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
September 11–12, 2025

Meeting Minutes

Day 1

I. CALL TO ORDER AND INTRODUCTIONS

Nicole C. Kleinstreuer, Ph.D., Acting Director, DPCPSI, welcomed participants, NIH staff members, and members of the public to the open session of the Council of Councils. The virtual meeting began at 10:00 a.m. on Thursday, September 11, 2025. The meeting attendees are identified below. Dr. Kleinstreuer then reviewed the day's agenda.

A. Attendance

1. Council Members

Council Members Present

Chair: Nicole C. Kleinstreuer, Ph.D., Acting Director, DPCPSI, NIH
Executive Secretary: Franziska B. Grieder, D.V.M., Ph.D., Director, Office of Research Infrastructure Programs (ORIP), DPCPSI
Monica Gandhi, M.D., M.P.H., University of California, San Francisco, San Francisco, CA
Rafael Irizarry, Ph.D., Dana-Farber Cancer Institute and Harvard T.H. Chan School of Public Health, Boston, MA
Karen C. Johnston, M.D., M.Sc., University of Virginia, Charlottesville, VA
Barbara Kelley, Hearing Loss Association of America, Bethesda, MD
Richard D. Krugman, M.D., University of Colorado School of Medicine, Aurora, CO
Kevin C. Kent Lloyd, D.V.M., Ph.D., University of California, Davis, Davis, CA
Jennifer Jaie Manly, Ph.D., Columbia University Medical Center, New York, NY
Lauren Silvis, J.D., Tempus, Inc., Washington, DC
Russell N. Van Gelder, M.D., Ph.D., University of Washington School of Medicine, Seattle, WA

2. Liaisons

Andrew A. Bremer, M.D., Ph.D., M.A.S., FAAP, Director, Office of Nutrition Research (ONR), DPCPSI, and Acting Director, Office of Dietary Supplements (ODS), DPCPSI
Janine A. Clayton, M.D., FARVO, Director, Office of Research on Women's Health (ORWH), DPCPSI
Josh C. Denny, M.D., M.S., Chief Executive Officer, *All of Us* Research Program Office, DPCPSI
Geri R. Donenberg, Ph.D., Director, Office of AIDS Research, DPCPSI
Matthew W. Gillman, M.D., S.M., Director, Environmental influences on Child Health Outcomes (ECHO) Program Office, DPCPSI
Susan K. Gregurick, Ph.D., Director, Office of Data Science Strategy (ODSS), DPCPSI

Franziska B. Grieder, D.V.M., Ph.D., Director, ORIP, DPCPSI
Rebecca Meseroll, Ph.D., on behalf of **George M. Santangelo, Ph.D.,** Director, Office of Portfolio Analysis, DPCPSI
David M. Murray, Ph.D., Director, Office of Disease Prevention, DPCPSI
Vivian Ota Wang, Ph.D., Acting Director, Office of Strategic Coordination (OSC), DPCPSI
Jane M. Simoni, Ph.D., Director, Office of Behavioral and Social Sciences Research, DPCPSI
Marina L. Volkov, Ph.D., Director, Office of Evaluation, Performance, and Reporting, DPCPSI
Karina L. Walters, Ph.D., M.S.W., Director, Tribal Health Research Office, DPCPSI

3. *Ex Officio* Member Present

Matthew J. Memoli, M.D., M.S., Principal Deputy Director, NIH

4. Presenters

Andrew A. Bremer, M.D., Ph.D., M.A.S., F.A.A.P., Director, ONR, and Acting Director, ODS, DPCPSI
Ishwar Chandramouliswaran, Lead Program Director, ODSS, DPCPSI
Christopher G. Duncan, Ph.D., Program Director, Genes, Environment, and Health Branch, Division of Extramural Research, National Institute of Environmental Health Sciences (NIEHS)
Taylor Gilliland, Ph.D., Senior Scientific Advisor to the Director, DPCPSI
Susan K. Gregurick, Ph.D., Director, ODSS, DPCPSI
Franziska B. Grieder, D.V.M., Ph.D., Director, ORIP, DPCPSI
Michelle Hamlet, Ph.D., Program Leader, OSC, DPCPSI
Matthew J. Memoli, M.D., M.S., Principal Deputy Director, NIH
Ian C. Nova, Ph.D., Program Director, Division of Genome Sciences, National Human Genome Research Institute (NHGRI)
Sheri Schully, Ph.D., Deputy Chief Medical and Scientific Officer, *All of Us* Research Program Office, DPCPSI
Danilo A. Tagle, Ph.D., Director, Office of Special Initiatives, National Center for Advancing Translational Sciences (NCATS)
Frederick L. Tyson, Ph.D., Program Director, Genes, Environment, and Health Branch, NIEHS

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

Franziska B. Grieder, D.V.M., 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 August 8, 2025.

- The minutes from this meeting will be posted on the DPCPSI website.

C. Future Meeting Dates

The next Council meetings are scheduled to be held January 29–30, May 14–15, and September 10–11, 2026.

II. NIH UPDATE

Matthew J. Memoli, M.D., M.S., Principal Deputy Director, NIH, provided updates on NIH priorities, emphasizing that NIH's overall vision moving forward is to support innovation and focus on diseases currently affecting Americans to improve overall population health. NIH is prioritizing rigor and reproducibility and human-focused research, as well as efforts related to safety, transparency, and academic freedom. Dr. Memoli noted that both the House and Senate appropriations committees have advanced bills that support an approximately flat budget for NIH. In the event of a continuing resolution, NIH will receive the same budget as the previous year for the duration of the continuing resolution. Dr. Memoli pointed out that NIH currently has 13 open director-level positions, as well as several open positions in OD, and he asked Council members for their support in reaching out to the community to help identify potential candidates.

Dr. Memoli emphasized that NIH's current priorities support advancing health and scientific excellence in the United States, including building a highly skilled workforce with innovative ideas. He emphasized that NIH is interested in this type of diversity, as young scientists are likely to have new ideas. NIH also is prioritizing replication, data innovation, nutritional exposures and chronic disease, and measurable interventions to address health disparities. Dr. Memoli noted priorities related to improving the understanding of autism, expanding alternative testing models based in human biology, and improving foreign research oversight. He noted that NIH will emphasize practical solutions related to HIV/AIDS and focus on implementation rather than discovery.

Dr. Memoli outlined program and policy updates, emphasizing the aim of rebuilding trust in NIH with a commitment to scientific integrity. Focus areas such as reproducibility and replication, open access, and alignment with national standards for the U.S. government and HHS framework contribute to this effort. Dr. Memoli noted several changes intended to align NIH with these priorities. To provide a unified approach to funding, NIH reviews now will consider other factors (e.g., innovation, gaps, portfolio, strategic mission) in addition to the payline. Dr. Memoli reminded attendees that all peer reviews have been consolidated under the Center for Scientific Review (CSR), and the review criteria have been simplified. To support academic freedom, intramural research program scientists will no longer be required to obtain approval from their supervisors before publishing. Supervisors should be informed, and researchers will follow guidelines for government publishing. To encourage the development of novel alternative models, NIH is shifting its focus to human biology–based methods and ending funding opportunities exclusive to animal models.

Dr. Memoli explained that the oversight of foreign awards has changed. Foreign components now will be linked directly to the prime award, which will improve the consistency of reporting and oversight. Allowable publication costs also will be limited, and NIH plans to develop incentives for replication work. NIH also is working to develop a policy on gain-of-function research. Dr. Memoli noted the need to shift the culture toward consideration of both risks and benefits of any proposed research. He added that

NIH is interested in modernizing biosafety policies; the current policies are based on regulating recombinant and synthetic nucleic acid technologies, which now are used regularly.

Discussion Highlights

- Dr. Memoli clarified that directors of institutes and centers (ICs) will continue to make funding decisions after CSR review, but ICs now will be encouraged to consider additional factors beyond review scores.

- Dr. Memoli confirmed that NIH would continue to support basic HIV science, but its focus would be shifted toward implementation.

- Dr. Memoli commented that additional guidance on foreign award changes is expected soon.

- When asked about a change in funding mechanisms to fully fund 50 percent of grants in their first year, Dr. Memoli pointed out that ICs always have had the ability to fully fund some grants and that most do so regularly. NIH intends to set a specific goal for the first time, but this will be subject to congressional approval.

- In response to concerns about grants awaiting funding as the end of the fiscal year approaches, Dr. Memoli commented that funding is only about 3 percent behind where it was at this point last year.

- When asked for explanations of grant terminations related to alignment with administration priorities, Dr. Memoli responded that the White House has a task force that looks for violations of civil rights laws and identified certain universities as being in violation; enforcement action was taken against those universities. Other grants have been terminated because the research now is inconsistent with HHS priorities. Dr. Memoli directed attendees to NIH Director Jay Bhattacharya's priority statement, which indicates topics that have been prioritized.

- When asked whether he is concerned about confirmation bias in research funded according to administration priorities, Dr. Memoli replied that he does not control decisions made by policymakers.

III. DPCPSI UPDATES

Dr. Kleinstreuer provided updates on DPCPSI activities, announcing the inaugural *NIH-Wide Strategic Plan for Autoimmune Research,* launched in July, which proposes a coordinated approach to supporting research that addresses the health needs of the many Americans living with autoimmune disorders. The strategic plan prioritizes scientific inquiry focused on the most pressing needs and integrates community perspectives. This holistic approach is intended to enhance the understanding of disease pathogenesis and expedite the development of novel therapies. Dr. Kleinstreuer also noted the recent publication of two DPCPSI-sponsored National Academies of Sciences, Engineering, and Medicine (NASEM) reports on team science and burnout in the scientific workforce.

Dr. Kleinstreuer noted new initiatives through *All of Us*. The *All of Us* Collaboration Hub highlights ways that other entities can leverage the *All of Us* infrastructure and platform to advance crosscutting research goals. *All of Us* also has shifted to clinical genetic testing, delivering results that may lower program costs and that participants can use in health care. New programs include the Remote Blood Collection Study, which tests two home blood collection devices for research sequencing, and the Eyes on Health Research Study, which will collect ocular images from 5,000 participants.

The NIH–U.S. Food and Drug Administration (FDA) Nutrition Regulatory Science Program is a collaboration between NIH and FDA to generate rigorous scientific evidence to inform food- and nutrition-related policy decisions. The program aims to align nutrition science with real-world regulatory needs and reduce chronic disease. Another new initiative is the Military Women's Health Monthly Webinar Series, hosted by ORWH and the Uniformed Services University Military Women's Health Research Program.

DPCPSI is leading the development of the first-ever *NIH Strategic Plan for Disability Health Research*, which will outline agencywide goals and objectives for advancing research activities that promote the health and well-being of people with disabilities. Dr. Kleinstreuer emphasized that the strategic plan has been developed with extensive input and feedback from individuals and organizations with expertise in disability. A Council working group on disability health research also has been established.

Dr. Kleinstreuer noted the ECHO Symposium on Translating Science to Action, which will explore how early environmental factors influence child health and how that research can be translated into meaningful action.

Discussion Highlights

- Dr. Kleinstreuer stated that although this strategic plan is the first NIH strategic plan addressing disability research, NIH has also invested the past in research relevant to this subject and has several ongoing programs in this space.

IV. DISCUSSION ON CHANGES IN NIH POLICIES AND PROCEDURES

In response to requests at a previous meeting, Dr. Kleinstreuer opened a discussion of recent changes in NIH policies and procedures. She explained that NIH is assessing its policies and processes and at that time were to be released.

The Office of Management and Budget required NIH to fully multiyear fund 50 percent of ICs' remaining fiscal year 2025 (FY25) research project grant (RPG) budgets, denoting that half the remaining funds allocated for competing RPGs must be used to fully fund the entire approved project period in a single award. As a result of this requirement, NIH anticipates supporting fewer awards. Dr. Kleinstreuer noted that projecting funds for future fiscal years is difficult to determine at this time but emphasized her commitment to providing transparency and timely updates once budget decisions are finalized.

Dr. Kleinstreuer elaborated on the new award structure prohibiting foreign subawards from being nested under the parent grant. The new system structures foreign subawards as subprojects that are directly linked to the prime award. This change applies prospectively to all NIH grants and cooperative agreements with domestic and foreign entities; designed to enhance transparency and trackability; protect national security and the biomedical research enterprise in both monetary and nonmonetary foreign collaborations. Dr. Kleinstreuer emphasized NIH's commitment to support international scientific collaboration in a secure, justifiable, and responsible manner. In July 2025, NIH implemented a short-term solution allowing recipients to remove a foreign subaward concerning human subjects from an existing award and renegotiate the subaward as an administrative supplement continuously supporting the health and safety of research participants at international sites while enhancing NIH's ability to track foreign financial obligations.

Dr. Kleinstreuer clarified the review rules for the Council, explaining that the legislatively required second level of review for NIH grant applications is performed by national advisory councils or boards and that the Council serves this function for DPCPSI programs. The Council may recommend that an application be funded or not funded, and the Council may also defer a decision to allow the application to

be re-reviewed by the study section. Dr. Kleinstreuer noted that the DPCPSI Director makes the final funding decision based on staff and Council advice.

NIH's recent focus on prioritizing human-based research is intended to accelerate progress, encourage innovation, and improve the quality and validation of new approach methodologies. The shift away from funding opportunities focused exclusively on animal models of human disease, as noted by Dr. Memoli, is intended to broaden the scope of models and technologies that NIH supports. Researchers may propose any model or combination of approaches deemed appropriate to answer the research question. NIH will continue to support grants that use laboratory animal models if they are scientifically appropriate and have appropriate animal welfare oversight.

A new NIH policy outlines guidance for appropriate use of artificial intelligence (AI) in research applications. NIH will not consider applications that are entirely developed by AI or contain sections that are substantially developed by AI. NIH also limits the number of applications a principal investigator (PI) can submit to six per calendar year, including renewal, resubmission, and revision applications.

NIH recently released a unified strategy for strengthening collective impact across the agency by balancing scientific opportunity with mission-driven priorities. NIH also has an implementation plan to incorporate "gold-standard science," which many DPCPSI-led efforts support. Dr. Kleinstreuer reiterated that NIH remains firmly committed to upholding the highest standards of evidence-based science that benefit the health of Americans and to restoring public trust.

Dr. Kleinstreuer also noted that NIH is working to simplify the landscape of funding opportunities to empower more investigator-driven projects, reduce overly narrow funding opportunities, and minimize administrative burden. As part of this effort, NIH-wide parent announcements will be used for many funding opportunities. Nonparent notices will be used for opportunities required to move a particular initiative forward, and an initiative called Highlighted Topics will emphasize timely and important areas identified by institutes, centers, and offices (ICOs).

Discussion Highlights

- Dr. Jennifer Manly commented that the executive order on improving oversight of federal grantmaking as well as Dr. Bhattacharya's priorities for NIH raise serious concerns about the increasing politicization of NIH grant decisions. Award decisions have been delayed by additional layers of scrutiny, and new review processes appear to prioritize alignment with political agendas over scientific merit, with notices of award restricted in nontransparent ways. Dr. Manly emphasized that the involvement of political appointees in grant decisions has the potential to undermine the integrity of the scientific process and is at odds with NIH's declared commitment to transparency. She asked for clarification on justification for grantmaking decisions and safeguards to ensure that scientific rigor remains the primary funding criterion, as well as whether mechanisms will be developed to explain to investigators why their funding was delayed or changed. Dr. Kleinstreuer responded that DPCPSI works closely with partner ICs and grants management staff to administer grants, and she reiterated NIH's commitment to upholding the highest standards of scientific rigor. She commented that grants have been terminated based on misalignment with HHS and administration priorities. An appeals process is available, and many grants have been reinstated after undergoing this process. Part of the appeals process incorporates feedback to grantees on the rationale for grant termination.

- Dr. Kleinstreuer clarified that the 50 percent multiyear funding for RPGs applies only to a specific number of grants during a specific period in FY25.

- Dr. K.C. Kent Lloyd asked whether the prohibition on funding opportunities using exclusively animal models applies to animal repositories and primate centers. Dr. Kleinstreuer responded that NIH intends to broaden the technologies and model systems used to address complex research questions. DPCPSI is working with ORIP to update its strategic plan in ways that reflect its historic support for animal model–based research infrastructure and the new, broader scope that includes new approach methodologies (NAMs) and human-based technologies. She clarified that researchers can still submit proposals exclusive to animal models, such as primate centers, but NIH will no longer publicize funding opportunities that only consider animal models.

- Dr. Karen Johnston pointed out that many early career scientists are worried about the viability of research careers in the current environment, which contrasts with Dr. Memoli's emphasis on training future biomedical scientists as a priority. She asked what additional programs DPCPSI offers to retain the best early career scientific minds. Dr. Kleinstreuer responded that several programs are dedicated to early stage investigators and that the changes to the review process to reduce emphasis on paylines are intended to provide that support. Dr. Bhattacharya is encouraging IC directors to consider early stage investigators with innovative ideas, regardless of their place relative to the traditional payline cutoff. Dr. Vivian Ota Wang pointed out that supporting early stage investigators is one of the primary tenets of cutting-edge science at OSC and encouraged early stage investigators to apply. Dr. Kleinstreuer added that all categories of the High-Risk, High-Reward Research Program are open to early stage investigators and that two awards are specific to them; she reiterated NIH's commitment to funding those programs as the budget allows.

- Dr. Rafael Irizarry asked for clarification on the Council's role in initiatives presented to the Council with a large budget, but no vote scheduled, such as the Autism Data Science Initiative (ADSI) and Real-World Data Network. Dr. Kleinstreuer explained that these programs are administratively and logistically supported by DPCPSI, but they are not Common Fund programs. ADSI is an NIH Director's initiative supported directly by the NIH Director's discretionary funding, and the Real-World Data Network is a partnership across multiple programs and ICs and is built upon substantial foundational infrastructure. Dr. Grieder pointed out that Common Fund concepts presented to the Council include estimated budgets and that the Council approves the scientific concept and basic strategies in a public forum, but NIH makes the final decisions depending on its annual appropriation.

- When asked about the large number of new Council members awaiting approval, Drs. Kleinstreuer and Grieder confirmed that their nominations remain pending. Council members emphasized the importance of ensuring that the Council has robust and broad representation.

- Dr. Lloyd pointed out that the plan to release more NIH-wide funding opportunities reduces specificity and clarity, which may affect the review process, especially given its new centralization. Dr. Kleinstreuer commented that NIH is trying to reduce an excessive number of highly specific funding opportunities and added that NIH's focus is ensuring that its priority scientific research areas are covered by comprehensive funding opportunities with clear guidance.

- Dr. Kleinstreuer confirmed that the early independence funding opportunity approved at a previous Council meeting is still in the pipeline.

- Dr. Kleinstreuer explained that NIH is working to identify tools and processes to assess whether proposals were developed by AI. Limiting the number of applications from the same PI also will address this issue.

- When asked how NIH will demonstrate that it values research on less-studied topics, Dr. Kleinstreuer responded that NIH is committed to covering a broad range of important research areas. She was not aware of any intent to remove special emphasis panels, and CSR will continue to ensure that reviewers have the greatest degree of subject-matter expertise in proposed areas. Dr. Grieder added that IC-specific review groups now operate under the umbrella of CSR but still exist, and Dr. Kleinstreuer pointed out that the reviewer pool can be expanded at any time.

- Dr. Richard D. Krugman noted that science and academics have become increasingly subspecialized and that opportunities for crosscutting science are lacking. He asked that as crosscutting opportunities are considered, researchers think specifically about the impact of childhood abuse on physical, mental, and public health. Dr. Kleinstreuer replied that as NIH works to evolve the biomedical research portfolio, the agency must consider emphasizing more multidisciplinary approaches.

- Dr. Lloyd asked for clarification on the conflict between the statement that ICs have final funding decisions and the executive order on oversight of federal grantmaking, which stipulates that a special appointee oversees funding decisions. Dr. Kleinstreuer pointed out that the NIH Director is a senior political appointee, so final funding decisions rest with Dr. Bhattacharya as both NIH Director and a senior political appointee. She added that the NIH Director has always had the final determination in funding decisions.

V. 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 review of 109 ORIP applications with requested first-year direct costs of $467,336,924.

VI. ORIP STRATEGIC PLAN UPDATE

Dr. Grieder presented the current draft of the *ORIP Strategic Plan 2026–2030*. She emphasized that the plan reflects ORIP's mission and vision in the context of current policies and guidelines. ORIP's tagline is "Infrastructure for Innovation," and the office operates in alignment with its three guiding principles: (1) awarding extramural grants, including cooperative agreements and contracts; (2) organizing and executing targeted workshops to identify existing scientific gaps and opportunities; and (3) supporting training for uniquely qualified biomedical scientists.

ORIP's strategic plan supports the NIH mission and priorities, including focus on human health, emphasis and support for replicability and rigorous conduct of scientific experiments, and promotion of innovation while supporting academic freedom. Dr. Grieder emphasized that ORIP's programs support all NIH ICOs and span the research continuum from basic discoveries to real-world implementation. ORIP's goal is to support the needs of the extramural scientific community and investigators.

[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.

In alignment with this outlook, ORIP is committed to addressing current challenges across the biomedical landscape. This includes fostering rigor and reproducibility in science, promoting NAMs to complement other models, upgrading critically important research infrastructure, and addressing challenges presented by advancements in data science. Dr. Grieder provided an overview of ORIP's structure and emphasized that many of ORIP's programs fund resources and centers that have been supporting the biomedical enterprise for decades.

Dr. Grieder outlined ORIP's strategic planning process. She noted that ORIP staff have been working collaboratively and productively for more than 2 years to achieve the concepts and strategies that are reflected in the plan. This included a kickoff retreat, followed by working groups and other meetings with internal and external experts. ORIP began developing the text for its strategic plan about 6 months prior to the Council presentation.

The strategic plan is organized by four priorities: (1) Model Resources to Advance the Study of Human Diseases, (2) Modern Physical Infrastructure to Accelerate Research Discoveries in Human Health and Disease, (3) Innovative Cross-Disciplinary Research Training in Model Systems for Human Health and Diseases, and (4) Expanding Outreach and Awareness of ORIP Resources and Programs. ORIP also identified four crosscutting themes that are important for ORIP's programmatic operations: Conducting Responsible Stewardship to Maximize Research Efficiency; Enhancing Scientific Transparency, Rigor, and Reproducibility; Strengthening Resources and Infrastructure for Health Research; and Promoting Research and Training Opportunities.

Discussion Highlights

- The discussants, Dr. Lloyd and former Council member Dr. Susan Sanchez, provided their comments. Dr. Lloyd remarked that the draft plan provides a forward-looking overview of ORIP's priorities that enable the entire spectrum of NIH-wide biomedical research investments. He commented that the plan would benefit from (1) emphasizing the integration of NAMs into the research tool ecosystem, rather than as a substitute for *in vivo* systems to model human diseases; (2) reintroducing preparedness for pandemics to ensure resilience of the research enterprise; and (3) clarifying the biomedical workforce strategy regarding the critical role for veterinary scientists' unique contributions to NIH's mission.

- Dr. Lloyd also remarked that the plan is ambitious, with frequent reference to expansion of investments in human-based translational research, data-integrated technologies, AI/machine learning (ML)–driven resources, and high-performance computing. He underscored the importance of balancing existing and proposed competing priorities. He also noted that ORIP's support for its resources is better characterized as an assistive mechanism rather than as a fully supportive one. The host institutions contribute significantly to the costs of projects in all resource categories, and many depend on recovery of user fees.

- Dr. Grieder agreed on the importance of considering these points in ORIP's strategic planning. Dr. Kleinstreuer concurred and added that training opportunities for veterinary scientists should be broad and cross disciplinary. She remarked that the language changes regarding human-based models are aligned with the NIH Director's priorities and reflect prior feedback from Council members on the need to support further development and validation of NAMs. She also noted that the FY26 budget still is being determined.

- Dr. Sanchez commented that scientists are thoughtful and deliberate in their use of animals, and they welcome alternatives that can effectively answer critical research questions. She cautioned that many NAMs lack the standardization and validation required to meet NIH standards for

scientific rigor. Reproducibility is essential, and animal models remain the gold standard in many areas of biomedical research. She emphasized the importance of continuous support of these models for maintaining scientific rigor and readiness for future public health emergencies.

- Dr. Sanchez also underscored the importance of veterinary scientists in research. She added that investments in AI/ML technologies and human-centered translational research are important, but they should not come at the expense of ORIP's core programs, which support a wide range of disciplines and NIH ICs. She recommended that ORIP maintain clarity when stating its priorities and ensure continued support for infrastructure and expertise that have long enabled transformative discoveries in human health. Dr. Grieder agreed on the importance of these points.

- Dr. Monica Gandhi commented that the plan is responsive to Congress' discussions on indirect cost rates and animal research and underscored the importance of continued support for veterinary scientists.

- Dr. Johnston commented that the use of the term "model" in the plan occasionally was unclear. She suggested defining the types of models addressed (e.g., computational, human tissue, animal) and highlighting their complementary roles in research. She also suggested including more specific language regarding veterinary scientists in the plan, as well as in funding opportunities.

- Dr. Russ Van Gelder spoke on the importance of highlighting large resource centers, such as the National Primate Research Centers, that ORIP has supported for many years. He stated that these investments have been critical for research advancements. He also recommended including a statement on ORIP's commitment to enhancing research infrastructure in all NIH-related research endeavors without regard to any institution. Dr. Grieder noted that ORIP's resources reflect many years of investment and development. She clarified that construction funds are set aside for Institutions of Emerging Excellence. Additional policies are in place to ensure wide geographic distribution of ORIP funds.

VII. *ALL OF US* RESEARCH PROGRAM OFFICE CONCEPT CLEARANCE (NEW): ACCELERATING DISCOVERY THROUGH PARTNERED RESEARCH WITH *ALL OF US* TO ANALYZE PARTICIPANT BIOSPECIMENS [VOTE]

Sheri Schully, Ph.D., Deputy Chief Medical and Scientific Officer, *All of Us* Research Program Office, DPCPSI, outlined a new concept supporting use of biospecimens collected by *All of Us*. The X01 requires no funding from *All of Us* and is anticipated to support five projects of 1 to 3 years. Dr. Schully explained that the mission of *All of Us* is to accelerate research and enable individualized prevention, treatment, and care for "all of us." The program enacts this mission by nurturing partnerships for decades with 1 million or more participants across the United States and its territories, including many previously underrepresented in research. The dataset compiled by *All of Us* is one of the largest, richest biomedical datasets that is both broadly available and secure. The program hopes to catalyze an ecosystem of communities, researchers, and funders to make *All of Us* an indispensable part of health research. To date, *All of Us* has consented more than 865,000 individuals into the program, and about 600,000 have completed the initial steps, including an in-person visit or a donation of biospecimens, consent to use electronic health records for research, and completion of surveys. Biospecimens, typically blood or urine, from more than 609,000 individuals are stored at the Mayo Clinic biobank.

All of Us is embarking on partnered research studies, traditionally called ancillary studies, that will be funded by external entities. These projects will collect new types of data by exploring biospecimens or recontacting participants, and these new data will be integrated into the existing data ecosystem. New data will be available through the Researcher Workbench, and value must be returned to the participants. The

existing biospecimens have been designated as non-human subjects, so they will be deidentified. Further studies, such as participant recontact and embedded trials, will need institutional review board approval.

Six studies have currently been launched, and the program is developing partnerships across NIH to support innovative studies while preparing tools and resources to make the program's resources broadly available beginning with this concept, which will enable investigators to apply for access to NIH resources to conduct research. The investigators must have funding to be approved for the project and will reimburse the costs incurred by the biobank to pull and ship the sample. The hope is that this program will accelerate discovery, enable innovative and cost-effective research, and return value to participants by educating them about new assays. The X01 allows the program to ensure fairness and transparency in the application and review process, and this will help the field move toward achieving precision medicine for all. Two receipt dates are proposed in April and September 2026. Programmatic review will be conducted by the *All of Us* program and subject-matter experts from ICs as needed. Project support will be provided in 1-year increments. *All of Us* will review requests for scientific policy and core values, and researchers approved for access to specimens may launch their studies after securing their own funding.

Discussion Highlights

- The discussants, Drs. Gandhi and Krugman, provided their comments. Dr. Gandhi supported the proposal and asked for examples of the types of research expected, as well as the connection to chronic disease. She also asked about cost efficiency and limitations on topic, and she asked how implementation research would be involved. Dr. Schully explained that *All of Us* was designed to be disease agnostic and enrich the resource to represent people who have not traditionally been included in research. Part of the goal is to build clinical evidence for those underrepresented groups, so the program is planning to follow up with participant-provided information. Dr. Schully noted that the program is trying to be as creative and cost-effective as possible, such as by delivering at-home blood collection kits or partnering with entities that have sites across the United States. As an example of translation, the Broad Institute developed a polygenic risk score using these data that recently has been implemented in clinical care, and the Nutrition for Precision Health program is an intervention being conducted within *All of Us* to study the impact of diet on health outcomes.

- Dr. Krugman recommended approval of this project and commended use of the X01 mechanism. He asked about the topics of current research studies and encouraged the program to include past histories of child physical and sexual abuse in its surveys, particularly given the intent to re-contact participants for longitudinal surveys. Dr. Schully explained that every project is logged at the *All of Us* website, thereby supporting transparency. The program also intends to facilitate collaborations between researchers interested in similar topics, such as the many researchers currently studying chronic disease–related topics. Dr. Schully confirmed that a question about past abuse is in the reassessment module and noted that *All of Us* focuses on assessing the whole person and creating a complete picture of all participants.

- Dr. Irizarry expressed concerns with difficulties accessing the data and encouraged program representatives to work with independent researchers to ensure there are no unseen barriers.

- Dr. Schully clarified that investigators will receive no personal data on the biospecimens except sex at birth. *All of Us* works closely with its data resource center at Vanderbilt University to define the data life cycle and ensure high-quality data that are standardized across steps. Partners are provided with the format in which the program needs the data to be returned, and the partner has access for 9 months before the data are released to everyone, which allows them to conduct an impactful study showing how the data can be used for that research question.

- Dr. Schully emphasized that while this discussion addresses the concept, the actual program announcement is planned in the near future. The program intends to clearly request applications for projects that enrich the *All of Us* ecosystem.

- Dr. Van Gelder pointed out that the proliferation of large datasets has led some researchers to search for correlations without a hypothesis, leading to questionable results that cannot be reproduced. He asked about guardrails against this. Dr. Schully explained that although the platform is open, all projects must be listed, and all research is conducted in the cloud, so researchers are encouraged to share workspaces to support replication. Dr. Van Gelder encouraged the program to request that investigators present their queries. Dr. Schully added that the public can flag research that seems stigmatizing for review.

- Dr. Kleinstreuer asked about plans to ensure this announcement is disseminated across ICs. Dr. Schully confirmed that they plan to present the program at various ICs, as well as potentially to the Program Coordinating Committee.

Vote

A motion to approve the Accelerating Discovery Through Partnered Research with *All of Us* to Analyze Participant Biospecimens concept was forwarded and seconded. The motion passed with no abstentions.

VIII. OSC CONCEPT CLEARANCE (NEW): RNOMICS PROGRAM [VOTE]

Frederick L. Tyson, Ph.D., Program Director, Genes, Environment, and Health Branch, NIEHS, introduced the RNomics Program, an initiative aimed at advancing RNA science through the creation of a comprehensive toolkit for characterizing and sequencing the human RNome. The RNome encompasses all RNA molecules, and their modifications expressed in a cell, tissue, or organism at a given time. The proposed program would cost approximately $30 million per year for 5 years to support about 15 awards.

Dr. Tyson emphasized the complex, dynamic nature of RNA, highlighting its role beyond acting as a passive messenger. RNA is a versatile toolkit involved in regulation, translation, and catalysis, with modifications that influence gene expression and protein production. Unfortunately, current RNA sequencing technologies are inadequate for full-length transcript sequencing and modification mapping. Understanding RNA modifications is particularly important for human health, as researchers have identified more than 100 chronic diseases associated with RNA modifications. Many RNA databases exist currently, but they are not interoperable. The RNomics Program would directly address these technological deficiencies and foster an environment that adopts widespread standards that make databases interoperable.

Dr. Tyson then briefly reviewed other recent work on RNomics that helped lay the foundation for the RNomics Program. In response to a 2021 *Nature Genetics* manuscript highlighting the need for direct RNA sequencing technologies, NIEHS and NHGRI convened a conference in May 2022 with more than 400 participants. Together, the participants identified technologies needed to comprehensively characterize RNomes and needs related to infrastructure, bioinformatics, and other resources. NIEHS and NHGRI then commissioned a consensus report from NASEM, "Charting a Future for Sequencing RNA and Its Modifications," that outlined a 15-year plan for expanding RNA-based research through technological advancements and the development of chemical, biological, and data standards.

Ian C. Nova, Ph.D., Program Director, Division of Genome Sciences, NHGRI, elaborated on the RNomics Program's structure, which is broken into four initiatives. He emphasized that the program's focus is technology development rather than large-scale data generation, and the goal is to provide the research community with a suite of tools to investigate RNA and then begin generating tissue-specific

datasets after the technologies are benchmarked. As the program progresses, it will support the generation of first-of-their-kind reference datasets and RNA-based clinical biomarkers.

The largest initiative, representing approximately 50 percent of overall program funding, is the development of RNA sequencing technologies that can more accurately analyze RNA with base modifications. The emphasis will be on technologies that sequence complete transcripts and detect many modifications in a single measurement. This initiative will include both high-risk, high-reward sequencing technology grants and collaborative RNA sequencing technology development centers that could include investigators with expertise in many disciplines. The second initiative will aim to create molecular and computational tools that can help decipher the effects of RNA modifications. Dr. Nova envisions the use of various technologies, including sequencing, imaging, and computational algorithms based on AI and ML. The third initiative, focused on the development of RNomics molecular standards, will address the critical need for standard RNA molecules to ensure reproducibility across RNA technologies and serve as a platform for cross-comparison and benchmarking. Finally, the fourth initiative would establish an RNomics coordinating center to harmonize efforts and facilitate outreach. This center would generate standards for methodology, nomenclature, and database requirements for RNomics data; create community challenges to cross-compare techniques and computational tools; coordinate data production and facilitate the reference dataset selection and production based on predetermined benchmarks; and coordinate outreach by promoting user guides to help scientists and clinicians choose computational and sequencing methods based on their inquiry.

Finally, Dr. Nova noted several anticipated outcomes from the RNomics Program: the production of comprehensive tissue-specific datasets, an enhanced understanding of the mechanisms and overarching rules of RNA molecular physiology, the discovery of RNA-based clinical biomarkers, the production of RNA therapeutics and RNA-targeting drugs, and insights into the effects of environmental exposure on biology and human health.

Discussion Highlights

- The discussants, Drs. Lloyd and Manly, provided their comments. Dr. Lloyd expressed concerns about the program's ambitious scope and feasibility. He questioned whether the program could succeed within the proposed time frame and whether the foundational standards should be developed prior to launching a Common Fund initiative. Dr. Nova responded by citing existing technologies and the catalytic potential of providing "ground-truth" standards, which would accelerate development. He also cited the coordinating center, which would bring disparate technology development efforts together and provide end users with better tools for generating high-quality reproducible data. Dr. Tyson added that without Common Fund support, the necessary standards would likely remain undeveloped due to lack of incentive. Both Dr. Nova and Dr. Tyson emphasized that the time is right to launch this project.

- Dr. Lloyd also expressed concerns about overlap between the proposed project and other Common Fund projects doing similar work, such as the Extracellular RNA Communication Program. Dr. Trish Labosky, who was the lead on that program, clarified that the RNomics Program focuses on different scientific objectives and deliverables and noted that the projects would be complementary.

- Dr. Manly supported the concept, highlighting its alignment with the NASEM report, which identified critical gaps in RNA research. She suggested that the concept clearance could more explicitly engage with current challenges in the RNA research landscape and describe how the program would align with FDA and European Medicines Agency guidance on RNA therapeutics and diagnostics. She also recommended incorporating community engagement and public

communication strategies to address the politicization of RNA science and enhance transparency. Drs. Tyson and Nova agreed, noting that the coordinating center would include outreach components to build public trust and support safe therapeutic development.

- Drs. Carolyn Hutter and Rick Woychik reinforced the program's timeliness and necessity, noting strong support from IC directors and alignment with broader research goals, including environmental health and gene–environment interactions. Dr. Woychik commented that the program is feasible in part because the research community sees credible ways to advance RNA sequencing technology.

Vote

A motion to approve the RNomics Program concept was forwarded and seconded. The motion received four years, two nays, and two abstentions.

IX. OSC CONCEPT CLEARANCE (NEW): ULTRA-PROCESSED FOODS PROGRAM [VOTE]

Andrew A. Bremer, M.D., Ph.D., M.A.S., FAAP, Director, ONR, introduced the Common Fund Ultra-Processed Foods (UPF) program, which aims to support robust multidisciplinary research across the lifespan on UPF-mediated mechanisms underlying chronic disease and adverse health outcomes and provide the evidence base needed to inform dietary guidelines, policies, and programs that promote disease prevention. Dr. Bremer noted the program would cost approximately $57 to $63 million per year for 5 years to support an estimated 20 awards.

Dr. Bremer emphasized that diet-related chronic diseases are the leading cause of death worldwide. In the United States, more than 1 million deaths and $1.1 trillion in health care costs and lost productivity per year are caused by diet-related chronic diseases. Epidemiological studies suggest an association between UPF-rich diets and an increased risk for adverse health outcomes. In the United States, about 60-66 percent of daily caloric intake is composed of UPFs depending on the population and age ranges studied. Dr. Bremer provided an overview of the NOVA classification system, which includes unprocessed or minimally processed foods, processed culinary ingredients, processed foods, and UPFs. Dr. Bremer stressed that the NOVA classification system does not consider the nutritional profile of UPFs when assigning them to one of the four groups.

Dr. Bremer briefly reviewed a seminal mechanistic study conducted by Dr. Kevin Hall at the Clinical Center, NIH, which showed a UPF diet caused participants to gain weight. When the participants were switched to an unprocessed diet, the reverse trend was observed. Another study currently underway shows in an interim analysis that diets constructed to be hyper-palatable and energy-dense result in consumption of ~1,000 more calories per day. Emerging epidemiological evidence suggests that UPF consumption adversely affects multiple organ systems, but the current data are mostly from observational studies, and a mechanistic understanding is needed. Moreover, no validated biomarkers of UPF exposure exist.

Dr. Bremer outlined the necessity for a UPF Common Fund program given the current national interest in expansive and comprehensive UPF-related research and noted that an NIH-wide UPF Working Group comprise of 17 ICOs helped guide the development of this program. A comprehensive portfolio analysis showed 34 extramural and intramural UPF-related projects across 12 ICOs between FY19 and FY23. The proposed UPF Common Fund program would also support the efforts of the new NIH–FDA Nutrition Regulatory Science Program, which aims to understand how food additives and preservatives affect metabolic health and contribute to the development of chronic disease. In addition, an interagency request for information from HHS, the FDA, and the USDA is open until September 23, 2025, to gain input from

the community about a uniform definition of UPF – the results of which would also inform the UPF Common Fund program.

Three components underscore the framework of the UPF Common Fund program: (1) strategic collaborations and partnerships, (2) research and communication centers, and (3) coordination and analysis centers. The budget is ~$300 million over 5 years. Dr. Bremer highlighted how the UPF program aligns with the Common Fund criteria by developing tools to help consumers make informed dietary choices and generating data to improve nutrition policies and inform industry on best practices for UPF reformulation to create healthier options. Deliverables will include an understanding of the mechanisms through which UPF consumption affects the risk for developing chronic diseases and adverse health outcomes; biomarkers of UPF consumption; a publicly available processed food database and tools to determine the level of food processing and identify UPF ingredients; data to inform interventions specific to prevention of diseases from UPF consumption; data to inform FDA regulatory decisions on UPFs, UPF ingredients, and manufacturing processes; and materials to educate the public and health care professionals about UPFs.

Discussion Highlights

- The discussants, Drs. Manly and Krugman, provided their comments. Dr. Manly expressed concerns about the program's ambitious scope and feasibility. She requested that Dr. Bremer provide additional information about the UPF Common Fund program for further Council discussions. Previous research has provided evidence for the role of UPFs in chronic diseases, but she noted that changes to policy are hindered by structural challenges, such as industry influence on regulatory organizations and administrative reluctance to address the social drivers of diet-related disease. Dr. Manly emphasized that the Common Fund program needs to acknowledge and address these structural challenges, which limit return on investment, and recommended that the concept address these issues.

- Dr. Manly also expressed concerns that the lucrative wellness industry promotes individualized but ineffective solutions. The UPF Common Fund program does not address the commercialization of health or highlight potential pharmacological interventions. She commented that research that focuses on monitoring, compliance, and enforcement of UPF-related policy changes is needed.

- Dr. Bremer responded that during the inception of the UPF Common Fund program, NIH staff engaged in a series of discussions with FDA to understand the data required to initiate regulatory changes. He acknowledged the importance of health disparities and suggested that private sector participation will allow for the formulation of healthier products. Intervention studies also could be included in the program. Dr. Bremer reiterated that the program aims to provide the information needed to modify the food system and make population-specific healthy foods available.

- Dr. Krugman also expressed concern about the program and suggested that additional discussion is needed. He asked when the working group began developing the concept and requested clarification on the proposed NIH RMS/Program Management budget line item. Dr. Bremer responded that meetings of the UPF Working Group began in the summer of 2024 – well before the current administration – and explained that the NIH RMS/Program Management line item would allow subject-matter experts from the various ICOs to be involved (e.g., program officers, project scientists, grant management specialists, etc.).

- Dr. Bremer clarified that the mortality statistic presented includes all diet-related diseases. Dr. Irizarry recommended the addition of a life expectancy statistic.

- Dr. Irizarry recommended that the program use randomized clinical trials to ensure that the underlying causes of diseases are related to UPFs rather than calorie intake, particularly given the many confounders present in observational studies. Dr. Bremer emphasized that research conducted through this program would indeed include randomized clinical trials and be rigorous.

- Ms. Lauren Silvis noted that diet-related research has been chronically underfunded for years and recommended that research conducted under this concept support policy solutions to regulate the food industry.

- Dr. Johnston emphasized that health outcomes will not improve until underlying structural challenges are addressed.

- Dr. Van Gelder commented that the deliverables lack sufficient details and recommended that the proposal be removed from consideration and be revised to address the Councilors' concerns.

The Ultra-Processed Foods concept was withdrawn from motion; it will be revised to address Council feedback.

X. ADJOURNMENT FOR THE DAY

Dr. Kleinstreuer thanked council members for their thoughtful input and robust discussions and adjourned the meeting for the day at 5:23 p.m. on September 11, 2025.

Day 2

XI. WELCOME AND RECAP OF DAY ONE

Dr. Kleinstreuer called the second day of the meeting to order at 10:01 a.m. on September 12, 2025, and outlined the day's agenda.

XII. AUTISM DATA SCIENCE INITIATIVE (ADSI)

Taylor Gilliland, Ph.D., Senior Scientific Advisor to the Director, DPCPSI, introduced ADSI. Autism is an extremely heterogeneous neurological and developmental condition with symptoms that present typically within the first 2 years of life, although diagnosis is often delayed. The wide-ranging symptoms and variable clinical presentations lead to a broad scope of needs for treatment, services, and support. Rates of autism diagnosis have increased steadily, driven in part by improved quality and accessibility of diagnostic screening and recognition of the condition, as well as changes in diagnostic criteria and increased awareness of signs of autism. A strong genetic component is a known risk factor; non-genetic components may include parental health factors, prenatal conditions, neurological syndromes, and environmental factors and exposures that can lead to complex gene–environment interactions (i.e., the exposome).

ADSI aims to gain new knowledge about autism to improve the health and well-being of people on the autism spectrum. Priority research areas include new, emerging, or understudied factors that contribute to autism and how multiple nongenetic factors might interact with genetics to affect the condition, as well as how such complex gene–environment interactions, when considered with the changes in awareness and diagnosis, explain the increase in autism diagnosis in the United States. ADSI also intends to assess current interventions for use in better addressing the needs of autistic individuals across the lifespan.

ADSI will accomplish its goal through four interconnected strategic aims: (1) combining and integrating existing data relevant to autism, (2) collecting new information to fill gaps in the understanding of the etiology of autism, (3) analyzing the combined existing and new datasets, and (4) validating the results and methods independently. The ADSI research opportunity announcement uses the Other Transaction Authority mechanism, which often is used to support research initiatives that rapidly address an evolving research topic and invite nontraditional collaborators. Dr. Gilliland clarified that investment in ADSI is in addition to the existing NIH autism research portfolio. Researchers applied to support the four strategic aims in several allowable configurations—those who applied to provide independent validation could not be funded for other tasks—and each applicant also was required to submit plans for community engagement and data management and sharing.

Dr. Gilliland addressed concerns about the intent of ADSI, noting that all data used by ADSI-funded investigators must comply with any applicable laws and regulations ensuring protection, security, and confidentiality of data collected from research participants. ADSI will not require research teams to submit data to NIH for deposit into a centralized repository, and each research team will independently implement any dataset aggregation, data generation, and data analysis activities.

Dr. Gilliland pointed out that the high number of applications and short timeline required ADSI to recruit many internal and external reviewers with the appropriate subject-matter expertise. Expert reviews of the applications assessed the overall impact, feasibility, and likelihood of achieving the proposed goals. After expert review, NIH staff conducted a programmatic review and prioritization of the applications. High priority applications were presented to an executive committee composed of senior leadership from multiple ICs. Dr. Gilliland listed some proposed causal factors and interventions to be investigated.

Based on concerns expressed during previous council meetings, Dr. Gilliland addressed how the ADSI is both related to and different from the Real-World Data Network initiative. ADSI is a research initiative that will fund independent investigators to work with existing datasets and generate new data, whereas the Real-World Data Network is a separate data infrastructure initiative that will link data sources into an NIH network and provide computational analysis resources. Dr. Gilliland reiterated that ADSI does not support a centralized data platform, but the Real-World Data Network will leverage existing infrastructure to build a more powerful and secure network. The Real-World Data Network also will be a resource for many conditions, whereas ADSI focuses solely on autism. Dr. Gilliland emphasized that these separate and distinct initiatives share a commitment to the collaborative engagement of community partners and ensuring data privacy, security, and confidentiality.

Discussion Highlights

- Dr. Irizarry asked why autism was selected for this investment, given the evidence that the increase in prevalence is caused by changes in diagnostic approaches, as well as the lack of autism-associated morbidity and the abundance of existing studies. He encouraged ADSI to confirm the increase in incidence before searching for its explanation. Dr. Gilliland suggested that unanswered questions in autism could benefit from a targeted approach to leveraging existing data. He noted that autism prevalence data are provided by the Centers for Disease Control and Prevention. Dr. Kleinstreuer added that this was identified as a very high priority by both the administration and the HHS Secretary.

- When asked about the identities of subject-matter experts recruited to review the applications, Dr. Gilliland explained that many experts requested to participate anonymously, but he assured attendees that their expertise was appropriate. Dr. Lloyd expressed concern about this change in transparency, noting that NIH grant reviewers always have been listed publicly.

- Dr. Gilliland explained that ADSI data will not be required to be added to the Real-World Data Network, but it will be an option. He clarified that previous analyses of autism-related data are not considered inadequate, but that ADSI intends to connect datasets that are not currently interoperable to drive new insights.

- Dr. Lloyd asked what precautions the program will take to ensure data analysis will be protected from confirmation bias, given comments from leadership supporting disproven theories of autism etiology. Dr. Gilliland responded that integrating independent validation from the beginning will support reproducible results that can be trusted.

- When asked about community involvement in developing the proposal, Dr. Gilliland explained that given the speed of the proposal, the team relied heavily on NIH experts who have worked with the autism community for decades. Dr. Bhattacharya and Kleinstreuer held a listening session with the autism community in June, and the results were used in building the ADSI program. Dr. Gilliland confirmed that the community was part of the targeted reviewer recruitment.

- Dr. Van Gelder pointed out the dissonance between centralizing peer review at CSR and exempting a large-scale project like ADSI from CSR-based review panels. He also noted that many grant proposals have been unable to secure funding because of mandates on upfront funding, yet this proposal was rushed to be funded in the current fiscal year. Dr. Van Gelder noted that Director's programs can bring the community together for public scientific meetings and asked whether a public forum is planned for this project. Dr. Gilliland encouraged attendees to recommend activities after the award launch and assured Council members of the program's commitment to transparency.

- When asked about the timeline for researching this complex condition and the probability of discovering interventions, Dr. Gilliland responded that ADSI awards have a project period of 2 to 3 years, and one category focuses on interventions.

XIII. REAL-WORLD DATA NETWORK

Dr. Kleinstreuer provided more information on the Real-World Data Network, which is intended to build upon existing infrastructure to connect data into an interoperable network that maintains high standards of security but facilitates more complex analyses of large, multivariate datasets. She pointed out that many data analysis programs already rely on real-world data, so the goal of this network is to link those datasets for use with cutting-edge analysis tools that will allow researchers to better separate signal from noise and identify contributing factors to adverse health outcomes and chronic disease. This network will work closely with many collaborators to ensure good stewardship of data and work at speed and scale. One partner, the Centers for Medicare & Medicaid Services, has agreed to provide de-identified data on individuals with a diagnosis of autism spectrum disorder. Another partner, the National Clinical Cohort Collaborative (N3C), was formed to gather information on COVID-19 from electronic health records but has expanded to include many other disease endpoints. The NIH Data COUNTS program, another partner, embeds individuals within health care institutions to improve and curate data systems.

Researchers interested in using the Real-World Data Network can submit a data use request, which will be reviewed for probability of technical success, policy alignment, and privacy. The request is then reviewed by institutions with data matching the request; institutions can choose not to participate. The network will harmonize all data pulled from the appropriate sources and create a secure workspace with the approved data and linked external datasets. Access to that workspace will be exclusive to authorized researchers,

and all analysis will be performed in that enclave. Only aggregated results will be exportable following an additional review step, and all activity will be logged for compliance and limited to 1 year.

Discussion Highlights

- When asked about time limits for data access, Dr. Kleinstreuer explained that most institutions allow multiple data pulls, which will provide researchers with snapshots of data at several time points. Exact limits may depend on agreements with health care institutions. Following a request for case studies for new research that this network would enable, Dr. Kleinstreuer suggested that this information could be added to the agenda for a future meeting.

- Dr. Van Gelder emphasized the significant likelihood of false discovery in such a large dataset and asked where the total dataset would be hosted. Dr. Kleinstreuer reiterated that access will be provided in a closed environment that does not allow researchers to download raw data, so this analysis workbench will facilitate reproducible, high-quality analyses and application of models that can be independently validated and verified.

- When asked about original limitations on N3C data, such as high degrees of missingness and the need for training, Dr. Kleinstreuer commented that the team is aware of the need for training and has multiple associated initiatives. Dr. Susan Gregurick, Director of ODSS, explained that the missingness in N3C predicated the work of Data COUNTS, which works to fully provenance data. Data that enter N3C will be consistently mapped. Dr. Kleinstreuer also confirmed that pediatric populations are represented in several datasets.

XIV. NIH COMMON FUND VENTURE PROGRAM UPDATE

Michelle Hamlet, Ph.D., Program Leader, OSC, DPCPSI, provided an update on the Common Fund Venture Program, which consists of initiatives that meet both Common Fund and Venture-specific criteria. The Common Fund criteria ensure novel, broadly impactful research projects of up to 10 years that advance the missions of multiple NIH ICOs. Venture ideas also must be bold, focused, and rapidly implemented relative to Common Fund programs. Project periods are up to 3 years, and the maximum award is up to $5 million per year.

Dr. Hamlet provided updates on the four current initiatives. The Development and Application of Imaging Technologies for Oculomics initiative supports the development and application of novel non-invasive eye imaging technologies that will allow identification of specific biomarkers for systemic diseases. Since last year, three awards have been issued for projects developing advanced retinal imaging technology to identify biomarkers of vascular disease; assess blood flow patterns in the retina that could signal neurological issues; and enhance imaging technology with visible light, high-resolution, cross-sectional images of eye tissues to identify early signs of degenerative neurological disease. The Systems Biology Data Platform uses public–private partnerships to connect independent datasets to improve understanding of biological pathways. The first phase is nearing completion, and the second phase will include establishment of a centralized data management system and continuing work on common data models and harmonization tools.

The Newborn Screening by Whole Genome Sequencing Collaboratory aims to expand whole-genome sequencing across state public health laboratories to enhance early diagnosis of treatable genetic conditions in newborns. A research opportunity announcement was issued in March 2025, with applications received in May and one award anticipated by the end of September. The final current initiative, Advancing Noninvasive Optical Imaging Approaches for Biological Systems, aims to develop less invasive optical imaging techniques by addressing the issue of light scattering within biological tissues. A notice of funding opportunity was published in 2024, applications were received in March

2025, and notices of award were recently issued for four projects. These projects focus on developing imaging that integrates reflection matrix optical coherence tomography with wavefront shaping, increasing the depth of photoacoustic tomography, developing synthetic wavelength imaging by mixing two captured optical fields, and using shortwave infrared technology Raman imaging. These awards will have a design phase followed by a testing phase culminating in *in vivo* demonstrations after 3 years.

The newest Venture initiative, Targeting RNA in Disease with Novel Technologies, aims to develop technologies that target RNA to identify new treatments for otherwise intractable diseases. Although proteins are the traditional target of therapies for human disease, targeting RNAs could expand the proportion of the human genome that can be therapeutically targeted. RNAs also have been implicated in many diseases; Dr. Hamlet outlined the example of myotonic dystrophy, which is caused by RNA dysfunction. Technologies for addressing RNA problems exist in the laboratory for research but have not yet been therapeutically translated, showing the timeliness of this initiative.

Discussion Highlights

- When asked about evaluation metrics, Dr. Hamlet explained that the program is currently developing protocols that can be used to evaluate initiatives at multiple levels. Her team also intends to evaluate the Venture Program itself to determine if it has been an effective way of supporting rapid development of clinical products.

- In response to a question about the differences between the Venture Program and the Advanced Research Projects Agency for Health (ARPA-H), Dr. Ota Wang commented that the Venture Program has been able to identify high-risk, high-reward topics and implement initiatives early. Dr. Van Gelder noted that the Venture Program project in vision science seems technologically mature but was not pursued prior to the Venture initiative, whereas the ARPA-H effort in this field seems less achievable.

- Dr. Hamlet clarified that the initiatives used several different award mechanisms, including Other Transaction Authority awards, cooperative agreements, U awards, and challenges, but opportunities were specific to the initiative topic. Dr. Lloyd asked whether recent discussions of changing rules related to patents generated with NIH funds might affect Venture Program applications; Drs. Hamlet and Ota Wang did not have information on this topic but intend to monitor it.

XV. REVIEW/VOTE ON THE COUNCIL OPERATING PROCEDURES

Council members pointed out that the vote on the RNomics proposal received four yeas, two nays, and two abstentions. According to Council procedures, concepts must be approved by a majority of the appointed members to pass. Because the Council currently has 10 appointed members, this concept did not receive a majority vote. Dr. Kleinstreuer proposed an *ad hoc* meeting within the next 2 months to revisit and discuss the concept. She asked Council members, especially those with concerns about this concept, to provide feedback in writing within the next 2 weeks so program staff can adequately address concerns.

Dr. Kleinstreuer outlined the suggested changes to the Council operating procedures. Language regarding the requirement to bring foreign applications and applications with foreign projects to the Council has been adjusted to ensure consistency with the current policy. Dr. Kleinstreuer emphasized that the Council's review requirements have not changed; the changes ensure consistent use of the terms "foreign entities and projects" throughout the subsection. When the final policy has been published, this section of the operating procedures will be revisited, and any necessary changes will be brought back to the Council.

The references to diversity supplements have been removed from the procedures because NIH is not currently awarding such supplements. To better reflect the voting process, the procedures have been modified to specify that a vote will be taken to approve or disapprove a concept; Council may also request modifications to a concept, and if modifications are made, a vote will be taken to approve the concept with clearly stated modifications. If additional information or clarification on the need for the concept is required, the Council may request to defer the concept; deferred concepts will be discussed and cleared at a future meeting. These options will be applied to the next meeting.

Vote

The motion to approve the Council operating procedures, as discussed, was forwarded and seconded. The motion passed with no abstentions.

XVI. OSC PROGRAM CLOSEOUT: EXTRACELLULAR RNA (ExRNA) COMMUNICATION PROGRAM

Danilo A. Tagle, Ph.D., Director, Office of Special Initiatives, NCATS, presented on the closeout of the Common Fund ExRNA Communication Program. He noted that the program was launched in 2013 to address scientific and technical challenges and answer pervading questions at that time. The queries were related to the types of cellular RNAs that are released, how exRNAs are protected outside the source cell to affect target cells and distant organs, the impact of exRNAs in health and disease states, and ways to harness the potential of exRNA communication for diagnosis and treatment.

The program was implemented in two stages. Stage 1 was focused on understanding exRNA biogenesis and function, origin, and targeting, as well as creating an atlas of human exRNA reference profiles that would determine clinical utilities for biomarkers and therapeutic agents. Stage 2 was focused on exRNA carrier separation technologies beyond ultracentrifugation that would allow vesicular separation from non-vesicular carriers, as well as the ability to isolate and analyze single vesicles. Stage 1 ran from 2013 to 2019. Stage 2 was launched in 2019 and was offset by about 3 years of no-cost extensions due to the COVID-19 pandemic. The program formally ended in 2025.

Key biological and clinical insights resulting from Stage 1 included the development of ontologies to standardize the language of this emerging field; identification of diverse classes of circulating small RNAs from different biofluid sources; and demonstration of the clinical potential of exRNA for liquid biopsies, including the non-invasive detection of biomarkers for nearly 30 diseases. The team demonstrated that some stem cell–derived exRNA molecules carried within exosomes are protective against disease and are regenerative for damaged tissues. Other projects included tackling a controversy of whether food-derived microRNA can lead to disease in humans.

Key biological and clinical insights resulting from Stage 2 include the discovery that different carriers transport specific types of exRNA cargo. This work deepened the understanding of how exRNAs are packaged and transported between cells. Another key discovery is the identification of supermeres as a major non-vesicular carrier of exRNA. The team also developed sophisticated tools and technologies for separating extracellular vesicles, including microfluidics-based purification methods for isolating cell-specific extracellular vesicles from body fluids. They also enabled single-vesicle isolation, developed analytical tools and computational analysis of exRNA profiling data, and characterized diverse RNA expression patterns. The team also demonstrated that ML models can help identify biofluid-specific exRNA features.

The ExRNA Communication Program developed many resources, including data, software, protocols, and reagents. Links to these resources are available at the ExRNA Research Portal. The program also established an open-access data portal that serves as a central hub to provide access to exRNA data, tools,

educational materials, and protocols for biofluid collection and exRNA analysis. Furthermore, the ExRNA Atlas contains a curated catalog of small RNA sequencing data from thousands of samples across various biofluids and disease states. The resource also includes standardized data and protocols, which will help address systematic biases and enable cross-study comparisons.

These efforts have yielded more than 950 publications that have been cited more than 100,000 times. Dr. Tagle emphasized that many of these publications represent the highly collaborative activities within the funded projects. The ExRNA Atlas contains more than 10,000 human exRNA profiles that have been downloaded more than 550,000 times. The Extracellular Vesicle Antibody Database has been accessed nearly 9,000 times since its launch in 2020. The exceRpt tool has included nearly 150,000 samples being processed and analyzed; 91 percent of data submitted were from non-consortium users. Furthermore, the MicroRNA Data Resource has been accessed nearly 1,500 times since the resource was launched in 2019.

Dr. Tagle emphasized that this resource has served as a catalytic investment and has supported accelerated activities within the field. The extracellular-based biomarkers and RNA-based therapeutics have been applied to more than 1,600 clinical trials. He also noted that the team pivoted to a single-vesicle isolation protocol during the COVID-19 pandemic to develop technologies for detecting SARS-CoV-2. From these efforts, four projects were supported, resulting in 32 publications, 14 patent filings, and several FDA filings and submissions.

In summary, the ExRNA Communication Program teams have helped establish exRNA as intercellular communications, showed the potential for exRNA as novel therapeutics, discovered vesicular and non-vesicular carriers with distinct exRNA cargo, and showed that exRNA molecules can be obtained as liquid biopsies and could be a source of biomarkers. The consortium also has developed methods to separate and characterize exRNA carriers from vesicular and non-vesicular forms, helped develop diagnostic tests for COVID-19 using exRNA carrier technologies, helped address the role of food-derived microRNA in affecting human health, and demonstrated a potential for exRNA molecules as drug-delivery vehicles.

Discussion Highlights

- Dr. Gandhi asked for clarification on the role of exRNA production to indicate active SARS-CoV-2 replication and infection. Dr. Tagle explained that the technique is based on microfluidic separation technologies. Because RNA molecules are secreted in biofluids, the process is non-invasive. The process can be completed within 30 minutes of collection, and the separation platform can distinguish symptomatic and asymptomatic infections.

- Dr. Tagle clarified that the 950 publications were all generated by consortium members who have cited their NIH-supported grants. Many of these publications reflect the collaborative efforts of multiple funded groups. He added that the researchers used RNA-seq protocols for identification. They found that secreted RNAs from diseased cells differ in vesicle size and cargo.

- Dr. Lloyd also asked how the consortium's accomplishments will help inform the RNomics program. Dr. Tagle stated that the program has generated relevant resources and tools and provided insight on various functions of RNA, both within and outside cells. Overall, this work provides a strong foundation for the RNomics group to build upon in future studies. Dr. Labosky added that the RNomics program will focus on RNA modifications. Many ExRNA team members will be involved in the RNomics program.

- Dr. Lloyd asked about plans to sustain the program's resources for the community. Dr. Tagle noted that the program has engaged multiple scientific societies that could play a role in this space. He emphasized that the resource serves primarily as a portal for existing databases, and it

has garnered significant interest within the research community. Dr. Labosky also emphasized that the ExRNA program has been focused on synergy and collaboration since its inception.

XVII. ODSS CONCEPT CLEARANCE (RENEWAL): EARLY STAGE AND ESTABLISHED BIOMEDICAL DATA REPOSITORIES AND KNOWLEDGEBASES [VOTE]

Susan K. Gregurick, Ph.D., Associate Director for Data Science, NIH, and Director, ODSS, DPCPSI, presented a concept clearance renewal for the Biomedical Data Repositories and Knowledgebases (DRKB) program. She explained that this program is widely supported by NIH's ICOs. The team is seeking data repositories and knowledgebase resource projects with unique value propositions that will deliver scientific impact, employ and promote good and efficient data management, engage user communities, address governance of biomedical data with the life cycle of data in mind, and promote long-term preservation.

Dr. Gregurick stated that the program is aligned with the *NIH Strategic Plan for Data Science 2025–2030*. Goals of the program include developing scientific impact in the communities that these resources support, promoting good data management, engaging communities, adopting and contributing to open metrics, providing sufficient metadata and semantic annotations to allow the data to be searchable and findable, and supporting a data life cycle analysis process. These efforts will modernize NIH's data ecosystem, sustain NIH's data repositories, and strengthen research infrastructure. The data repositories and knowledgebases must address four main components of their funding announcement: fulfilling a scientific need or addressing a gap, promoting good and efficient data management and dissemination, engaging the research community, and providing governance processes for life cycle management of data and data assets.

Christopher G. Duncan, Ph.D., Program Director, Genes, Environment, and Health Branch, Division of Extramural Research, NIEHS, explained that the DRKB program grew out of a history of NIH supporting data repositories and knowledgebases through several different mechanisms. The current phase includes program announcements with special receipt, referral, and/or review considerations (PARs) for early-stage and established DRKBs. A total of 18 ICOs currently participate in the program. In response to feedback from the cross-NIH DRKB working group, the concept seeks to renew the U24 PAR as a single notice of funding opportunity focused on enhancing and managing established strategic biomedical data resources.

So far, the program has had 10 receipt dates, with the final two dates for the current phase scheduled for the near future. A total of 45 competing awards have been made to date across NIH. Dr. Duncan noted that approximately half of the competing awards represent instances where existing resources were transitioned from alternative funding opportunities or mechanisms within the same administering ICO. Around 69 percent of the awards are for knowledgebases, and 31 percent are for data repositories. Dr. Duncan briefly highlighted the 45 resources, as well as the supporting ICs. He noted that the resources span a range of domains and focus areas and represent critical core community resources; many of the resources have crosscutting and cross-domain impact.

Ishwar Chandramouliswaran, Lead Program Director, ODSS, DPCPSI, remarked that the DRKB network represents a major strength of the program. The program supports an annual meeting, which has helped foster a community around biomedical data repositories and knowledgebases funded by NIH. Previous discussion topics have included data curation, sustainability, metrics, and metadata. Ultimately, the goal of these meetings is to establish a forum around data resources to generate ideas for collaborative projects, optimize the data resources, and develop a shared vision for the future of the NIH data resource landscape.

The program requirements for the reissue include addressing an NIH institute-specific scientific mission priorities, as well as program priority; demonstrating community needs and continued engagement; demonstrating quality of the data and associated services; and implementing effective governance practices. These requirements are reviewed by a special emphasis panel with criteria to review data resource projects, as opposed to research projects. The U24 mechanism is used, and projects are funded for up to 5 years with budgets requesting actual needs. New features of the reissue include an emphasis on established data resources, collaborations on crosscutting topics, responsible stewardship, and an optimized data resource landscape. Mr. Chandramouliswaran emphasized that these approaches will lower the barriers for data sharing, improve discovery and reuse of NIH-funded datasets, increase the efficiency of operations and optimize costs, and disentangle data resources from research projects. He emphasized that the program is fundamental to creating a modernized biomedical data ecosystem.

Discussion Highlights

- The discussants, Drs. Johnston and Irizarry, provided their comments. Dr. Johnston remarked that this concept demonstrates a continued prioritization of creating and making high-quality biomedical data available to advance human health. She stated that this program is critical to supporting NIH's biomedical research ecosystem, including for early career investigators. She requested clarification on the community's usage of the data resources and asked whether the reissue will include an external advisory committee. Mr. Chandramouliswaran commented that the established repositories demonstrate usage, utility, and impact based on various metrics; the program is working to implement consistent evaluation metrics. He also clarified that a scientific advisory board or expert community will be required. Dr. Johnston underscored the value of community engagement in this space.

- Dr. Irizarry also spoke on the importance of engaging potential users, and he emphasized the significance of this resource for modern biomedical research. He asked how NIH will evaluate and prioritize the resources that have significant impact in small but critical research areas, given that the small user base might be deprioritized. Dr. Gregurick explained that co-funding is dependent on the availability of funds, as well as the ability to cross many ICs' missions.

- Dr. Irizarry also requested further details on specific criteria and metrics that will be used for assessing efficiency of operations, and he wondered about assurances for long-term sustainability. Mr. Chandramouliswaran noted that researchers in the network have expressed enthusiasm regarding improving efficiency of operations, particularly by implementing common metadata elements, improving the search and discovery functions using persistent identifiers, and enhancing other core technical capabilities. He also noted that these infrastructure developments are important for sustainability.

- Dr. Irizarry also asked about connections to other initiatives. Dr. Gregurick noted that the program is linked to the Generalist Repository Ecosystem Initiative, which will focus on making connections between awards through shared metadata and connection points with application programming interfaces. She also spoke on the benefits of making biomedical data assets available through the Real-World Data Network. In response to a follow-up question from Dr. Irizarry, Dr. Gregurick explained that real-world data is observational data and often originates from health care settings. Dr. Kleinstreuer emphasized that bringing together different types of data enables multifaceted and multivariate discovery analyses.

- Dr. Krugman asked whether only NIH-funded datasets will be included in the resource. Dr. Gregurick clarified that the data can be funded by any organization. NIH-funded investigators are encouraged to deposit their data into a data resource primarily funded by NIH and regarded as

appropriate by the scientific community. This initiative is focused on promoting the infrastructure of data repositories and knowledgebases.

- Dr. Van Gelder underscored the importance of creating widely usable data and knowledge repositories. He asked about plans for restructuring repositories to comply with the new structural guidelines for subcontracts versus subawards. Dr. Gregurick confirmed that the program will adhere to such guidelines, and the team will work with international funding collaborators to ensure that the work is sustained.

- Dr. Van Gelder requested clarification on the proportion of funding from DPCPSI OD compared with partner co-funding. He asked about the capabilities of ICs to sustain the resources after the funding ends. Mr. Chandramouliswaran explained that the ICs provide the primary funding based on their research needs and program priorities. OD will augment the funding to address crosscutting themes, common topics, and collaborative aspects that span multiple ICs.

- Mr. Chandramouliswaran noted that the program is focused on the overall biomedical data landscape, with an emphasis on encouraging connections among repositories, making the data reusable, and improving the flow of data and metadata. This work will be driven by use cases and questions that the community wants to address.

Vote

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

XVIII. CLOSING REMARKS

Dr. Kleinstreuer expressed appreciation to the Council members for their thoughtful input, careful feedback, and robust discussions. She noted that an *ad hoc* virtual meeting will be scheduled within the next 2 months to discuss the RNome concept clearance, and members were encouraged to send written feedback on the concept within the next 2 weeks. The next regular Council meeting is scheduled for January 29–30, 2026 and will be held in person.

In response to a question from Dr. Lloyd, Dr. Kleinstreuer also clarified that direct awards to foreign institutions are still allowed, but they must be approved individually by the IC council. She agreed to follow up with any available additional information on restrictions for subawards for foreign applicants.

XIX. ADJOURNMENT

Dr. Kleinstreuer adjourned the meeting at 2:10 p.m. EDT on September 12, 2025.

XX. CERTIFICATION

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

Kleinstreuer, Nicole (NIH/OD) [E]
Digitally signed by Kleinstreuer, Nicole (NIH/OD) [E]
Date: 2026.01.13 13:54:04 -05'00'

Nicole C. Kleinstreuer, Ph.D.
Chair, NIH Council of Councils
Acting Director, DPCPSI, OD, NIH

Date

FRANZISKA B. GRIEDER -S
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Date: 2025.12.04 16:27:33 -05'00'

Franziska B. Grieder, D.V.M., Ph.D.
Executive Secretary, NIH Council of Councils
Director, ORIP, DPCPSI, OD, NIH

Date