, and data use. Since the concept is guided by a bioethics framework, all proposals will require a clearly articulated bioethics issue.

The concept will provide a scientific foundation for informing and developing guidelines, training materials, and other resources. It will address knowledge gaps in RBRR related to environmental health and non-genomic data. Quality RBRR will benefit current conversations in areas such as climate change, environmental justice, community engagement, data management, and DEIA.

Mr. O’Fallon invited Dr. Adam Berger to comment on OSP’s interest in and involvement with the RBRR concept. Dr. Berger, Director of the OSP Division of Clinical and Healthcare Research Policy, said that partnerships like this collaboration are major components of OSP’s larger bioethics program. RBRR is “a quintessential bioethics issue,” he noted. He said that OSP is extremely excited about the partnership.

Mr. O’Fallon summarized the concept, and turned to the Council discussants for their comments.

Dr. Ingram was the first Council discussant. She said that one of the issues in her mind is the difference between human biospecimens, which are overseen by IRBs, and environmental samples. She supported the concept of having an opportunity to look at different ways of reporting back to different types of communities. She commented that there needs to be an assessment of whether RBRR works or not. She said that community engagement will be very important, particularly to identify the most effective means of RBRR communication.
Dr. Goldman was the second Council discussant. She said she supported the initiative. She noted that people in environmental health have been dedicated to RBRR for a long time, involving their concerns about environmental justice and community-based participatory research, along with a commitment to right-to-know. She felt that sometimes IRBs can be the biggest obstacle to RBRR, due to their reluctance to reporting back information lacking a precise context about the meaning of results to a person’s health. A clinical test can be interpreted in the context of an individual’s health, but physicians may not be familiar enough with environmental tests to provide interpretation. She said that many of the environmental labs do not produce consistent results, making interpretation difficult. Many of the measurements do not have precise yardsticks yet, and the EHS units of measurement are not well understood by the general public. She recognized that data to knowledge is important, but community capacity to understand results is as well. She hoped that some of the research would involve helping researchers to build that type of capacity. She expressed strong support for what she characterized as “a daunting task” that is even more complicated than genomics. She mentioned that environmental research findings are now being entered into publicly accessible datasets, many of which are likely to be accessed by people who are not experts in environmental health or epidemiology or exposure science. They may be generating findings from data science perspectives. She wondered what the obligations would be for those secondary users for communicating those findings back to the people from whom the data was collected.

Dr. Ingram observed that it would be important to include the idea of active next steps in RBRR. She noted that there is not always an answer. Dr. Goldman agreed that it is a major issue, with researchers generating data that prompt action, but not necessarily knowing what that action might be. There should be communication with the people who do local public and environmental health, in a timely fashion.

Dr. Miller pointed out that there is a national society of genetic counselors and a whole field in that area. It should be considered how to build up a professional infrastructure to provide such services in the environmental health field. Dr. Balshaw agreed, and noted that it had come up in the exposome workshop series in 2022. The field needs people with that expertise.

Dr. Penning asked whether any thought had been given to the “more harm than good” issue, in the sense that research results may impact home values, health insurance, and other sensitive areas. Mr. O’Fallon agreed that those are important conversations to be held in the context of the ethical implications of RBRR. Dr. Berger agreed that there is a need for EH counselors similar to genetic counselors. Dr. Penning added that an exposed community is only one stakeholder, and that the polluters themselves may be open to receiving RBRR.
Dr. Geller said that he was excited to see NIEHS embarking on RBRR research. He said that EPA had been facing some of the issues Dr. Penning raised, both at the national and the local levels. He hoped to see approaches to those kinds of issues emerging from the RBRR research. Regarding the community engagement efforts described by Dr. Woychik, he asked Mr. O'Fallon if those issues had come up in early discussions with community partners. Mr. O'Fallon said that it is a hot topic within Research to Action and Partnerships for Environmental Public Health.

Dr. Kavanagh asked about social media, and whether it would be interesting to include some of the companies like Meta and others. Mr. O'Fallon said it was an interesting concept.

When discussing home values, Dr. Goldman pointed out that realtors, banks, and other such entities are part of their communities, and need to be taken into account. She said the concern may not only be the value of a property itself, but about potentially resulting stigma, citing mercury research as an example.

Dr. Hertz-Picciotto agreed that information without interpretation is challenging. She felt that RBRR done well can stimulate interest in environmental health and science. Regarding the stigma issue, she pointed out that it is different with RBRR, which mainly concerns individuals, while stigma is more associated with community or regional elements. She noted that in the history of working with Native American communities, there are sometimes strong environmental departments, and there may be some models for investigators to explore regarding RBRR. She asked about an RFA that had requirements for RBRR and a formula for funding it. Mr. O'Fallon said there may be a bioethics supplement that she had seen. Dr. Hertz-Picciotto noted that a lack of supplemental funding to carry out RBRR may be intimidating to some researchers, so funding dedicated to the process would be important.

Dr. Ingram noted that dissemination done well can enrich consideration of environmental issues with communities. She commented that there could be some very useful information mined from social media.

Dr. Balshaw called for a vote on the concept. Dr. Kavanagh moved to approve the concept; Dr. Penning seconded. The Council voted to approve the concept.

X. Gene-Environment Interactions in Alzheimer’s Disease: A Potential Path to Precision Prevention and Treatment

Dr. Jason Richardson, from the Robert Stempel College of Public Health and Social Work at Florida International University, presented his work on gene-environment interactions in Alzheimer's disease (AD).
He provided details about the prevalence of AD, and emphasized that “it is not normal aging.” Genetic risk factors, which are well-known, can only explain some of the widespread occurrence of AD; environmental risk and protective factors need much more attention, he noted. Modifiable risk factors include:

- Education
- Cardiovascular and metabolic risk factors
- Lifestyle, e.g., tobacco and alcohol consumption
- Environmental exposures such as pesticides and air pollution

Much of his work has involved elevated serum pesticide levels and risk for AD. He has conducted studies involving DDT, which was banned in the U.S. in 1972, but remains in use to control vector borne diseases in some countries. Research has shown that DDE (a DDT metabolite) levels are higher in Mexican- and African-Americans. Also, cognitive dysfunction associated with pesticide exposure differs by race/ethnicity.

Dr. Richardson described AD pathology, and the mechanism of action associated with DDT. Given that mechanical depolarization of the cell increases APP and Aβ secretion, and that pharmacological depolarization/increase in neuronal activity increases secretion, his hypothesis is that an environmental agent (DDT), which is known to induce depolarization because of its modulation of the sodium channel, will have similar effects. He presented considerable data to support the hypothesis, including results showing that:

- DDT and DDE alter firing of mouse and human neurons
- DDT causes cognitive dysfunction and neurodegeneration
- APOE genotype modifies cognitive effects of DDE in AD
- There was enhanced neurodegeneration in APOE4 mice treated with DDT

Dr. Richardson addressed how this information might be used to translate to humans. In terms of therapeutics, two drugs have been approved for AD treatment since 2003, but current therapies are not disease-modifying. A precision medicine approach will be to detect latent physiological processes leading to molecularly tailored interventions. The disease population is quite heterogeneous, and the goal is to identify subsets of the disease population who will respond to specific therapeutics, leading to personalized therapeutic intervention. Overall:

- Environmental factors play a role in AD
- Interplay between genetic susceptibility and environment is likely a key mechanism
- Identification of genetic susceptibility and environmental contributors may lead to early identification
• Understanding mechanisms may lead to a personalized approach to treatment/prevention

Dr. Richardson concluded by listing his current research projects.

Dr. Miller asked Dr. Richardson what he would do with unlimited funds in looking at various cohorts, related to the observation that DDT is very environmentally persistent and keeps very well in biobanks. Dr. Richardson said that one of the biggest problems with biobank samples is that they are not very diverse, limiting the distribution of genetics. He noted that he has been working with a consortium led by a Texas colleague that will help address that issue.

Dr. Woychik asked a question related to gene-by-environment effects. He wondered if Dr. Richardson had ever seen a case where a gene locus was made homozygous by balancing a mutant allele with a wild type allele whose expression is altered or turned off as a consequence of an epigenetic modification. Dr. Richardson said that he had. For example, an amyloid precursor protein is clearly epigenetically regulated. Dr. Woychik and Dr. Richardson further discussed up-regulation of APOE, and the role of epigenetic effects.

Dr. Hertz-Picciotto said it was exciting to see this type of gene-environment work being conducted. Dr. Richardson concurred, adding that he was heartened that the AD field has been very open to GXE research.

XI. Council Discussion

Dr. Sheila Newton, Deputy Director of the NIEHS Office of Strategic Coordination, Planning and Evaluation, led the Council in a discussion focusing on new ideas for NIEHS Strategic Planning. She described the development process for the 2024-2028 Strategic Plan, which currently stands in the input phase, with the online tool for comments and input now open through April 20, 2023. A virtual Open Space Technology meeting is scheduled for April 11, 12, and 14. Dr. Woychik asked Dr. Newton to describe Open Space Technology, which had been used effectively in formulating the current and prior NIEHS strategic plans. She provided information about how the meeting technology works. Review of other inputs is ongoing. She asked Council members to consider the following discussion questions:

• What do we want to be known for/to have achieved by 2029?
• What is the status and potential of the priorities that have grown out of our current Strategic Plan? (the 6 areas of strategic focus, among other goals)
• How are these areas going to evolve in this timeframe?
• What new opportunities are on the horizon for environmental health sciences that we should be embracing as new strategic priorities?
The current areas of strategic focus are:

- Precision Environmental Health
- Exposomics
- Mechanistic Toxicology
- Computational Biology/Data Science
- Environmental Justice/Environmental Health Disparities
- Climate Change and Health

Dr. Hertz-Picciotto discussed the call for the new California initiative for climate action, which requires that every project have deliverables in two years. This forced applicants to re-think what research can be conducted that will lead to community actions that will change the situation. She asked what the actionable research is and how are those areas identified, working with community partners. She added that if NIEHS does that in a systematic way, it would be an enormous accomplishment. Dr. Newton said her idea fit with the theme of moving toward translation.

Dr. Kavanagh said that one of the new areas worth considering involves COVID, with One Health in mind in a holistic sense. He said it would be important in terms of being prepared for the next epidemic or pandemic.

Dr. Penning endorsed embracing the idea of environmental health for changing times, which would include climate change and human health, and COVID, with its enormous imprint on the U.S. health system as a whole. He said the emphasis is currently on treating disease, but should go back to health wellness and prevention. He noted that there is an enormous amount of data available now, and the field should embrace the idea of artificial intelligence and machine learning for a variety of environmental health metrics, predictive toxicology being one example. He discussed technological advances such as non-animal models (NAMS). He sees those elements as part of the changing times. “This progress was not evident four or five years ago,” he added.

Dr. Balshaw said that there had been a push since 2009 to begin to develop microphysiological systems, which have now evolved into NAMS. He asked where the next such advances might be coming from. Dr. Penning said he did not have an answer, but it is certainly worth thinking about. He noted that with NAMS, there has been an effort to go from a single organ-on-a-chip to multiple systems, such as organoids.

Dr. Miller commented about the identity of the institute. He said there are many ideas, but not everything can be done. He said that one idea that came up in the Catalytic Workshop series was that since every institute now does genomics in some way; therefore, the mission of NHGRI has changed from just doing genomics research to being a center for improving genomics technologies and the applicability of genomics
data. He asked if NIEHS should be thinking about how to make sure everyone is doing exposomics right, as the field is expanding. He said it goes beyond just funding R01s to an infrastructure approach, in a structural/tactical way. Dr. Newton said there is some activity in that space, with HHEAR and other efforts to integrate environment across the NIH, providing tools to sister institutes. It has also been a strategic plan theme. Dr. Miller noted that CHEAR and HHEAR were more about providing services to other places, versus the technologies that they could then take advantage of themselves.

Dr. Holian mentioned the importance of the induction of inflammation in environmental impacts. Inflammation is known to be the primary driver of most human diseases, and the field should determine how the environment impacts the development of an inflammatory response in the different organ systems that are affected. That is clearly a role for NIEHS to exercise leadership, he observed. Although the institute obviously cannot do everything, inflammation should be one of the core elements of research.

Dr. Hertz-Picciotto noted the importance of the immune system and its response to the environment in the rise of certain diseases in recent years, such as autism, diabetes, and obesity.

Dr. Goldman wondered if there is a way for NIH to catalyze real change in what is available to scientists for assessing exposure, just as NIHGRI did for genomics. To develop useful new tools would require partnerships with industry, as well as non-directed funding.

Dr. Geller pointed out that there are now measures of cumulative effects of environmental exposures. He said he was interested in developing a better phenotype for vulnerability. He endorsed the concept of environmental counselors.

Dr. Balshaw wondered if there was a role for the strategic plan to change the dialogue focusing on the vulnerable to focusing on the resilient, helping to build resilience in vulnerable populations. Dr. Geller agreed with the idea.

Dr. Kavanagh described a small environmental counselor program in Seattle called Master Home Environmentalists (https://www.lung.org/local-content/wa/mhe-program). He felt that NIEHS should consider developing training in that area and devoting some resources towards it.

Dr. Woychik noted that the proposed environmental health counseling would be counseling for individuals, but what about the context of counseling not to individuals but to the public health, creating public health messages around various environmental exposures. He asked if NIEHS is doing a good job of that. For example, RBRR is typically designed to report back to individuals, but could it be fashioned to report back to groups? He cited recent publication on hair straightening products.
Dr. Goldman said there are people who specialize in that area, as well as academics who conduct research. There is enormous variation in how people perceive environmental health messaging, she noted. There are training programs to train people to become professional communicators. It is unlike genetic counseling, however. There is no licensing board or official credentialing. She said that people doing that type of work at a community level must have some sensitivity to how those messages impact individuals. It is not a field that has been as well developed and matured as it should be.

Dr. Miller said that people pursuing an MPH in environmental health should be able to acquire a certification in environmental health counseling. They probably have 80% of what is needed, but would likely need additional training in the counseling aspects. NIEHS could be very helpful in defining the needed competencies. Dr. Goldman disagreed, in that the skills required for counseling should not be underestimated, and the MPH in environmental health does not include that type of content. The counseling skills are not easy, and not every MPH student would be qualified.

Dr. Miller said he was envisioning a subset of those people who have the MPH training. He noted that there is already much scientific and community expertise and relationships with the community, but it would be a good group to recruit from. Dr. Goldman said that forming interdisciplinary teams would be a good approach. Dr. Newton observed that it would be an exciting area to pursue.

Dr. Trevor Archer asked Council members if there is one area in the EHS field that is ripe for an advance.

Dr. Hertz-Picciotto said there is much to learn from young people, high school and undergraduates. Dr. Archer felt that was a very interesting concept, adding that it would be useful to tap into their ideas. He noted that NIEHS has several programs designed to bring high school and undergraduate students to the institute. Dr. Janet Hall added that communication at all levels will be important, particularly to incorporate the environment across the different fields of medicine. She also mentioned that it will be helpful to educate the media, including social networking.

Dr. Holian said that scientists at all levels should be involved with messaging, with incorporation fundamental biological mechanisms and understanding of environmental health impacts being crucial.

Dr. Kavanagh agreed that there should be investment in crafting the most effective messages, along with the training necessary to disseminate environmental health messages.
Dr. Balshaw added that fundamental understanding of the context of how environmental exposures are influencing health is sometimes more important than “you've been exposed to this, therefore you are at risk of that.”

   XII. Adjournment

Dr. Woychik thanked everyone who had been involved in the meeting, and everyone involved in preparing for the meeting. Dr. Archer agreed that it had been a productive meeting. Dr. Balshaw felt there had been much valuable input from Council, and appreciated that it had been possible to conduct the meeting at least partially in person. Dr. Woychik thanked Dr. Kavanagh for his Council service.

He adjourned the meeting at 4:01 pm, February 22, 2023.

CERTIFICATION:

/s/ Rick Woychik, PhD
Chairperson
National Advisory Environmental Health Sciences Council

/s/ David Balshaw, PhD
Executive Secretary
National Advisory Environmental Health Sciences Council

Attachment:
Council Roster