National Diabetes and Digestive and Kidney Diseases Advisory Council
National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Department of Health and Human Services

I. CALL TO ORDER
Dr. Rodgers

Dr. Griffin Rodgers, Director, NIDDK, called to order the 217th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 10:00 a.m. on September 9, 2021, via Zoom videoconference. This meeting was conducted using a two-tiered webinar format. The panelist tier consisted of NIDDK's Advisory Council members and NIDDK staff members who presented during the meeting. The audience tier was available to members of the public and allowed them to view and listen to the meeting.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Ms. Tracey Brown
Dr. Iain Drummond
Dr. Penny Gordon-Larsen
Dr. Barbara Kahn
Dr. Mark Nelson
Dr. Richard Peek
Ms. Ceciel Rooker
Dr. Kathleen Sakamoto
Dr. Michael Snyder
Dr. Ronald Sokol
Ms. Lorraine Stiehl
Dr. Gary Wu

Subject Matter Experts:
Dr. Linda Baker
Dr. Elizabeth Seaquist

Ad hoc members:
Ms. Dawn Edwards
Dr. Keith Norris
Dr. Debra Haire-Joshu
Dr. Philipp Scherer

Ex-officio members:
Dr. Cindy Davis
Dr. Ian Stewart

Also Present:
Dr. Griffin Rodgers, Director, NIDDK and Chair of the NIDDK Advisory Council
Dr. Karl F. Malik, Executive Secretary, NIDDK Advisory Council
Dr. Matthew E. Portnoy, Deputy Director, Division of Extramural Activities
Dr. Gregory G. Germino, Deputy Director, NIDDK
Dr. William Cefalu, Director, Division of Diabetes, Endocrinology and Metabolic Diseases, NIDDK
Dr. Stephen P. James, Director, Division of Digestive Diseases and Nutrition, NIDDK
Dr. Robert A. Star, Director, Division of Kidney, Urologic, and Hematologic Diseases, NIDDK

B. NIH and NIDDK PANELISTS/SPEAKERS

Dr. Bruce Tromberg, Director, National Institute of Biomedical Imaging and Bioengineering
Dr. Katrina Serrano, Program Director, Office of Minority Health Research Coordination, NIDDK
Dr. Karen Teff, Co-Director, Office of Obesity Research; Program Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, NIDDK

C. ANNOUNCEMENTS

Dr. Rodgers

Dr. Rodgers noted that this is NIDDK's fifth consecutive virtual Council meeting. Due to the delta variant, NIH has not yet determined whether the Council meeting for January 2022 will be in-person or virtual. He urged members to stay tuned to the NIDDK Advisory Council website for updates.

Council Member News

Dr. Rodgers recognized two subject matter experts who joined the meeting:

- **Linda A. Baker, M.D.**, is a Professor of Pediatric Urology at the University of Texas Southwestern Medical Center in Dallas. She is Director of Pediatric Urology Research at University of Texas Southwestern and Children's Medical Center.
- **Elizabeth Seaquist, M.D.**, is Professor of Medicine and Director of the Division of Diabetes, Endocrinology, and Metabolism at the University of Minnesota Medical School and holds the Pennock Family Chair in Diabetes Research.

Dr. Baker will participate in discussions within the Kidney, Urologic, and Hematologic (KUH) subcommittee. Dr. Seaquist will participate in discussions within the Diabetes, Endocrinology, and Metabolic Diseases (DEM) subcommittee.

Dr. Rodgers also recognized four individuals serving as *ad hoc* members during this Council meeting:

- Dawn Edwards is a Wellness Ambassador for the Rogosin Institute in New York.
- Debra Haire-Joshu, Ph.D., R.N., is the Joyce Wood Professor and holds joint appointments in the Washington University School of Medicine and the Brown School of Public Health at Washington University in St. Louis, Missouri.
- Keith Norris, M.D., Ph.D., is the Executive Vice Chair for Equity, Diversity, and Inclusion and Professor of General Internal Medicine at UCLA.
- Philipp Sherer, Ph.D., is Professor of Internal Medicine and Cell Biology and the Gifford O. Touchstone, Jr. and Randolph G. Touchstone Distinguished Chair in Diabetes Research at University of Texas Southwestern Medical Center.

Drs. Haire-Joshu and Scherer will participate in discussions within the DEM subcommittee. Ms. Edwards and Dr. Norris will participate in discussions within the KUH subcommittee.

Dr. Rodgers also introduced Dr. Cindy Davis, who will serve as an *ex officio* member representing the United States Department of Agriculture (USDA), where Dr. Davis serves as National Program Leader for Human Nutrition in the Agriculture Research Service. She will participate in the Digestive Diseases and Nutrition (DDN) subcommittee. She replaces Dr. David Klurfeld, who retired last winter after serving as an *ex officio* member representing USDA for many years.

In Memoriam

Dr. Rodgers reported the recent passing of several NIDDK grantees and staff members:

- **Dr. James Heubi**, a long-time NIDDK awardee, was a pediatric gastroenterologist and hepatologist at Cincinnati Children's Hospital Medical Center, where he was at times the Director of the Division of Pediatric Gastroenterology, Hepatology, and Nutrition; Director of the Clinical Center for Translational Science and Training; and Associate Dean for Clinical Research. Dr. Heubi played an active role in the NIDDK-funded Childhood Liver Disease Research Network (CHiLDReN). He was instrumental in describing, characterizing, and identifying the genetic defects in bile acid synthesis disorders, one of the genetic causes of progressive neonatal cholestasis. With **Dr. Kenneth Setchell**, he formulated and tested cholic acid therapy for these disorders. The first treatment for any childhood cholestatic liver disease approved by the U.S. Food and Drug Administration in 2015, this treatment has saved the lives of many affected children and avoided the need for liver transplantation.
- **Dr. Paul Frenette**, distinguished hematology physician and NIDDK grantee, died July 27. Dr. Frenette identified mechanisms behind sickle cell-mediated blood vessel blockages and discovered key roles of the nervous system in blood stem cell trafficking. He taught medicine and cell biology at Albert Einstein College of Medicine, where he founded and directed the Ruth L. and David S. Gottesman Institute for Stem Cell and Regenerative Medicine Research. He was an elected member of the American Society of Clinical Investigation and the Association of American Physicians. He served on boards and scientific committees focused on stem cell research and hematology, editorial boards of *Blood* and *The Journal for Clinical Investigation*, and multiple NIH panels.
- **Dr. Barbara Murphy**, a leading nephrologist who specialized in advanced research on predicting and diagnosing kidney transplant outcomes, passed away in July from glioblastoma. Originally from Ireland, she served at Mount Sinai Hospital in Manhattan starting in 1997. In 2012, she was named Chairwoman of the Department of Medicine at the Icahn School of Medicine at Mount Sinai, making her the first woman to run a department of medicine at an academic medical center in New York City. Her research focused on genetics and genomics of predicting the results of transplants and why some kidneys are rejected. The work has been licensed to two commercial entities.
- **Dr. Tadataka "Tachi" Yamada**, gastroenterologist and former NIDDK Advisory Council member, passed away on August 4. He is remembered for an impressive 50-year career as a physician-scientist and leader. He made critical discoveries in gastric acid secretion and the activation of peptide hormones, and

he was devoted to the work of the National Academy of Medicine. He was especially recognized for his work in global health, developing medicines and vaccines for diseases such as tuberculosis and malaria, and was formerly the president of the Bill and Melinda Gates Foundation Global Health Program.

- **Dr. H. James Hofrichter** died suddenly on August 5. A brilliant scientist, Dr. Hofrichter was senior investigator and section chief in NIDDK's Laboratory of Chemical Physics (LCP). His research focused on sickle cell hemoglobin polymerization, time-resolved spectroscopy, and protein folding. He was instrumental in changing sickle cell research from biochemical phenomenology to rigorous physical chemistry.

NIDDK Staffing News

Dr. Rodgers also announced several awards to staff members of NIDDK's Intramural Research Program:

- **Dr. G. Marius Clore**, section chief in the Laboratory of Chemical Physics, was awarded the Khorana Prize from the Royal Society of Chemistry in London. The award recognized work to develop nuclear magnetic resonance-based methods to characterize protein assembly and aggregation in amyloidosis, a rare disease in which abnormal proteins build up and interfere with normal organ function.
- **Dr. Barbara Rehermann**, section chief in the Liver Diseases Branch, was elected to the German National Academy of Sciences *Leopoldina* for her work in microbiology and immunology. The *Leopoldina*, founded in 1652, is the world's oldest continuously existing academy of natural sciences and medicine.

Dr. Gregory Germino then reported that Dr. Rodgers was recently recognized by two organizations.

- Dr. Rodgers was a 2021 honoree of the American Association of Kidney Patients (AAKP) National President's Award. Dr. Rodgers was selected for his courage and leadership during the national COVID-19 pandemic and for his ongoing commitment to long-term scientific research, discovery, and innovation to prevent and treat kidney disease and save human lives.
- Dr. Rodgers also received the Research Service Award from the American Gastroenterological Association. The award recognizes people whose work has significantly advanced gastroenterological science and research. The award notes that through Dr. Rodgers' leadership, NIDDK-supported advances in genetics, the gut microbiome, and other factors are leading to more personalized and, ultimately, more effective treatments.

Dr. Rodgers announced the retirement of long-time NIDDK staff member, **Dr. William Knowler**, after 46 years at NIH. Since 1979, Dr. Knowler has served as Chief of NIDDK's Diabetes Epidemiology and Clinical Research Section in the Phoenix Epidemiology and Clinical Research Branch (PECRB) in NIDDK's Intramural Research Program. He has devoted decades of research into the behavioral, genetic, and environmental factors contributing to the development of type 2 diabetes and its complications, particularly among American Indian populations. Dr. Knowler and PECRB scientists have worked closely with the Southwest American Indian

population, who have the world's highest reported prevalence of type 2 diabetes, to gain valuable insights into the disease's risk factors and development. Dr. Knowler played a pivotal role in making sure American Indians were well-represented in the Diabetes Prevention Program's diverse participant pool, which helped ensure the study's results could be extrapolated to the communities at highest risk for the disease.

Dr. Rodgers also recognized staff who have gone "above and beyond" as volunteers helping unaccompanied children who have been arriving at the southern U.S. border in large numbers. This has become a national priority and the Department of Health and Human Services (HHS) has asked staff to consider volunteering to support the response and help ensure that the United States can successfully meet the needs of these children while they are in its care. Five employees and one Commissioned Corps officer from NIDDK deployed in this capacity between April and June 2021. These deployments involved long hours under challenging circumstances.

Lastly, Dr. Rodgers noted that he and NIDDK Executive Officer **Ms. Camille Hoover** recently spoke with Federal News Radio about NIDDK's many efforts to work towards diversity, equity, and inclusion. NIDDK's workforce continues to give the Institute top rankings both at NIH and in the Federal Government as a great place to work.

Dr. Rodgers reminded Council members and others that another way to stay abreast of NIDDK events is to follow the agency on Twitter, Facebook, YouTube, and Instagram.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 216th COUNCIL MEETING

Dr. Rodgers

The Council approved, by electronic poll, the Summary Minutes of the 216th Council meeting, which had been sent to them in advance for review.

Dr. Malik noted that a recent audit of the Council Minutes identified some missing information in recent rounds. Amendments to these Minutes have been developed and posted in the Electronic Council Book for Council review. The Council approved these amendments by electronic poll.

III. FUTURE COUNCIL DATES

Dr. Rodgers

Dr. Rodgers did not review all the upcoming meeting dates but noted that NIH has not yet determined if the January Council Meeting scheduled for January 26-27, 2022, will be virtual or in-person. Updated information will be posted on the Council website.

IV. ANNOUNCEMENTS

Dr. Malik

Confidentiality

Dr. Karl Malik reminded Council members that material furnished for review purposes and discussion during the closed portion of the meeting is considered confidential. The content of discussions taking place during the closed session may be disclosed only by the staff and only under appropriate circumstances. Any communication from investigators to Council members regarding actions on an application must be referred to the Institute. Any attempts by Council members to handle questions from applicants could create difficult or embarrassing situations for the members, the Institute, and/or the investigators.

Conflict of Interest

Dr. Malik reminded Council members that advisors and consultants serving as members of public advisory committees, such as the NIDDK Advisory Council, may not participate in situations in which any violation of conflict of interest laws and regulations may occur.

Responsible NIDDK staff shall assist Council members to help ensure that a member does not participate in, and is not present during, the review of applications or projects in which, to the member's knowledge, any of the following has a financial interest: the member, or his or her spouse, minor child, or partner (including close professional associates), or an organization with which the member is connected. To ensure that a member does not participate in the discussion of, nor vote on, an application in which he/she is in conflict, a written certification is required. A statement is provided for the signature of the member, and this statement becomes a part of the meeting file. Dr. Malik directed each Council member to a statement in his or her meeting folder regarding the conflict of interest in review of applications. He asked each Council member to read it carefully, sign it, and return it to NIDDK before leaving the meeting.

Dr. Malik pointed out that when the Council reviews applications in groups without discussion—also called "*en bloc*" actions—all Council members may be present and may participate. The vote of an individual member in such instances does not apply to applications for which the member might be in conflict.

Regarding multi-campus institutions of higher education, Dr. Malik said that an employee at one campus may participate in any particular matter affecting another campus, if the employee's financial interest is solely at one campus and the employee has no multi-campus responsibilities.

V. REPORT FROM THE NIDDK DIRECTOR

Dr. Rodgers

Budget Update

Dr. Rodgers updated the Council on the current budget and the status of NIH appropriations for Fiscal Year (FY) 2022. He reviewed the FY 2021 Omnibus Appropriations Package that was signed into law in December 2020, which included $42.934 billion for the NIH, a $1.475 billion increase over FY 2020. This law included funding for targeted programs such as the BRAIN Initiative, Alzheimer's disease research, and opioid research. NIDDK received $2.132 billion in the law, an $18

million (0.8 percent) increase over FY 2020. These amounts do not include funds from the Special Diabetes Program.

In April, President Biden released a FY 2022 budget request, sometimes called the "skinny" budget, which only provides high-level budget guidance. Dr. Rodgers highlighted the following key dates in the process since the May Council meeting:

- **May 25 (House) and May 26 (Senate)**: Appropriations Subcommittees for the Departments of Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS-Education) held budget request hearings for the NIH.
- **May 28:** President Biden released his full budget request for FY 2022.
- **July 29:** The House passed a minibus that included the Labor-HHS-Education appropriations bill. (Markups took place earlier in July.)

The FY 2022 President's budget request called for a $9 billion increase in the overall NIH budget, or a 21 percent increase over FY 2021 levels; this includes an $87.4 million increase for NIDDK. This would be the largest single-year nominal-dollar increase in NIH's history.

The House minibus bill that passed on July 29 included $49.4 billion for NIH, a $6.5 billion (about 15 percent) increase over the FY 2021 enacted budget. This includes a nearly 5 percent increase for NIDDK from $2.132 to $2.238 billion.

The Senate has not yet introduced its FY 2022 Labor-HHS-Education appropriations bill, but the bill and markups are expected soon.

The Biden Administration has proposed $6.5 billion to establish the Advanced Research Projects Agency for Health, or ARPA-H, to promote high-risk/high-reward, innovative research similar to that supported by the Defense Advanced Research Projects Agency (DARPA) for defense and ARPA-E for energy innovation. The House bill included $3 billion for ARPA-H. Diabetes was specifically mentioned as an initial focus area, and the broad scope of ARPA-H may include other areas of interest to NIDDK.

Dr. Rodgers participated in an NIH listening session about ARPA-H that included NIDDK stakeholders, including the American Gastroenterology Association, the Endocrine Society, and the American Society of Nephrology. Other NIDDK stakeholders participated in listening sessions hosted by the White House Office of Science and Technology Policy.

Congressional Activities

Dr. Rodgers also updated the Council on Congressional activities:

- On May 19, Dr. E. Dale Abel, Chair of Internal Medicine and Chair in Diabetes Research at the University of Iowa Carver College of Medicine, testified before the House Appropriations Labor-HHS-Education Subcommittee on behalf of the Friends of NIDDK. This was the first Public Witness Day since the start of the pandemic.
- The House and Senate Appropriations Labor-HHS-Education Subcommittees held FY 2022 budget request hearings for the NIH in May. Topics related to

NIDDK included: pediatric kidney disease, sickle cell trait, diabetes, and cystic fibrosis. Other topics were discussed as well, including COVID-19 and structural racism and health disparities.

- On June 7, Representative Jim McGovern of Massachusetts and Senator Cory Booker of New Jersey gave opening remarks at the American Society of Nutrition meeting, sharing their vision of the future of the field of nutrition science.

Council Questions and Discussion
Comment from Council: *Where will ARPA-H be located administratively?*

Dr. Rodgers answered that discussion is ongoing but there is interest in co-locating it as a separate entity within NIH to facilitate a close working relationship with the 27 NIH Institutes and Centers.

VI. UPDATE: DIRECTOR, NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING
Dr. Bruce Tromberg

Dr. Rodgers introduced Dr. Bruce Tromberg, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) since 2019. Dr. Tromberg was previously Professor of Biomedical Engineering and Surgery at the University of California, Irvine. He specializes in the development of optics and photonics technologies for biomedical imaging and therapy. He has co-authored more than 450 publications and holds 23 patents in new technology development and bench-to-bedside clinical translation, validation, and commercialization of devices. He has also trained more than 80 students and fellows.

Dr. Tromberg thanked Dr. Rodgers for the introduction and explained that he will discuss the origins and work of NIBIB as well as the trans-NIH initiatives with which he is involved, including the Rapid Acceleration of Diagnostics (RADx) initiative in response to the COVID-19 pandemic.

Dr. Tromberg explained that NIBIB was created in 2000 by an Act of Congress that was signed into law by President Bill Clinton. The law was based on the finding at that time that: "Basic research in imaging, bioengineering, computer science, informatics, and related fields is critical to improving healthcare but is fundamentally different from the research in molecular biology on which the current national research institutes at the National Institutes of Health…are based." The goal of forming NIBIB was to "ensure the development of new techniques and technologies for the 21st century," recognizing that these disciplines "require an identity and research home at NIH that is independent of the existing institute structure." NIBIB accepts non-hypothesis-based research, which has become the Institute's signature.

Dr. Tromberg explained that human health has become a top priority of engineering, transforming engineering education and leading to a 5-fold increase in the number of biomedical engineering departments in the country to more than 130 currently. Each year, another 1,600 undergraduate students and 60 faculty join the field. Biomedical

engineering programs have played a large role in increasing diversity in schools of engineering. For example, the male-female distribution in biomedical engineering is roughly 50-50.

Another trend in the field are partnerships between medical and engineering schools, producing "physicianeers." The first program that actively encouraged this was the University of Illinois at Urbana-Champaign, followed by Texas A&M University. In addition, many centers for engineering and medicine are being established around the country, improving human health through innovation, technology development, and commercialization and entrepreneurship.

Dr. Tromberg explained that NIBIB accounts for about 1 percent of the total NIH budget, and NIBIB actively collaborates with virtually all of the ICs within the NIH. When combined with investments at other ICs, the total NIH investment in bioengineering is $5.65 billion, or 13.5 percent of the NIH budget. The growth rate for bioengineering funding has been about 2.5-times the NIH budget growth rate.

Bioengineering is at the intersection of animate and inanimate materials and includes many different technologies including therapeutic devices, imaging technologies, engineered biology, and sensors and point-of-care devices, all tied together with computer modeling, computation, and machine intelligence. Examples include tissue chips and organoids; as well as synthetic biology, which involves thinking of cells as programmable units that can be modeled computationally. Advances in materials and manufacturing are increasing access to these technologies, which are connected across the internet.

NIBIB is also involved in supporting therapeutic devices including deep tissue surgery using external energy—such as using focused ultrasound, microwaves, or fiber optic probes. These complex combinations of hardware and computational techniques require understanding of basic physics as well as human biology. One of the defining characteristics of the field is the belief that there is an equation or equations to represent the phenomena of human biology, resulting in a merger of physics, engineering, and machine learning and machine intelligence. An example of this is implantable electrodes that function as operating computer interfaces that use machine learning to convert brain signals into words or movement.

To accelerate progress in these areas, NIH will soon launch the Biomedical Engineering and Technology Acceleration (BETA) Center. This Center represents a significant workforce development opportunity to introduce diversity in terms of intellectual activity as well as backgrounds. The director of the Center will also serve as NIBIB Associate Director for Diversity, Equity, and Inclusion. Dr. Rodgers is chairing the search committee for the new director, and the search will start in the coming weeks. Dr. Tromberg asked the Council to think of possible candidates for the position as well as opportunities for collaboration with the Center.

Dr. Tromberg also explained that NIBIB has focused on applying its major strengths to addressing the COVID-19 pandemic. It established a multi-center national network, Medical Imaging and Data Resource Center (MIDRC), focused on imaging and artificial intelligence (AI). Hosted at the University of Chicago, it is funded by NIBIB

and co-led by the American College of Radiology, the Radiological Society of North America, and the American Association of Physicists in Medicine. The goal is to curate and integrate AI-ready imaging datasets to help advance and accelerate algorithms that can be used for diagnosis and prognosis. The Center aims to have 60,000 images available with validated and ultimately FDA-cleared computational tools that can be rolled out to hospitals and community centers to improve their quality of care.

Dr. Tromberg also described the work of the RADx program, which focuses on diagnostic test technology for COVID-19. He explained that, as part of the 4th congressional appropriation for COVID relief, NIBIB received $500 million on April 24, 2020, a portion of the $1.5 billion that NIH received to expand COVID testing technology and access to testing. At that time, the only way to test for COVID was through a laboratory. Patients had to be symptomatic to get a test, and there was a shortage of test kits. Needing accessible testing for more people, NIBIB launched RADx Tech on April 29, 5 days after receiving the appropriation.

RADx programming falls into two categories: (1) innovation and new platforms; and (2) expansion of existing platforms. Dr. Jill Heemskerk, NIBIB Deputy Director, and Dr. Tromberg lead these programs, which are overseen by the Office of the Director of NIH. Dr. Francis Collins, NIH Director, and Dr. Larry Tabak, NIH Principal Deputy Director, have been involved since the launch.

Two other programs are related to the RADx initiative:

- RADx-RAD, which supports forward-looking technologies; and
- RADx-UP, which is a $500 million program designed to bring technologies to underserved populations and focus on demonstration projects to increase understanding of testing efficacy and effectiveness.

RADx has formed partnerships with the Biomedical Advanced Research and Development Authority (BARDA), the HHS Assistant Secretary of Health, the Food and Drug Administration (FDA), the Department of Defense, the White House, and the Centers for Disease Control and Prevention (CDC).

The fast launch of the program was possible because it was leveraged from the existing Point-of-Care Technologies Research Network, established by former NIBIB Director Dr. Pettigrew in 2007. The entire Network agreed to focus operations on COVID-19. The group created three cores: a validation core to independently evaluate proposed technologies for funding; a clinical studies core with a standard trial design, digital health platform, and a single Institutional Review Board (IRB); and a deployment core to address issues of supply chain and manufacturing, build the user community, and link the partners working across the country.

The fundamental operations include:

- review and fund ideas;
- test and validate new technologies; and
- provide expert guidance.

Every project was teamed with at least six experts who became an instant board of directors, creating a public/private partnership of enormous scale.

The result was an innovation funnel that received 716 applications in 2020, followed by another 108 applications in 2021, from small businesses, academic groups, start-ups, mid-size companies, and large companies. These were put through a multi-stage review that included a 1-week, intensive "shark tank" process. Of the 824 completed applications, 35 made it through the review process and received support for manufacturing and expansion. He pointed out that NIH usually focuses on early-stage research, but in this case, it was necessary to get tests designed, completed, and onto the marketplace. The process condensed what normally takes 5 or 6 years into 5 or 6 months.

The 35 products that made it into manufacturing include point-of-care and home tests with turnaround times of 30 minutes and performance comparable to lab tests. The program has also supported laboratory tests. Eighteen percent of the phase 2 funded tests used highly innovative nanoscience technologies. Dr. Tromberg noted that some of the home antigen tests, when used twice in 1 week, perform as well as the traditional PCR tests and typically sell over the counter for $20-25 for two tests. He also noted that preliminary data indicate that even children can effectively nasal swab themselves, which may help workflow, especially with in-school testing.

Dr. Tromberg outlined major milestones of the project so far, including:

- expanded capacity from virtually zero in September 2020 to a cumulative capacity of 667 million tests through July 2021;
- an estimated 5 million tests/products a day in July 2021;
- 28 Emergency Use Authorizations granted, including the first over-the-counter Emergency Use Authorization and three "at home" tests;
- more than 100 companies supported;
- more than $1 billion invested in biotechnology companies; and
- more than $1.3 billion in private capital raised, exceeding the federal investment.

Dr. Tromberg also highlighted other accomplishments related to the pandemic. The Consortia for Improving Medicine with Innovation & Technology (CIMIT) at Massachusetts General Hospital, which is the coordinating center for the project, has developed a website, whentotest.org, which helps individuals and organizations determine when testing would help stem the spread of COVID-19. It includes guidance for businesses, community organizations, and schools.

In all, the RADx program has distributed almost 3 million tests around the country in partnership with public health agencies, the RADx-UP program, and the CDC. After some initial hesitancy, the at-home testing has now caught on with the public, with some areas experiencing shortages of tests.

Dr. Tromberg explained that the RADx program is enabled by digital health infrastructure, although uptake of this information into state and federal databases has been slow. The variants have complicated the process, and there are 75,000 samples in

the previously described validation core to validate the tests with multiple variants.

Future directions for the program include continuing to develop new technologies, including nanomaterials, synthetic biology, application-specific integrated circuits (ASICs), and waveguides that perform better than classic lateral flow assays. Developments are also underway in pooling at the point of care, which would give PCR level sensitivity to groups at the point of care.

Ongoing challenges to progress include the reporting infrastructure, which in many cases still relies on lab results delivered by fax and mail, making it difficult to identify hot spots quickly enough to prevent outbreaks. In a recent study, NIBIB Intramural investigator Dr. Kaitlyn Sadtler and colleagues showed that the number of actual cases in July-August 2020 was actually 5-6 times higher than recorded. Undiagnosed cases continue to persist, especially with the variants, leading to lagging and incomplete test data. There continues to be a need for better, more accessible, faster tests as well as more complete reporting.

Dr. Tromberg noted the investment in multiplex tests for differential COVID, flu, and RSV diagnoses. He also acknowledged the need for faster, more accurate, and cost-effective surveillance genotyping with appropriate informatics in laboratory and point-of-care settings.

Dr. Tromberg explained that NIBIB intends to make RADx a permanent structure to take advantage of these networks to develop new technologies for other pathogens and enhance preparedness for the next pandemic.

Council Questions and Discussion

Comment from Council: *Given that viruses mutate, what thresholds or criteria do you use to decide when to modify the rapid test? Do you use data from other countries to anticipate what may emerge in the United States?*

Dr. Tromberg explained that NIBIB launched the Variant Task Force in January. There is now a pool of 75,000 samples that include early variants as well as the more recent delta variant, and work will include testing samples of variants and evaluating test performance. He pointed out that the FDA makes decisions to modify the tests.

Comment from Council: *Is there an external source that is making sure that the specifications for the tests are what the manufacturers claim they are?*

Dr. Tromberg explained that this is the goal of the validation cores at Emory University and the Georgia Institute of Technology. If the FDA identifies post-market issues with the test, RADx is ready to build studies to validate that. RADx representatives meet with the FDA several times per week and the FDA gives RADx projects priority, which is a driver for companies to participate in the network. This type of program provides independent validation, and it allows the FDA to specify what they are looking for to an independent group of academics and industry experts.

Comment from Council: *A problem faced by bioengineers working on engineered tissue is that they require tiny sensors. Do you see any signs of synergy between organ*

builders and sensor makers? What are the opportunities in this area?

Dr. Tromberg said this is an area of enormous activity and growth. The next round of the RADx process may well focus on cyborg tissue and organs-on-a-chip with an innovation funnel launched in this area. NIBIB's Blueprint MedTech Program is doing this with neurotechnologies. Dr. Tromberg added that this would be different from the ARPA-H effort previously mentioned.

Comment from Council: *With the investment of both federal dollars and private capital, is there an opportunity for NIH to share in the benefits as these companies generate revenue? Could this be a sustainability model for this program?*

Dr. Tromberg said this has been discussed, but the group settled on the normal Bayh-Dole governance with respect to intellectual property. However, other models may emerge via ARPA-H, as it will not be operating under similar time pressures. He pointed out that the companies are still assuming risk even though the program tries to stabilize companies through longer-term contracts. Without stabilization, testing capacity can disappear. This happened when the virus decreased substantially after vaccination started, then surged again with the delta variant. This is an area for healthcare economists to consider.

Comment from Council: *What obstacles prevent point-of-care antibacterial resistance testing for body fluids? Urologists treating patients with urinary tract infections still use a shotgun therapy with antibacterial drugs. Can that be refined?*

Dr. Tromberg stated that companies are heavily influenced by what they perceive to be their markets and will invest in the design and introduction of new technologies based on that. NIH is helping to reduce that risk. For example, the Small Business Innovation Research program at NIH is a $1.2 billion NIH-wide investment that helps facilitate that risk reduction. RADx has shown that by banding together and creating consensus and an open science approach, it is possible to create a public/private partnership with more than 1,000 people across the country all pulling in one direction. There will be continuing change in the country and in perceptions of what can be delivered at the point of care and at home. This also relates to telemedicine and telemetry, including wearables and *in vitro* diagnostics, whether they are prescribed or over the counter.

Comment from Council: *How does the Institute think through the myriad technologies that are in development? What type of assessment is needed from clinicians and patients who might use these technologies?*

Dr. Tromberg stated this is a central issue. That is why NIBIB has formed partnerships with CDC, FDA, BARDA, and others, to facilitate interaction between the bioengineering community and public health. Selective application of technologies designed to move collaboratively to solve specific problems, especially in crises, is important. The community needs to be engaged and help move along the iterative process of design, build, test, and deploy for a specific purpose. Many of the problems faced by medicine and public health trace back to antiquated approaches that are not optimized to the current situation. NIBIB not only studies efficiency and effectiveness, but it also "studies the studies" in the hope of taking the information back to our

colleagues and continuing to grow.

Comment from Council: *How does NIBIB's work relate to treatment and prevention of diseases of concern to NIDDK and to the current efforts towards precision health?*

Dr. Tromberg said that prevention is key, and NIBIB aspires to create technologies that follow the health trajectory and provide patients and their providers the right information to alter that trajectory if it is going in the wrong direction. For example, the reason to test for COVID-19 is primarily for prevention: determining who has COVID-19 and then taking steps to prevent its spread.

Dr. Tromberg stated that an element to this will be better ways to measure biologic processes over time, rather than in snapshots with great time intervals that do not allow course corrections. An example is the continuous glucose monitor. There is enormous potential and he hopes to engage the NIDDK community in partnerships.

VII. UPDATE: HEALTH EQUITY WORKING GROUP

Dr. Germino

Dr. Germino gave a progress report on NIDDK's efforts to develop a Health Equity and Health Disparities Implementation Plan in support of the NIDDK Strategic Plan (see VIII).

Spurred by the devastating effects of COVID-19 on communities and the longstanding health inequalities magnified by the pandemic, NIDDK started a year-long Council Forum in September 2020 that focused on structural racism and social determinants of health and their effects on the NIDDK workforce and research programs.

At the January 2021 Council Forum, the discussion centered on health disparity research, including ways to encourage more research in this area. For example, one factor contributing to the lower success rate for black researchers is that they tend to propose research on topics with lower award rates, such as health disparities. The Council agreed with a recommendation to establish a Working Group to develop a Health Equity and Health Disparities Implementation Plan for NIDDK's Strategic Plan. External experts, NIDDK staff, and the broader community recognized the urgency of weaving throughout the Strategic Plan themes of inclusion, diversity, and stakeholder engagement, with a goal of achieving health equity by eliminating health disparities. Dr. Germino noted that the overarching theme of the NIDDK Strategic Plan is: empowering a multidisciplinary research community, engaging diverse stakeholders, and leveraging discoveries and connections among diseases across NIDDK's mission to improve prevention, treatment, and health equity—pursuing pathways to health for all.

To develop the Health Equity and Health Disparities Implementation Plan, the NIDDK established a Working Group that includes representatives from each of NIDDK's extramural programmatic Divisions, the Division of Extramural Activities, the Office of Scientific Program and Policy Analysis, the Office of Minority Health Research Coordination, and the Office of the Director. The group has been meeting regularly since January 2021, and has identified four broad scientific themes that loosely follow

the research framework described by Dr. Pamela Thornton at the January 2021 Council meeting.

Theme 1: *Determine how structural racism and other social determinants of health intersect with biological processes to cause disease.*

Many of the conditions within NIDDK's mission are linked. For example, obesity is a risk factor for fatty liver disease and type 2 diabetes; diabetes raises the risk for kidney disease. In addition to shared biological causes and contributors, such as genetics and inflammation, these diseases also share social and structural determinants of health, such as differences in access to care, environmental exposures, and access to healthy food and places to exercise. As a result of the shared pathways to disease development, many individuals have more than one disease in NIDDK's mission area. Work in this area may include examining how discrimination, stigma, economic distress, and other factors can result in inflammation, dysregulated cortisol release, metabolic disease, and disruption of biological systems.

Theme 2: *Determine how to mitigate the effects of social determinants of health to improve health and eliminate disparities.*

Addressing longstanding, complex, and widespread systems and stressors, such as structural racism, and mitigating the psychological, social, and physical burdens on people and communities is a long-term effort. This includes identifying interventions and approaches to help people compensate for and/or overcome barriers that prevent equitable access to healthy environments and health resources. Examples include community health worker interventions, transportation support, language access, or peer support strategies.

Theme 3: *Address the upstream causes of social determinants of health and health disparities from an NIDDK perspective.*

Referred to as "Next Generation Research" by Dr. Thornton, root cause studies focus on understanding and mitigating fundamental conditions that lead to health disparities. Interventions in this space can have the greatest impact on relieving multiple health disparities and supporting health equity, but these are also the most complex to achieve, as they will require multisectoral partnerships. This work could include policy-oriented studies, including research that addresses structural barriers and social determinants of health directly. The challenge will be to define where and how NIDDK can most effectively leverage its expertise and modest resources.

Theme 4: *Engage communities and build partnerships.*

Work related to this theme would focus on integrating an understanding of community members' lived experience and research priorities into NIDDK's work, building sustainable partnerships with diverse stakeholders, and centering equity into research efforts.

Related to the logistics of developing the Implementation Plan, the Working Group intends to establish four subgroups—one for each of the themes—that will each be co-

chaired by an external expert in the health disparity and health equity field and an NIDDK program officer. Each subgroup will include six additional external experts, as well as NIDDK staff members. The Working Group has finalized a slate of external experts and will send out invitations shortly.

In addition, the Working Group would also form a steering committee comprised of the co-chairs of each subgroup to help coordinate the various elements of the Implementation Plan into a cohesive whole. The Working Group also plans to have a series of community engagement sessions to solicit community input throughout the process. Relevant community members may not be reached through the standard Request for Information (RFI) processes, so alternative methods will be used.

The Working Group has also identified background information that may be useful for deliberations, including:

- NIDDK portfolio review
- National Institute of Minority Health and Health Disparities (NIMHD) Strategic Plan
- RFI input obtained during the development of NIDDK's Strategic Plan
- Summaries of meetings held by subgroups of the NIDDK Strategic Plan Council Working Group
- Relevant literature

In terms of a timeline, the Working Group intends to kick off the effort this fall with an orientation meeting, followed by a steering committee meeting and two sets of subgroup meetings, with work continuing between meetings. Community input will be solicited throughout the process. The goal is to complete the process by the Advisory Council meeting in September 2022. The deliverable will be a multilevel research framework and Implementation Plan that will include a summary of high priority research gaps and achievable research opportunities.

Council Questions and Discussion

Comment from Council: *To ensure direct input from community members, should you consider having a community or patient representative on each subgroup? Involving multiple community members can help build trust within the community and re-establish good relationships.*

Dr. Germino explained that the Working Group has discussed this at length, including how to practically involve community members to get a wider perspective. The Working Group's initial thoughts were that engaging a larger number of community representatives throughout the process would provide better representation compared to having a single representative on each subgroup.

The need for direct community input to this effort was reiterated by several Council members, including the importance of adding community or patient representatives to subgroups, and Dr. Rodgers assured the Council that the Working Group will take another look at this issue.

Comment from Council: *Basic scientists struggle to integrate diversity and*

underrepresented issues into their work. Might there be an opportunity to look at fundamental pathways of stress and immune suppression that arises out of social inequality, and housing and economic disadvantage?

Dr. Germino explained that this area is embedded in theme 1, which looks at biological connections and how social determinants of health and structural racism manifest by creating or resulting in disease. Examining biological processes has been an NIDDK strength, and linking basic science research to social determinants of health will be important to achieving health equity.

VIII. UPDATE: NIDDK STRATEGIC PLANNING PROCESS

Dr. Germino

Dr. Rodgers invited Dr. Germino to update Council with highlights of the draft NIDDK Strategic Plan.

Dr. Germino reminded Council that the Strategic Plan was developed as an overarching research plan for the Institute and is meant to complement disease-specific planning efforts. NIDDK has received valuable input from its external Working Group, from Council, and from a public request for information (RFI). Based on this input, NIDDK staff developed a first draft that was sent to the Working Group for review in the spring of this year. Staff then posted a revised draft on the NIDDK website for public comment this summer, as another RFI, and are currently reviewing those comments.

The NIDDK Strategic Plan has four major scientific goals:

1. Advance understanding of biological pathways and environmental contributors to health and disease;
2. Advance pivotal clinical studies and trials for prevention, treatment, and cures;
3. Advance research to disseminate and implement evidence-based prevention strategies and treatments in clinics and community settings–to improve the health of all people, more rapidly and more effectively; and
4. Advance stakeholder engagement—including patients and other participants as true partners in research.

Dr. Germino noted that several issues crucial to NIDDK's mission are addressed throughout the Strategic Plan. These include:

1. Achieving health equity by eliminating health disparities among minority groups and those who are underserved;
2. Improving women's health;
3. Strengthening the biomedical research workforce diversity and training; and
4. Ensuring that NIDDK serves as efficient and effective stewards of public resources.

The Strategic Plan also contains this overarching theme:

"NIDDK is committed to empowering multidisciplinary researchers, engaging diverse stakeholders, and leveraging connections among diseases across our mission to improve prevention, treatment, and health equity—pursuing pathways to health for all."

Dr. Germino explained that "stakeholder" is a common word in the Plan and refers to the diverse communities who share NIDDK's interest in improving health and quality of life for those with diseases within the Institute's mission, including, for example, patients and caregivers, others who participate in research, healthcare and other organizations that would deliver interventions studied in clinical research, industry, and others. These individuals and organizations are all also potential partners in the research process.

He then outlined research opportunities and examples for each scientific goal in the Strategic Plan.

Scientific Goal 1: Advance understanding of biological pathways and environmental contributors to health and disease
Research Opportunities:

- **Identify and characterize factors that affect human health**, such as genetic and molecular pathways, the microbiome, inflammation, and other biological, environmental, and social factors that affect disease risk. Related topics include disease-related differences between males and females, understanding how the body's organs, tissues, and cells signal to each other, and brain-body connections. Stakeholder engagement includes gathering perspectives of patients who provide precious tissue and other biological samples to make new discoveries possible. Other collaborations, including with industry, can help move foundational discoveries through the research pipeline to potential therapeutics.
- **Analyze links between biology, behavior, and environment,** to increase understanding of disease heterogeneity and to give insights into health disparities. For example, knowing that a biological process varies with factors such as stress or poverty can help refine research questions and reveal previously unrecognized connections between biological responses and the environment.
- **Develop innovative technologies and resources**, such as new cell lines, animal models, organoids, and tissue- or organ-on-a-chip systems that more accurately reflect human health and disease. Advancing data science and biorepository resources will also aid foundational research discoveries.
- **Enhance and diversify the workforce** to solve complex, multidisciplinary research questions. Training in new techniques and technologies in areas such as bioengineering, imaging, genomics, proteomics, and social science will advance a broad array of research studies. Collaborations between basic scientists and physician scientists can help bridge the gap between discovery and real-world clinical needs.

Scientific Goal 2: Advance pivotal clinical studies and trials for prevention,

treatment, and cures in diverse populations
Research Opportunities:

- **Enhance development/testing of diagnostics, therapeutics, and prevention strategies,** such as by translating basic science discoveries to clinical studies through multidisciplinary team science; developing precision medicine approaches; developing interventions that address social determinants of health; integrating innovative clinical trial designs into research; and making research participation in healthcare more feasible with improved technology, such as wearable devices for monitoring nutrients, metabolites, hormones, and activity.
- **Increase participant diversity in clinical trials**, including sufficient representation of women and minority populations and efforts toward including patient- or participant-oriented outcomes to reflect that patients' priorities sometimes differ from researcher-selected outcome measures. Developing innovative and inclusive outreach strategies could also help to address hurdles to diverse enrollment.
- **Bolster workforce development and training** of people in a variety of roles in clinical studies, including principal investigators, clinical study coordinators, community partners, and others.
- **Use data science to improve clinical studies,** including the use of electronic health records and artificial intelligence technologies while addressing key ethical concerns, such as protecting individual privacy and eliminating potential bias in AI technologies.
- **Optimize infrastructure and resources for clinical research,** including facilitating the startup process for clinical studies through approaches for reusing existing infrastructures and other efforts. Resources include biorepositories, which may link genomic, metabolomic, and other -omic data to information on presence or absence of a disease, hormone levels, or other measures.

The Strategic Plan also addresses NIDDK's unique role in "filling the gap"—sponsoring clinical studies that are not likely to be supported by the pharmaceutical industry or other funders. For example, studies of behavioral interventions, comparative effectiveness research, and the exploration of other uses for generic medications.

Scientific Goal 3: Advance research to disseminate and implement evidence-based prevention strategies and treatments in clinics and community settings—to improve the health of all people, more rapidly and more effectively
Research Opportunities:

- **Improve dissemination and implementation research to accelerate the reach of prevention/treatments**, such as by testing multi-level, multidisciplinary approaches that link medical settings with social services or other organizations to treat the whole person. These types of studies would address social determinants of health, such as socioeconomic disadvantages, structural racism, lack of access to healthcare, or limited availability of nutritious and affordable foods in the community. Incorporating sustainability into the research design will help enable the continuation of intervention delivery in healthcare or community settings over time, after the research project is concluded.

- **Evaluate programs/policies initiated by communities, others.** Because the diseases in NIDDK's mission place substantial burden on public health, many communities and policymakers are pursuing efforts toward disease prevention or management. Research to evaluate these programs and policies, often referred to as natural experiments, can determine their effects on health and identify opportunities for implementing promising efforts in other settings and populations.
- **Study major unanticipated events,** such as a pandemic, with an eye toward future implementation of preparedness and response efforts.
- **Engage and partner with stakeholders,** including those who would benefit from an intervention, as well as those involved in disseminating and implementing the intervention. This includes healthcare systems, community organizations, school systems, and digital technology vendors.
- **Enhance workforce** training and diversity, as well as multidisciplinary approaches.

Scientific Goal 4: Advance stakeholder engagement — including patients and other participants as true partners in research
Research Opportunities:

- **Involve stakeholders (patients, caregivers, patient advocacy organizations, and others) in each step of the research process.** Potential areas for engagement include providing input into research priorities, the design of studies involving volunteers or analysis of human tissue samples, and participant recruitment. Stakeholders can also serve in leadership roles on steering and other committees.
- **Ensure representation of populations affected by NIDDK diseases.** To ensure such representation, including populations that have been marginalized, it is necessary to recognize the inherent inequities they experience and identify ways to make involvement in research feasible for and appealing to them. Building trust is also essential, particularly for minority populations that have been historically underrepresented in these efforts.
- **Address barriers to stakeholder engagement.** This includes medical literacy, costs, time, transportation, childcare, and other practical challenges.

Stewardship Opportunities
Next, Dr. Germino discussed some ways NIDDK can continue to demonstrate good stewardship of public resources.

- **Increase diversity of the research workforce.** Multiple approaches to address this topic are addressed in the Strategic Plan. For example, researchers could bring opportunities directly to communities of people underrepresented in science, so they could maintain their community and support networks. For instance, data science is particularly well suited to work in communities with few existing resources because extensive research infrastructure is not required.
- **Enhance research training and career development.** Avenues include training and incentivizing mentors, seeking input from next generation researchers to build training and career development programs that better meet their needs, and promoting a broader research experience by building bridges across disciplines.

- **Attract and retain physician/surgeon scientists.** One approach would be to connect these individuals with the field of data science, as that field would have the flexibility to be woven into clinical training. Additionally, collaboration between clinical researchers and data scientists would enhance translation of big data into clinical application.
- **Promote data science.** This includes promoting proper data collection, storage, and sharing; increasing training in bioinformatics and biostatistics; and encouraging interdisciplinary collaboration among data scientists and researchers who focus on diseases within the NIDDK mission.
- **Improve rigor and reproducibility.** The Strategic Plan addresses multiple aspects of this, such as the use of unique identifiers for datasets and reagents, standardization, and ensuring data and resources can be found, used, and reused.

Process for Strategic Plan Formal Council Review and Concurrence
Dr. Germino informed Council that members will receive the final draft of the NIDDK Strategic Plan for review in mid-November. A virtual meeting on Council concurrence will be held on November 23, 2021. The NIDDK plans to release the final Strategic Plan in December.

Dr. Germino announced that he had many people to thank for their work on the Strategic Plan. This includes:

- Our Council, the Working Group members, and those who sent comments in response to public RFIs.
- The five external co-chairs of the Working Group subgroups: Drs. Gary Wu, Penny Gordon-Larsen, Barbara Kahn, Elizabeth Seaquist, and former Council member Mr. Richard Knight.
- The five NIDDK staff co-chairs of the Working Group subgroups: Drs. Chris Mullins, Averell Sherker, Pamela Thornton, Ellen Leschek, and Matt Portnoy.
- The Lead Strategic Plan Development Team in NIDDK's Office of Scientific Program and Policy Analysis: Drs. Lisa Gansheroff, Rebecca Cerio, Sandeep Dayal, Rob Tilghman, and Julie Wallace, along with the Office Director Dr. Heather Rieff.
- The many other external Working Group members and NIDDK staff who participated in the Strategic Plan development. They will be listed in the Strategic Plan itself.

<u>Council Questions and Discussion</u>
Before opening up to general questions from the Council, Dr. Germino asked the external co-chairs of the Strategic Plan Working Group subgroups if they would like to comment, including Drs. Gordon-Larsen, Kahn, Wu, and Seaquist.

Dr. Barbara Kahn pointed to how several Working Group subgroups converged on many of the same ideas, including diversity and inclusion, as well as the concept that data science may benefit communities with few existing resources. Another important theme that emerged was encouraging scientists from diverse institutions to participate in NIDDK research. Given the ambitious nature of these goals, she asked about the

process for implementing and prioritizing among these ideas and initiatives.

Dr. Germino recognized that priority setting is a complex process that considers factors such as research opportunity, available resources, and impact of the research. The NIDDK plans to develop implementation plans for their communities.

Dr. Wu pointed out common themes across Working Group subgroups, such as opportunities for cross-disciplinary research. Implementation is an important component, especially in underserved communities. Prior projects can provide a roadmap, so he urged careful consideration of examples described in the Strategic Plan.

Dr. Gordon-Larsen referred to a previous session about the incorporation of issues of diversity, equity, and inclusion into the basic sciences, pointing out this is an important area for the Council and NIDDK to consider.

Dr. Seaquist observed that she has seen a change in how and in what context structural racism, diversity, and inequity are discussed, and this Strategic Plan reflects that. Data science using electronic medical records may present an opportunity to study the whole population. However, effective use of that data requires solving the problems associated with electronic medical records and clinical data.

Dr. Germino then opened discussion to the other Council members.

Comment from Council: *Adding to Dr. Gordon-Larsen's point, translation from basic science to clinical care should be bi-directional. An example is research into Long QT Syndrome, which reached deeper insights when basic observations were combined with information from patients with the identified gene. This may be true of other mutations causing disease in certain populations, such as sickle cell and other diseases in African Americans.*

Dr. Germino pointed out that having multidisciplinary researchers working with diverse stakeholders and communities could help to promote bi-directional flow of information. The goal of health equity requires the cooperation of a variety of people playing different roles.

Comment from Council: *When it comes to implementation, NIDDK lacks effective mechanisms to bring people together for larger grants. What novel, innovative mechanism can we use to bring people together where the sum is greater than the individual parts?*

Dr. Germino said that different approaches and strategies have been used to build research communities. The RC2 program is one example. He recognized the importance of thinking about how best to build structures that can support the kind of collaborative science described in the Strategic Plan.

Comment from Council: *Implementation science should include early stakeholder input to help identify what is likely to work as we move forward, especially in terms of building diversity—including diversity of perspectives and input—and building trust in communities at NIH and NIDDK. Interaction among the Plan's goals is necessary to build*

real-world ideas.

Comment from Council: *When basic science explores pathways and molecular mechanisms that might explain social determinants of health, there is the potential to unintentionally stigmatize a community. The engagement of community members in the basic science itself—and the communication to community members of that research and science—is important.*

Dr. Germino agreed that this is an important point and one that should be discussed beyond the Council and even outside of NIH. More than half of NIDDK's research budget goes to investigator-initiated projects where the Institute has some oversight but is not actively involved as participants as it is with consortia. It is an important conversation to have in the research community at large, as it may be beyond what NIH can do alone.

Comment from Council: *Is there a role for the Common Fund to take on some of these large challenging issues that have been discussed today, to enhance what can be addressed on an Institute level?*

Dr. Germino explained that the Common Fund is something NIDDK actively participates in. Many program staff members wear multiple hats, including in the Common Fund and other trans-NIH efforts, participating in the design of research questions. Examples include the Human Microbiome Project, the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, and many others that have benefited the communities, science, and disciplines represented at NIDDK. NIDDK actively looks for opportunities to build partnerships and broaden stakeholders to achieve our research mission.

Comment from Council: *Is the move of the Office of Nutrition Research out of NIDDK having an impact on NIDDK's portfolio?*

Dr. Germino said that the NIDDK portfolio has not changed. The hope is that the relocation of the office into the NIH Office of the Director will result in the expansion of opportunities for promoting research into nutrition, for example, by leveraging the All of Us investment. The Office moved less than a year ago and the transition is still at the early stages.

Comment from Council: *Surveys of patients from clinical trials and recruitment efforts related to burden of disease, drug therapy, and clinical trials are becoming more important. NIDDK should encourage this kind of survey even at a basic science level because of the potential impact on outcomes that patients need and want.*

No staff or Council response required.

Comment from Council: *When you solicited comments on the Strategic Plan from the research community, did you receive many comments? What was the nature of the input? What are the next steps in that process?*

Dr. Germino said that the comment period recently closed and the comments are currently being processed. The plan is to review the public comments, make edits as necessary in response to those comments, then send the revised draft to the Working Group for review.

After considering Working Group comments, a version will be submitted to the Council prior to the November 23 meeting.

Comment from Council: *Is there something unique in the portfolio of NIDDK that could be addressed in the Strategic Plan that would be different from the other NIH Institutes?*

Dr. Germino acknowledged that there are many common and cross-cutting themes. The report will include call-out boxes and illustrative examples of how this would be implemented in NIDDK's mission areas. With the breadth of conditions and target organs, it is difficult to do justice to the full breadth of possibilities.

Comment from Council: *Does the Strategic Plan look at cross-mission areas, such as children transitioning to young adults, and the possibility of working with the* Eunice Kennedy Shriver *National Institute of Child Health and Human Development (NICHD)? Pediatric patients are affected by different social determinants of health and disparities in access to care and medications when compared to adult patients, and the transition between childhood and adulthood is important from a nutritional standpoint and affects obesity.*

Dr. Germino explained that, while the Plan does not call out for partnerships with specific NIH Institutes, this issue does fall in the NIDDK mission area as well as that of other Institutes. An important focus of the Plan is strengthening relationships and identifying cooperative strategies. The transition from childhood to adulthood is important to a variety of disease states, including chronic kidney disease. An NIH policy changed a couple of years ago so that clinical studies must have a scientific reason for not including participants across the lifespan.

IX. CONCEPT CLEARANCE

Dr. Rodgers then turned to Concept Clearance by Council, a step required before ICs can publish funding opportunity announcements, or FOAs. To streamline this process, summaries of the concepts were supplied to Council members for their review before the meeting.

The meeting included descriptions of six concepts: three by the Division of Diabetes, Endocrinology, and Metabolic Diseases, and three by the Office of Minority Health Research Coordination. Cleared concepts will be made publicly available on the NIDDK website.

Division of Diabetes, Endocrinology, and Metabolic Diseases Concepts
Members of the DEM staff presented three concepts on behalf of the division. Dr. Karen Teff started by presenting one new initiative, and Dr. Cefalu presented concepts for reissue FOAs:

- **Elucidating the Heterogeneity in the Restoration of Hypoglycemia Awareness in Type 1 Diabetes Mellitus (T1DM):** Dr. Karen Teff started by presenting a new initiative on T1DM. Repeated episodes of hypoglycemia result in impaired awareness of hypoglycemia (IAH) and blunting of counter-regulatory responses (CRR) required to restore normal glycemia. T1DM individuals with IAH experience severe hypoglycemic episodes with increased risk of morbidity and mortality. New

technologies including continuous glucose monitors (CGM) and artificial pancreas devices alert patients to declining levels of glucose, reduce hypoglycemic events and restore hypoglycemia awareness in some but not all individuals. T1DM patients with IAH are often excluded from clinical trials resulting in minimal progress in our understanding of the clinical characteristics or physiological mechanisms that predict an individual's ability to restore hypoglycemic awareness or improve CRR. A clinical consortium is proposed to identify clinical and physiological factors that restore awareness of hypoglycemia and improve CRR in adults with T1DM and IAH. The consortium will: 1) determine if a hybrid closed-loop system and hypoglycemia avoidance education can restore awareness of hypoglycemia and improve CRR; 2) identify glycemic metrics associated with restoration of hypoglycemia awareness and improvements in CRR; and 3) validate current self-report assessments with physiological measurements. The study will follow participants for 2 years. The primary outcome variables will be a measure of hypoglycemia awareness and a physiological measure derived during a hypoglycemic, hyperinsulinemic clamp.

- **Continuation of Mass Spectrometric Assays for the Reliable and Reproducible Detection of Proteins/Peptides of Importance in Type 1 Diabetes Research:** Dr. William Cefalu presented this continuation concept on mass spectrometry (MS)-based assays, which have several inherent advantages when compared to traditional ELISA. The main research goal of this initiative is to develop MS-based assays for peptides and proteins of interest to empower the type 1 diabetes (T1D) research community and facilitate precision medicine. Priority will be given to assays that are more likely to have an impact on clinical research, but assays that might be of interest to the basic research community can also be developed. A pilot project for this initiative has already led to the development of a novel targeted MS-based assay for C-peptide that does not require the use of antibodies, sophisticated MS instrumentation or separation, and can be performed in a standard clinical chemistry laboratory. This assay is likely to be easily multiplexed with a similar insulin assay that is under development. The next phase of this initiative will further validate the assays for insulin, glucagon, and C-peptide and develop standards, reference materials, and MS-based assays for other targets that will be prioritized based on feedback from the T1D research community.
- **Continuation of New Investigator Gateway Awards for Collaborative T1D Research:** Dr. Cefalu also presented this renewal concept for the New Investigator Gateway Award in T1D Research, which is designed to ensure that a robust pipeline of talented new investigators will continue to embark on successful careers in T1D research. In addition to providing support for preliminary research, the Gateway program provides an opportunity for new Program Directors/Principal Investigators (PD/PIs) to pursue their studies within the intellectual environment of a select number of large, ongoing collaborative research programs. Embedding awardees within an established scientific framework in each of these consortia will provide unique opportunities for New and Early-Stage Investigators to increase their understanding of key questions in the field, to network, and to establish unique and potentially long-lasting collaborations that will propel their careers forward. It is anticipated that the Gateway award will provide the support needed to enhance the success of future R01 submissions from New Investigators interested in pursuing careers in T1D

research.

Council Questions and Comments

Comment from Council: *For the Restoration of Hypoglycemia Awareness project, not all patients who experience decreased awareness are using a hybrid closed-loop pump; some still use multiple daily injections of insulin. Did you feel you had to start with a common protocol for insulin delivery? What about participants overriding the commands on the closed-loop pump?*

Dr. Teff noted that providing a hybrid closed-loop pump to all participants would ensure that study participants have a common baseline. Additionally, offering newer technology may encourage participation in the study. She added that hypoglycemia awareness education will help participants overcome issues they may have with glucose control and address concerns related to overriding pump commands.

Comment from Council: *Why is the MS assay initiative specific to type 1 diabetes when type 2 diabetes research will also benefit? Also, a similar project is underway that hopes to validate assays for diabetes and obesity research, which may present another opportunity to work together.*

Dr. Cefalu responded that the assays are going to be available and used for type 1 and type 2 diabetes. Dr. Salvatore Sechi, NIDDK, added that there is also a similar project that has more emphasis on type 2 diabetes and obesity research. These two groups have been working together for assays of common interest performing inter-laboratory validation.

Comment from Council: *The Restoration of Hypoglycemia Awareness initiative is a uniquely NIH type of project because it will use a commercially available tool that lacks appropriate clinical guidance. This initiative may help identify which patients would benefit most from a hybrid closed-loop system. Additionally, Council members commended NIDDK for using a multicenter clinical trial mechanism to achieve sufficient patient enrollment.*

No staff or Council response required.

Comment from Council: *How successful has the Gateway initiative been to get new investigators into type 1 diabetes research?*

Dr. Cefalu responded that the DEM subcommittee would receive an update on this project later in the day. For the full Council, he asked Dr. Kristin Abraham, NIDDK, to give a brief update.

Dr. Abraham informed the Council that the pilot phase implemented through the Human Islet Research Network funded six awardees. In the 3 years since those awards were made, 5 out of 6 awardees have now earned R01s in those topic areas. Meanwhile, the NIH/NIDDK version just made the first round of awards recently. Preliminary feedback from the awardees and their mentor investigators has been very positive.

Office of Minority Health Research Coordination (OMHRC) Concepts

Dr. Katrina Serrano presented three concepts on behalf of OMHRC.

- **Scientists Helping to Accelerate Research Potential (SHARP): A Pilot Mentoring Program:** Critical to the success of the NIH mission is promoting diversity in the extramural scientific workforce. Over the years, NIDDK and OMHRC have initiated programs that have trained several thousands of individuals from communities underrepresented in the scientific workforce. However, very few of these efforts have seemed to make a difference in increasing the proportion of underrepresented groups that have been successful in obtaining NIH R01 awards. While these efforts have supported the career development of biomedical scientists to pursue independent careers in the scientific workforce, additional strategies to promote the transition of junior faculty to tenured faculty are needed. Mentoring has long served an essential role in developing a scientific workforce, and research shows that it is critical to supporting the careers of underrepresented junior faculty. This proposed initiative would provide support to mentors to provide NIDDK Diversity R21, advanced (postdocs and junior faculty) Diversity Supplement, and MOSAIC K99/R00 scholars with professional skills and evidence-based mentoring to allow them to advance and succeed in NIDDK-relevant, independent academic research careers. At the end of the program, it is expected that at least 30 percent of the Diversity R21 and MOSAIC scholars will have successfully applied for an R01 grant.
- **Continuation of NIDDK Partnerships with Professional Societies to Enhance Scientific Workforce Diversity and Promote Scientific Leadership:** The overarching goal of this NIDDK Partnerships with Professional Societies to Enhance Scientific Workforce Diversity and Promote Scientific Leadership program is to support educational activities that enhance the diversity of the biomedical, behavioral, and clinical research workforce. This program focuses on the role that professional societies play in enhancing the scientific workforce. Since FY 2012, the OMHRC has awarded R25 grants to professional societies such as the Endocrine Society, the Academic Pediatric Association, the American Gastroenterological Association, the American Society of Andrology, and the American Psychological Association. The programs developed by these professional societies have been largely successful. By fostering the diversity of professional societies, the diversity of the overall biomedical and behavioral research workforce will be enhanced as well. Thus, continued support of this program is essential to ensuring that the scientific workforce better reflects the diverse backgrounds and experiences of the U.S. population.
- **Continuation of Advancing Gender Inclusive Excellence – Coordinating Center:** The final initiative presented by Dr. Serrano was a renewal of NIDDK participation in an initiative led by the NIH Office of Research on Women's Health. The overarching goal of the Advancing Gender Inclusive Excellence (AGIE) - Coordinating Center is to support a coordinating center that will provide the organizational framework for the management, direction, and overall coordination of all common activities aimed at investigating the strategies, approaches, barriers, and interventions to women attaining leadership positions in many areas of science. The AGIE - Coordinating Center will design and implement data collection methods; ensure data quality; develop strategies for the dissemination of findings; and serve as

a resource hub for future programs. This research will add to the understanding of the strategies, approaches, and barriers that range from interpersonal interventions to changes in the structure and culture at the institutional level. The coordinating center will make data available to those who want to study and implement such strategies. This proposed initiative aligns with NIH's focus on diversity in biomedical research, as well as NIDDK's goal of preserving a stable pool of talented new investigators from diverse backgrounds.

Council Questions and Comments

Comment from Council: *The presentation on the SHARP initiative included data that showed that 40 percent of R21 recipients did not progress to receiving an R01. Did those data include investigators who never went on to apply for an R01?*

Dr. Serrano responded that 28 out of 64 R21 participants did not submit an R01. The SHARP mentoring program would help support these investigators, including encouraging them to submit an R01 application.

Comment from Council: *How will the SHARP mentors be chosen? Will the mentors and the quality of their mentorship be evaluated during the 5-year program or only at its end? What if it becomes apparent that a mentor needs more training during the course of the program? Consider asking for feedback from mentees partway through the program.*

Dr. Serrano responded that OMHRC would have criteria for mentor qualifications and eligibility. The plan is to select senior investigators who have received substantial NIH funding to assist mentees with grantsmanship. Part of the program evaluation would include whether mentors and their mentorship strategies are effective.

Comment from Council: *Centers of Biomedical Research Excellence (COBRE) is a similar mentorship program in general medicine that assists young investigators in getting their first R01 grant. This program uses two types of mentors: senior mentors, as well as peer mentors who have just received their first R01 grant. Peer mentors may be at a late assistant professor or associate professor level and are especially valuable due to their recent experiences with the grant process. This dual-mentor strategy is effective and could work well for the SHARP program.*

Dr. Serrano appreciated this insight and noted that, while plans for SHARP include assigned cohorts that would function as peer mentors, she will further consider this suggestion.

Comment from Council: *How did OMHRC come up with the plan to assign 11 mentees per mentor? It may be too difficult for each mentor to spend enough time with the mentees to be beneficial.*

Dr. Serrano explained that each mentor will have to apply to the program so they could best judge their own ability to fulfill the program expectations. The total number of mentees per mentor at the end of the program would be 11, with mentees being added each year until that number was reached. This includes several NIDDK R21 investigators per year, a Mosaic K99 R00 scholar per year, and some diversity

supplement scholars per year across mentors. At the end of the fifth year, these would total 11 mentees per mentor.

Additionally, there may be a year or two when some mentors are not assigned a mentee. In some years of the program, there would be a transition of mentees—i.e., some will leave the program and new ones will replace them.

Comment from Council: *The need for greater diversity is certainly there, but has OMHRC accounted for the fact that there might initially be fewer mentees interested in participating in the SHARP program than expected?*

Dr. Serrano noted that OMHRC has some program outcomes for the NIDDK Diversity R21 program, which shows that underrepresented investigators are building successful early career paths and successfully applying for R21 grants. They just have not yet been successful getting an R01.

Comment from Council: *A more flexible approach with assigning mentees to mentors might be to give mentors who requested it fewer mentees and less funding for the 5 years. That would enable OMHRC to fund more mentors.*

Dr. Serrano thanked Council for this suggestion and requested Council input on what might be an ideal number of mentees per mentor. After some discussion, it emerged that Council would consider 5 to 6 mentees per mentor a more reasonable number.

Comment from Council: *Are the investigators who are receiving R21 grants MDs or PhDs? The pandemic has had a disproportionate effect on physician-scientists.*

Dr. Serrano responded that physician-scientists (MDs or MD/PhDs) are well-represented among R21 grant holders.

Comment from Council: *Regarding the gender inclusion initiative, the COVID-19 pandemic has disproportionately affected younger women investigators with family obligations. In addition to challenges faced by all investigators, there may be added burdens for parents that impact their competitiveness as clinical investigators. Will the Coordinating Center address this problem?*

Dr. Serrano confirmed that the Coordinating Center could gather data and perhaps issue some intervention strategies for institutions. Dr. Rodgers reminded Council that COVID's disproportionate effect on underrepresented scientists was also discussed early in the pandemic as an emerging area of concern.

Dr. Malik oversaw a motion for concurrence from Council regarding the six concepts presented. The motion was made, seconded, and approved by Council members via electronic poll.

Dr. Rodgers then announced that the Open Session of the Full Council was in recess at 1:53 p.m. Eastern Daylight Time.

X. INTRAMURAL RESEARCH PROGRAM UPDATE (Executive Session)

Following a short recess, Council met in Executive Session to hear an update on the Intramural Research Program led by Dr. Michael Krause.

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under 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 2).

XI. INTRAMURAL RESEARCH PROGRAM IMPLEMENTATION PLAN (Executive Session)

Council continued to meet in Executive Session with Dr. Krause to discuss plans to implement the recommendations of the Blue-Ribbon Panel Review.

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under 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 2).

ADJOURNMENT DAY ONE
Dr. Rodgers

The first day of the 217th meeting of the NIDDK Advisory Council was adjourned at 4:00 p.m. on September 9, 2021.

DAY TWO

XII. OPEN SESSION OF SUBCOMMITTEE MEETINGS

See Minutes posted on NIDDK Council Minutes Website.

XIII. CLOSED SESSION OF THE SUBCOMMITTEE MEETINGS

A portion of the meeting was closed to the public in accordance with the determination that it concerned matters exempt from mandatory disclosures under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. and Section 10(d) of the Federal Advisory Committee Act as amended (5 U.S.C. Appendix 2).

Members absented themselves from the meeting during discussion of and voting on applications from their own institutions, or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect.

XIV. CLOSED SESSION OF THE FULL COUNCIL

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under 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 2).

CONSIDERATION OF REVIEW OF GRANT APPLICATIONS.

A total of 2417 grant applications (1505 primary and 912 dual), requesting support of $970,372,945 were reviewed for consideration at the September 9-10, 2021, meeting. An additional 517 Common Fund applications requesting $410,591,105 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1183 applications requesting $408,025,238 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level. The expedited concurrence actions were reported to the full Advisory Council at the September 9-10, 2021, meeting.

XV. ADJOURNMENT

Dr. Rodgers

Dr. Rodgers expressed appreciation on behalf of the NIDDK to the Council members, presenters, and other participants. He thanked the Council members for their valuable input. There being no other business, the 217th meeting of the NIDDK Advisory Council was adjourned at 12:45 p.m. on September 10, 2021.

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

Griffin P. Rodgers, M.D., M.A.C.P.
Director, National Institute of Diabetes and Digestive and Kidney Diseases, and
Chairman, National Diabetes and Digestive and Kidney Diseases Advisory Council