National Institutes of Health

National Advisory Allergy and Infectious Diseases Council

Minutes of Meeting

September 9, 2024

The 208th meeting of the National Advisory Allergy and Infectious Diseases Council (NAAIDC) convened at 5601 Fishers Lane in the Grand Hall at 10:30 a.m. on **Monday, September 9, 2024**. Dr. Jeanne Marrazzo, Director, National Institute of Allergy and Infectious Diseases (NIAID) presided as chair.

In accordance with the provisions of Public Law 92-463, the meeting was open to the public from 10:30 a.m. to 11:45 a.m. and from 1:00 p.m. to 4:10 p.m. The meeting was closed to the public from 8:30 a.m. to 10:30 a.m. and from 11:45 a.m. to 12:00 noon for review and consideration of individual grant applications. Notice of the meeting was published in the *Federal Register*.

Meeting Attendees

Council Members Present:

Dr. Grace Aldrovandi
Dr. Linda Bockenstedt
Ms. Emily Brown
Dr. Mary Estes
Dr. James Gern
Dr. Keith Jerome
Dr. Laurence Morel
Dr. Guy Palmer
Dr. Maria Pascual
Dr. R. Stokes Peebles
Ms. Seema Shah
Dr. Stephanie Taylor

***Ex Officio* Members Present:**

Dr. Victoria Davey
Dr. Jeanne Marrazzo

***Ad Hoc* Members Present:**

Dr. Dusan Bogunovic
Dr. Joaquin Espinosa
Dr. Bernard Khor

Council Members Absent:

***Ex Officio* Members Absent:**

Dr. Daniel Jernigan

NIAID Senior Staff Present:

Dr. Hugh Auchincloss
Dr. Carl Dieffenbach
Dr. Emily Erbelding
Dr. Jill Harper
Dr. Cliff Lane
Dr. Ted Pierson
Dr. Kelly Poe
Dr. Daniel Rotrosen

I. Review of Grant Applications

The National Advisory Allergy and Infectious Diseases Council convened in closed session to consider applications in allergy and immunology, microbiology and infectious diseases, and AIDS.

Funding Actions: The Council reviewed 4,960 research and training applications with primary assignment to NIAID for a requested amount of $1,709,844,189 in first-year direct costs and recommended approval of 2,577 applications with $979,348,782 in first-year direct costs.

II. Remarks of the Director, NIAID—Jeanne Marrazzo, M.D., M.P.H.

Dr. Marrazzo opened the Council session by welcoming visitors to the meeting.

Dr. Marrazzo acknowledged the contributions of three retiring Council members—Drs. Linda Bockenstedt, Keith Jerome, and Stephanie Taylor—and presented them with plaques and certificates of appreciation for their service. She then welcomed three *ad hoc* members: Dr. Dusan Bogunovic, Columbia University Medical Center; Dr. Joaquin Espinosa, University of Colorado Anschutz Medical Campus; and Dr. Bernard Khor, Benaroya Research Institute.

Consideration of Minutes of Previous Meeting

Council considered the minutes of the June 3, 2024 meeting and concepts that had been presented and approved them as written.

Staff and Organizational Changes

Dr. Marrazzo announced appointments and transitions that have taken place at NIH and NIAID since the last Council meeting.

Dr. Carolyn Hutter has been named Director of NIH's Office of Strategic Coordination, and Dr. Geri Donenberg has been appointed NIH Associate Director for AIDS Research and Director of NIH's Office of AIDS Research (OAR).

After 18 years of stellar service to the Institute, NIAID Principal Deputy Director Dr. Hugh Auchincloss will retire at the end of September.

Three key people have been selected to join Dr. Marrazzo's leadership team in the Immediate Office of the Director: Dr. Lucas Buyon, Health Science Policy Analyst and Scientific Special Assistant; Dr. Robert Eisinger, Senior Advisor to the Director; and Dr. Tara Palmore, Senior Medical Advisor.

In the Division of AIDS (DAIDS), Dr. César Boggiano is the new Director of the Vaccine Research Program.

In the Division of Allergy, Immunology, and Transplantation (DAIT), Dr. Bruce Burnett is the new Chief of the Office of Regulatory Affairs.

Dr. Chelsea Boyd has been named Director of the Office of Extramural Research Policy and Operations in the Division of Extramural Activities.

Meetings and Events

On June 27, Dr. Marrazzo and NIH Director Dr. Monica Bertagnolli visited Whitman-Walker's Max Robinson Center, a community-based research site in Washington, DC, in celebration of Pride Month.

On July 9, Dr. Marrazzo met with NIAID's first year clinical fellows.

Dr. Lee Hall and his colleagues hosted Dr. Marrazzo for a World Mosquito Day briefing on July 20.

On July 31, Dr. Marrazzo visited the Gaithersburg and Frederick Vaccine Research Center (VRC) facilities, which included the Vaccine Immunology Program, the Production Program, and the Clinical Materials Program.

Dr. Marrazzo highlighted recent meetings with international colleagues from China, Australia, Japan, and the World Health Organization, along with an 8-day trip to South Africa, which included visits to tuberculosis and HIV care facilities.

Budget Update

The President's FY 2025 budget request was submitted to Congress on March 11, 2024, which proposed an overall increase for NIH of 5.6 percent or $2.76 billion above the FY 2024 enacted level. The budgets for NIAID and most other institutes and centers (ICs) remain flat at the FY 2024 enacted level.

Dr. Marrazzo presented NIAID research areas proposed for earmarks—Congressional directives where NIAID is required to spend a specified amount of money for a stated purpose. New target research requirements for FY 2025 include National Biocontainment Laboratories and Valley Fever Vaccine.

Legislative Update

In June, NIH's Office of Legislative Policy and Analysis held a Lunch and Learn presentation for Congressional staff on Long COVID. Dr. Marrazzo, Dr. Bertagnolli, and staff from several NIH institutes participated.

On July 10, Dr. Marrazzo briefed members of the GOP Doctors Caucus on NIH/NIAID research on H5N1 as part of a larger multi-agency briefing. Representatives from the Assistant Secretary for Pandemic Responses Office, Center for the Biomedical Advanced Research and Development Authority, FDA, CDC, and USDA also participated. Other NIAID staff have done similar briefings since there has been a lot of Congressional interest in NIAID's H5N1 portfolio.

On August 27, Congressional appropriations staff visited Rocky Mountain Laboratories (RML). Dr. Marshall Bloom led the site visit, which included a tour of the RML facilities and updates from investigators about a broad range of research.

Other Information Items

Dr. Marrazzo began with an update on HIV, noting that we aren't where we need to be with HIV. She mentioned that epidemics are growing in several regions outside of Sub-Saharan Africa, and resources available for HIV have decreased and remain short of what is needed to realize 2030 goals.

Dr. Marrazzo attended and was involved in several presentations at the 25th International AIDS Conference in Munich, from July 22 to 25, 2024. She presented a few highlights from the Conference,

including promising results from the long-acting pre-exposure prophylaxis (PrEP) studies of injectable lenacapavir in cisgender women and injectable cabotegravir during pregnancy; the next Berlin patient who has had sustained HIV remission without antiretroviral therapy after a heterozygous CCR5 allogenic stem cell transplant; and vaccine development, especially focusing on the success of germline targeting.

To help address the syphilis epidemic, NIAID recently awarded 10 grants to support innovative projects in syphilis diagnostics.

Dr. Marrazzo gave an overview of the H5N1 highly pathogenic avian influenza outbreak, which included selected facts about the outbreak, number of reported human cases in the United States, and number of reported infections in animals. On June 5, NIAID released its H5N1 Influenza Research Agenda, which focuses on four key objectives for advancing H5N1 influenza basic research and translating findings into strategies and interventions that can benefit people. She then highlighted recent NIAID-funded H5N1 research results that have helped inform the response.

Mpox, which has been endemic in Africa for a long time, has mutated and spread and become a public health emergency. NIAID released its Mpox Research Agenda, which outlines planned and ongoing projects led by the Institute as part of a broader mpox research effort. Dr. Marrazzo then acknowledged Dr. Cliff Lane and his team for leading the randomized, controlled trial of tecovirimat in the Democratic Republic of the Congo.

Dr. Marrazzo provided updated statistics on COVID-19. She emphasized the challenges of Long COVID and provided examples of recent NIAID-funded studies on Long COVID pathogenesis. NIAID is launching a new initiative, Researching COVID to Enhance Recovery-Treating Long COVID (RECOVER-TLC), that will build on the successes and lessons learned from the National Heart, Lung, and Blood Institute's RECOVER project. RECOVER-TLC will focus on running clinical trials for Long COVID and testing and investigating more potential treatments.

She concluded with brief updates on malaria vaccines and pregnancy, and a study on the molecular basis for cognitive impairment in lupus that is potentially modifiable.

III. Guest Speaker—Ted Pierson, Ph.D., Director, Vaccine Research Center, NIAID

Dr. Ted Pierson began by giving an overview of VRC's mission—to perform basic science research that enables the development of novel vaccines and biologics targeting infectious diseases of global health importance.

VRC has a broad basic and translational research portfolio and was originally founded to conduct research that would lead to the development of HIV vaccines. VRC's portfolio has expanded considerably since its inception to include many other viruses. In addition to virology research, VRC also works on *Mycobacterium tuberculosis*, malaria, cancer, discovery science in immunology and virology, and platform technology development.

Dr. Pierson introduced additions to VRC faculty and leadership: Dr. Nicole Doria-Rose established the Antibody Immunity Section; Dr. Sarah Andrew launched the B Cell Immunobiology Section; and Dr. Tongqing Zhou launched the Structural Virology and Vaccinology Section. He also noted that Dr. Jason Gall is the new Chief of the Vaccine Production Program and Director of VRC's Strategic Planning and Development.

Dr. Pierson concluded by highlighting some of VRC's scientific advances related to CAP256-VRC26, a neutralizing HIV monoclonal antibody; HIV vaccines; a protective monoclonal antibody that binds the

underside of the influenza virus neuraminidase; neutralizing antibodies to influenza H5; strategies for COVID boosting regimens that can prevent infection and transmission; and development of anti-malarial monoclonal antibodies.

IV. Report of the Allergy, Immunology, and Transplantation Subcommittee—Daniel Rotrosen, M.D., Director, DAIT

Dr. Rotrosen welcomed the subcommittee members to the 208th meeting of the National Advisory Allergy and Infectious Diseases Subcommittee meeting.

Dr. Rotrosen presented the following scientific and Division activities:

Staff and Organizational Changes

Bruce Burnett, Ph.D., Dr. Burnett has been selected as the Branch Chief of the Office of Regulatory Affairs. Dr. Burnett has more than 25 years of leadership experience in multiple aspects of the clinical development of drugs, biologics, and devices. After 9 years in the biotech industry, he was recruited to Duke University where he established and was appointed as the University's first Director, of their Regulatory Affairs and Quality program. For the last 7 years he has worked at NIH establishing and supporting the NIH Clinical Center Office of Research Support and Compliance. Dr. Burnett received his Ph.D. in organic chemistry/biochemistry from the Massachusetts Institute of Technology in 1982 under Nobel Laureate Dr. Har Gobind Khorana, followed by an NIH-funded postdoctoral fellowship at Harvard University/Harvard Medical School under Dr. Frederick Ausubel.

Taylor Poor, M.D., Ph.D., Dr. Poor joined the Allergy, Asthma, and Airway Biology Branch in August 2024 as a Medical Officer. He completed medical school and the medical-scientist training program at the Feinberg School of Medicine at Northwestern University. Following graduate school, he remained at Northwestern University for internship and residency training in Internal Medicine at the McGraw Medical Center, followed by fellowship training in Pulmonary and Critical Care Medicine. He joined the faculty of the Division of Pulmonary and Critical Care Medicine in 2022, where his research focused on metabolic control of lung epithelial repair in models of lung injury, as well as pathophysiology of the host response pulmonary infection in critical illness.

Payal Patel, M.D., Dr. Patel joined the Allergy, Asthma, and Airway Biology Branch in May 2024 as a Project Manager. She received a medical degree from the Medical University of Lublin, Poland in 2013. Since then, she has worked as a coordinator, psychometric rater, and sub-investigator in psychiatric clinical research at CI Trials in California, and as a manager of psychometrics at Cenexel/CBH Health in Virginia. Prior to joining NIAID, she worked with Sunstone Therapies focusing on psychedelic research for mental health. Dr. Patel brings to NIAID her experience in clinical coordination and training of staff on protocols, source creation, monitoring, and safety assessments.

Selected Funding Opportunities

NIAID

RFA-AI-24-041: Novel Approaches for Radiation Biodosimetry and Medical Countermeasure Development (R21, Clinical Trial Not Allowed). The purpose of this notice of funding opportunity (NOFO) is to support exploratory and conceptual research projects in radiation research focused on medical countermeasures, biodosimetry, and animal model development to diagnose/mitigate/treat injuries arising from radiation exposure sustained during a radiation mass casualty incident. This NOFO will support development of preliminary data to help advance high-risk, high-reward projects needed for a

robust early product development pipeline that can lead to the advancement of much-needed radiation-exposure related tools and products.

Division Activities

Radiation and Nuclear Countermeasures Program

The NIAID/RNCP Biodosimetry Blue Ribbon Panel. On May 13 and 14, 2024, the RNCP convened an in-person Blue Ribbon Panel in Rockville, Maryland, comprised of radiation biodosimetry subject matter experts and thought leaders and experts from government, academia, and private industry. The goal was to inform future programmatic directions and to draft a strategic research agenda for the RNCP Biodosimetry Program. Discussions focused on 1) the status of development of assays or devices for the purpose of triage, assessing absorbed dose, or predicting health outcomes of acute or delayed injuries resulting from radiation exposure during a public health emergency, and 2) the need for a North American Biodosimetry Assessment Networking Group (BANG). This workshop provided opportunities to discuss progress and challenges related to this area of research so that all stakeholders can cohesively move the development of these approaches toward future regulatory approvals. Input from panel members is currently being incorporated into the final Strategic Plan document.

NIAID/BARDA Radiation Medical Countermeasures Radiation Portfolio Update Meeting. On May 23, 2024, a hybrid meeting was held in Washington, DC, between the RNCP and the BARDA Radiological Countermeasures teams. Eight RNCP and 10 BARDA team members attended the meeting to specifically discuss recently awarded RNCP product development contracts and grants. The purpose of these semi-annual meetings is to provide routine programmatic transparency, ensure that the funded research programs are aligned across both HHS agencies, and share information on potential transitions of promising candidates.

U01 Development of Microbiome-Related Approaches for Diagnosis/Mitigation/Treatment of Radiation Injuries Kickoff Meeting. On May 31, 2024, the NIAID/RNCP held (in a virtual format) its first annual meeting for this consortium of four awards issued in 2023. Topics covered during the meeting focused on elucidating the mechanisms of radiation injury in the gastrointestinal tract in rodent models and harnessing the power of the microbiome to develop countermeasures to mitigate radiation injury. It is intended that these 5-year awards will pave the way for future investigational new drug (IND)-enabling studies in large animal models for eventual approval by the FDA to treat radiation-induced GI injury. Attendees included government program staff, as well as members of the awardee institution laboratories.

U01 Novel Bioassay and Biodosimetry Devices Annual Meeting. On June 27, 2024, an in-person consortium meeting was held in Rockville, Maryland, by the NIAID/RNCP. The objectives of the meeting were to allow the investigators to meet in a forum that allowed for creative interactions and to provide background on their planned projects and progress since being awarded in 2020. The meeting enabled the exchange of ideas and refinement of research, while providing a framework for future collaborations among the investigators. The meeting was attended by the principal investigators, NIAID staff, regulatory members, and other government agencies (over 45 attendees). Plans were developed for collaborations and regulatory meetings within the consortium for the upcoming year.

Allergy, Asthma, and Airway Biology Branch

Alpha Gal Syndrome Investigator Meeting. On July 12, 2024, a virtual meeting was held by the NIAID/DAIT/AAABB for investigators funded to study Alpha Gal Syndrome. Representatives from seven research groups provided updates on their research and discussed potential collaborations, including a planned future clinical trial.

Basic Immunology Branch

Joint Adjuvant Comparison Programs Annual Meeting (hybrid). On June 5 and 6, 2024, the first joint meeting for the *Adjuvant Comparison and Characterization (ACC)* and *Advancing Vaccine Adjuvant Research for Tuberculosis (AVAR-T)* programs was held in Rockville, Maryland. The ACC program supports the systematic side-by-side comparison of immune responses induced by different adjuvants in combination with clinically relevant vaccine/antigen platforms. The AVAR-T program supports the systematic side-by-side comparison of immune responses induced by different adjuvants combined with *Mycobacterium tuberculosis* immunogens to facilitate the identification of novel tuberculosis vaccine candidates for clinical development and identification of potential correlates of protection. Both programs include integration of the data across species to establish immunological profiles in different mouse and nonhuman primate animal models and human cells. The contractors presented research progress and challenges, highlighted collaborations between the programs and with external investigators, and discussed approaches to leverage the knowledge gained. The ImmPort team presented information about the data repository and available tools. Attendees included NIH staff, IP-holders of adjuvants used by the contractors, and external stakeholders from the adjuvant community, including the Japan Agency for Medical Research and Development (AMED), Bill & Melinda Gates Foundations (BMGF), Coalition for Epidemic Preparedness Innovations (CEPI), and Defense Advanced Research Projects Agency (DARPA).

Cohort Studies to Improve Our Understanding of Influenza Immunity, Vaccine Response and Effectiveness in Older Adults. On July 9, 2024, the annual program meeting was held in Rockville, Maryland. This program is a partnership between DAIT and DMID. The goal of the program is to determine how changes in immune function in individuals 65 years of age and older impact protective immunity. Investigators supported by this program are characterizing immune responses in existing or new longitudinal cohorts and examining the role of pre-existing immunity to influenza generated by a history of natural infections and/or vaccinations. Three institutions received awards under this initiative: Jackson Laboratory (Duygu Ucar and George Kuchel), Dana-Farber Cancer Institute (Wayne Marasco), and Johns Hopkins University (Sean Leng). Awardees presented their research progress from each of their cohorts. The meeting provided a forum for researchers to exchange ideas and to discuss potential collaborations.

Animal Models for Basic and Applied Studies of Respiratory Viruses. On July 11 and 12, 2024, a hybrid workshop was held in Rockville, Maryland, to discuss the use of animal models for respiratory disease research. This workshop was developed by DMID and DAIT. The speakers presented their recent results using different animal models to understand the transmission, pathogenesis, and host immune responses caused by respiratory viruses. At the end of the meeting, speakers and NIAID extramural staff discussed the availability of resources, the further development of small animal models, as well as priorities for the development of novel reagents. Joy Liu, the Program Offer managing the DAIT Reagent Development SBIR program for non-mammalian and under-presented animal models, described the availability of novel antibodies for these animal models. The workshop provided a platform for building collaborations, sharing information, and leveraging resources.

Impact of Diet on Mucosal Immunity and Immune-mediated Digestive Diseases Workshop. On August 21 and 22, 2024, NIAID and the Office of Nutrition Research (Office of the Director, NIH), in collaboration with many other institutes and offices at NIH, held a workshop focused on identification of critical dietary factors that regulate the development and function of the gastrointestinal immune system. Topics covered in this workshop included the impact of early exposures, including diet (e.g., human milk and infant formula) and nutrition, on mucosal homeostasis, gut mucosal immune development, and the functional interactions of these biological systems with the gut microbiome, as well as their relationship to the development of digestive and immune-mediated diseases (e.g., inflammatory bowel disease and food allergies). Sessions centered on examining the current state of the science in the field, identifying

knowledge gaps, and proposing steps needed to address these gaps related to the role of nutrition in maintaining or altering intestinal homeostasis during health and disease states across the lifespan.

Molecular Mechanisms of Combination Adjuvants (MMCA) Annual Meeting. On September 5 and 6, 2024, the annual meeting of the Molecular Mechanisms of Combination Adjuvants program took place in Rockville, Maryland. Participating investigators presented updates on research findings from the first 3 years of their 5-year U01 grants. Presenters spoke about novel findings relating to mechanisms of adjuvanticity in vaccines containing multiple adjuvants. The meeting featured a robust discussion of a wide range of combination adjuvants, including elucidation of novel pathways involved in adjuvantation, cutting-edge analysis techniques, and unique vaccine delivery platforms. Investigators discussed next steps for their projects and how to proceed with developing their adjuvant combinations.

Transplantation Branch

HLA and KIR Region Genomics in Immune-Mediated Diseases Program. On July 11, 2024, a virtual annual steering committee meeting for the HLA and KIR Region Genomics in Immune-Mediated Diseases Cooperative Agreement program (HLA and KIR RGC), consisting of five U01awards, was held in Rockville, Maryland. This program supports studies that identify and characterize associations between polymorphisms in human leukocyte antigen (HLA) and killer cell immunoglobulin-like receptor (KIR) genetic regions and immune-mediated disease risk, progression and/or severity, and outcomes following organ, tissue, and cell transplantation. HLA and KIR regions contain high degrees of polymorphism between individuals and among racial and ethnic groups. Current projects are studying the role of HLA and KIR polymorphism in: 1) Asthma in African American cohorts; 2) Central nervous system paraneoplastic syndromes and related neuroimmune conditions; 3) Hematopoietic stem cells and cord blood transplantation; 4) Primary nephrotic syndrome and post-kidney transplant recurrence; and 5) Solid organ transplantation, including heart, kidney, liver, and lung allografts. The program continues to generate high quality, publicly accessible HLA- and KIR- genomic datasets and associated phenotypic data. The meeting was attended by the consortium members, extramural NIAID staff, and co-funding institutes, National Cancer Institute and National Institute of Neurological Disorders and Stroke. Presenters discussed project updates and scientific progress, areas of potential synergy, and the availability and limitations in immunogenetics analytical tools and data sharing methods.

Autoimmunity and Mucosal Immunology Branch

Autoimmunity Centers of Excellence (ACE) FY24-FY28 Kickoff Meeting. From July 15 to 17, 2024, the Investigator Kickoff meeting for the 2024 Autoimmunity Centers of Excellence (ACE) awards was held in Rockville. The goal of ACE is to foster collaboration between basic and clinical researchers, leading to better understanding of both the etiologies of autoimmune diseases and mechanisms of action for therapeutic interventions, ultimately leading to more efficient diagnosis and more effective treatments. In FY 2024, five new Basic ACE U19 cooperative agreements were awarded to Drs. Ignacio Sanz (Emory University), Virginia Pascual (Weill Cornell Medical College), Maureen Su (University of California Los Angeles), Shiv Pillai (Massachusetts General Hospital), and Drs. Betty Diamond and Anne Davidson of Feinstein Institute for Medical Research. Three new Clinical ACE UM1 awards were issued to Drs. Judith James (Oklahoma Medical Research Foundation), John Stone (Massachusetts General Hospital), and Julie Paik (Johns Hopkins University). On July 15, Clinical ACE investigators worked with AMIB clinical staff to initiate development of final clinical trial protocols. On July 16 and 17, investigators from both Clinical and Basic ACEs convened to provide overviews of their research plans for the new ACE awards and to initiate development of collaborative research across the network. Also attending was Dr. Victoria Shanmugam, Inaugural Director of the newly formed NIH Office of Autoimmune Disease Research, Office of Research for Women's Health (OADR-ORWH), which provided co-funding for five awards in FY 2024.

Development of Sample Sparing Assays for Immune Monitoring Annual Investigators Meeting. On May 30 and 31, 2024, Sample Sparing Assays investigators met in Rockville, Maryland, to present their research progress as they enter the final year of the current 5-year program. This program supports the development of assays that use extremely small sample volumes and are adaptable to high throughput set ups. The goal of the program is to develop and expand the use of these assays across DAIT and NIAID-funded research and beyond. This program has increased accessibility by leveraging sample collection approaches that patients can perform at home and by developing assays that use portable equipment useful in field work. Major accomplishments include the development of a variety of different proteomic and viromic assays, micro scale assays to measure immune cell function and antibody reactivity and specificity, serological assays to support arbovirus diagnosis and surveillance, and assays to assess gene regulatory profiling.

FY 2026 Research Concept Clearances Presented to Division of Advisory Council

The subcommittee endorsed and unanimously approved the following six Research Concept Clearances:

Asthma and Allergic Diseases Cooperative Research Centers (U19, Clinical Trial Optional). This initiative aims to investigate mechanisms underlying the onset and progression of diseases of interest, including asthma, rhinitis (allergic and non-allergic), chronic rhinosinusitis, atopic dermatitis, food allergy, and drug allergy.

CIVICs Data Management and Coordinating Center. The purpose of this renewal solicitation is to provide data management and program coordination services to the CIVICs network (Vaccine Centers and related Cores) in the areas of preclinical data and meta-data management services (studies include animal models and nonclinical trial human subjects research); development of harmonized data standards; and coordination of CIVICs network-related activities including cross-network communication and collaboration, CIVICs-wide meeting and webinar management, and tracking and distribution of CIVICs-generated reagents and other resources to CIVICs investigators and the broader research community.

Molecular Mechanisms of Combination Adjuvants (MMCA) (R01, Clinical Trial Not Allowed). This initiative supports studies on the mechanism of action of a combination of two or more vaccine adjuvants (combination adjuvant).

NIAID DAIT Clinical Products Center (CPC). This initiative will provide pharmacy and pharmaceutical oversight of national and international NIAID/DAIT-supported clinical trials as well as other NIH-funded clinical trials on an as-needed basis, to ensure study product integrity, participant safety, and pharmacy and pharmaceutical regulatory compliance.

Nonhuman Primate Reagent Resource (U24, Clinical Trial Not Allowed). This initiative will continue to provide support for a nonhuman primate (NHP) reagent resource that enables rigorous and reproducible research in NHP models through the development, production, and distribution of key NHP-specific immunologic reagents that are not commercially available or, if commercially available, are not optimized for use in NHPs.

Mucosal Immunology Studies Team (MIST) (U01, Clinical Trial Not Allowed). This initiative will support innovative basic research projects that focus on immune mechanisms and immune regulation at mucosal surfaces of the respiratory, gastrointestinal, and urogenital tracts.

V. Report of the Microbiology and Infectious Diseases Subcommittee–Emily Erbelding, M.D., M.P.H., Director, DMID

Dr. Emily Erbelding, Director of the Division of Microbiology and Infectious Diseases (DMID), chaired the NIAID Microbiology and Infectious Diseases Council Subcommittee meeting on September 9, 2024. She provided a DMID personnel update, recognizing new staff appointments made in the Division since the last Council meeting, including: Genevieve Holzapfel, Annie Bridwell, Feorillo Galivo, and Sushma Bhosle, who have all joined the Virology Branch; Quique Meijia–Galvis who recently transferred from the DMID Office of Clinical Research Affairs to the DMID Office of Clinical Research Resources; and Yunus Abdul, who joined the Office of Biodefense, Research Resources, and Translational Research.

Following staff introductions, Dr. Erbelding provided a report on recent activities of note:

- **Lassa Fever Virus Vaccine Protects NHPs from Lethal Disease –** In this DMID-supported study, nonhuman primates (NHPs) were administered a two-dose regimen of a candidate Lassa Fever Virus (LASV) vaccine or an irrelevant Rabies Virus-based vaccine to serve as a negative control. NHPs immunized with the LASV candidate vaccine developed strong humoral responses to LASV. Upon challenge with LASV, NHPs vaccinated with the LASV candidate vaccine survived to the study endpoint, whereas NHPs in the control group did not. This study demonstrates that the LASV candidate vaccine is a worthy candidate for continued development.
- **New Awards to Simplify Syphilis Testing Process** – DMID recently made 10 new grant awards focused on the development of improved diagnostic tools for congenital and adult syphilis.
- **Clinical trial to evaluate the safety of an investigational mAb (EV68-228-N) to treat EV-D68** – DMID is supporting a Phase 1 clinical trial being conducted through the DMID Infectious Disease Clinical Research Consortium (IDCRC) program to evaluate the safety of the investigational monoclonal antibody, EV68-228-N, how long it lasts in the body, and the most effective dose. The trial is being conducted in collaboration with academic medical centers across the United States through the IDCRC, which includes the NIAID-funded Vaccine and Treatment Evaluation Units (VTEUs).

FY 2026 DMID Concepts Presented for Clearance

The following concepts were presented to the Subcommittee:

Broad Spectrum Products Against Multiple Neurotoxin Botulinum Serotypes – This concept aims to stimulate discovery of novel products for treating Botulinum Neurotoxin (BoNT) toxicity with improved or innovative new characteristics compared to the currently FDA-approved treatment BAT® [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) - (Equine)]. The candidate therapeutics should be efficacious against the seven most clinically relevant BoNT serotypes (BoNT A-G). The Subcommittee expressed support for the concept and acknowledged the need to develop products for treating BoNT intoxication, including products that could reverse BoNT neuronal intoxication. Subcommittee members recognized the importance of developing the next generation of BoNT countermeasures to address a growing national security preparedness concern and agreed with the proposed plan to support translational research, including the generation of platform-agnostic new antitoxin agents, which could include biologics or drugs.

Rational Design of Vaccines Against Hepatitis C Virus (HCV) – This concept proposes to support translational research including the discovery and optimization of broadly protective vaccines for HCV, evaluation of immunogenicity in animal models, and other IND-enabling studies to support advancement of vaccine candidates into clinical development. The Subcommittee recognized the importance of developing a vaccine to prevent acute and chronic HCV. They agreed with the approach to continue some

of the objectives from the current iteration of the concept for this proposed renewal, but also suggested DMID consider an increased focus on the advancement of vaccine candidates towards clinical development. For example, they recommended decoupling animal model development and vaccine development and focusing on advancing HCV candidates based on the elicitation of the targeted immune response. One Subcommittee member discussed the importance of identifying the target populations and genotype breadth early in vaccine candidate development. Another Subcommittee member asked whether cross-protection against multiple genotypes is possible or if different vaccines may be needed for different genotypes. Program responded that cross-genotype protection is complex and while more still needs to be elucidated, a vaccine that is able to protect against some of the more prevalent genotypes could still have an impact.

***In Vitro* Assessments for Antimicrobial Activity** – This concept proposes to renew a longstanding DMID Preclinical Services program to conduct screening of candidate therapeutics for antimicrobial activity against a variety of pathogens, including newly emerged, highly pathogenic and/or drug-resistant strains. The Subcommittee recognized the clear and immediate programmatic value of the program, which provides broad *in vitro* screening capability, production of well-characterized challenge material, and development of methods to grow difficult-to-culture pathogens in support of countermeasure development for human infectious diseases. Subcommittee members noted that the antifungal testing and the library screening efforts are of particular importance and worthy of increased emphasis. The Subcommittee was interested in the metrics used to determine success of the program, the decision-making surrounding progressing products to further testing, and the types of sponsors that request services, which were shared during the presentation. The Subcommittee was very supportive of the use of the indefinite delivery/indefinite quantity (IDIQ) contract mechanism, observing that it offers flexibility and rapid response, which are essential to address public health emergencies and to permit efficient reporting of results for product developers dependent on making timely go/no-go decisions.

Impact of Initial Influenza Exposure on Immunity in Infants – This renewal concept proposes to establish, follow, and characterize longitudinal cohorts of infants and/or mother-infant dyads to determine how initial and repeated natural influenza infections and/or vaccinations shape infant and childhood immunity to future influenza exposures. The Subcommittee was highly supportive of this cohort study because it stands to provide foundational information to improve immune health and vaccine efficacy. They agreed on the importance of understanding early immune responses to influenza exposure in neonates and infants, and noted the research was likely to be more broadly relevant to other mucosal pathogens as well. Subcommittee members also stated that collecting samples from both infected and vaccinated cohort enrollees would provide the benefit of comparing outcomes to different types of influenza exposures. Two Subcommittee members asked for clarification on the current awards' timeline and if the renewal initiative would be an open or closed competition. The presentation before the Subcommittee members provided more detail on the timeline of the current awards and stressed that this will be an open competition to allow for the establishment of new cohorts or continuation of ongoing cohorts. One Subcommittee member remarked in the meeting that given how much research has been done on influenza there is surprisingly little known about the influenza imprinting response in infant cohorts, which emphasized the need for this initiative to continue.

Collaborative Influenza Vaccine Innovation Centers (CIVICs) – This concept proposes to renew support for a consortium of collaborative centers that will apply innovative approaches to advance the development of influenza vaccines that provide robust, durable, broadly protective mucosal and systemic immunity, as well as the improvement of the immunogenicity, breadth, and enhanced durability of licensed seasonal influenza vaccines. The Subcommittee expressed support for the continuation of this program, recognizing the importance of advancing the development of more durable, broadly protective, and longer-lasting influenza vaccines. One of the Subcommittee members asked how this program differs from DMID's Vaccine and Treatment Evaluation Units (VTEUs). Program clarified that the VTEUs are a

separate NIAID-supported resource for conducting clinical trials of vaccines and treatments. Program also addressed a question concerning required technology readiness level for products supported under the program and stated that investigators interested in submitting a proposal to this program must focus on vaccines that either need or have completed process development that will allow for Good Manufacturing Practice (GMP) release within a year of the contract initiation. Finally, program noted that, in the next iteration of this program, NIAID will support more discovery and development efforts to increase the number of novel vaccine candidates moving into preclinical development.

Clinical Research Operations Core – This concept proposes to provide operational support, management, and oversight for DMID clinical research activities, and manage and oversee a range of activities to advance clinical research priorities for DMID, including protocol development; site selection from across DMID's clinical infrastructure; budget development and oversight; management of end-to-end processes for study implementation; oversight of laboratory services and specimen management; and coordination among stakeholders to ensure timely dissemination of results. The Subcommittee recognized the importance of the proposed concept. They understood that to meet DMID's scientific priorities and achieve successful clinical trial outcomes to address critical public health needs, DMID's clinical trial infrastructure needs the flexibility to support operations and sites in order to respond rapidly during public health emergencies. Two Subcommittee members noted that this concept is in line with the lessons learned from previous clinical trials and pandemic response efforts, particularly with DMID's COVID-19 pandemic response efforts. These examples underscored the need for a Clinical Research Operations Core to effectively respond to future needs.

VI. Joint Meeting of the AIDS Subcommittee and AIDS Research Advisory Committee (ARAC)– Carl Dieffenbach, Ph.D., Director, DAIDS

Dr. Abrams welcomed everyone to the hybrid meeting. Dr. Abrams called for the Committee vote on approval of the minutes of the June 3, 2024 hybrid ARAC meeting. The minutes were approved.

Director's Report

Carl Dieffenbach, Ph.D.; Director, Division of AIDS (DAIDS)

Dr. Dieffenbach thanked Drs. Reuben Harris and Keith Jerome for their service on the ARAC. He announced that Dr. César Boggiano has been selected as the Director of the DAIDS Vaccine Research Program (VRP). He also thanked Dr. Jim Lane for his leadership in serving as the Acting VRP Director for the past year.

At the end of September 2024, Dr. Hugh Auchincloss will retire from federal service in his role as the Deputy Director of NIAID.

The NIH Director, Dr. Monica Bertagnolli, recently announced that Dr. Geri Donenberg has been selected as the new NIH Associate Director for AIDS Research and Director of the NIH Office of AIDS Research (OAR).

Budget Update

The President released the FY 2025 budget on March 11. The House released their version on July 9 and the Senate released their version on August 1. The FY 2025 House funding for NIAID has split into two ICs: National Institute on Infectious Diseases (NIID) for $3.3B and National Institute on the Immune System and Arthritis (NIISA) for $3.3B.

NIAID is scheduled on the House side to receive a very small increase and on the Senate side, should it be enacted, about a 2 percent increase. We anticipate a Continuing Resolution beginning on October 1, 2024. Interim paylines for FY 2025 are currently set at 8th percentile for established investigators and 10th percentile for early-stage investigators–hopefully these will improve for FY 2025 if and when we receive a budget.

Scientific Updates

The antiretroviral drug, maraviroc, improves kidney function after transplant in people with HIV. Maraviroc suppresses the activity of the CCR5 receptor – a collection of proteins on the surface of certain immune cells – and was associated with better renal function in kidney transplant recipients with HIV compared to people who took a placebo in a randomized trial. Study participants taking the drug maraviroc also experienced lower rates of transplant rejection than those taking placebo, but the difference was not statistically significant due to lower-than-expected rejection rates across the entire study population.

Long-acting injectable cabotegravir (CAB-LA) is safe and well tolerated as HIV pre-exposure prophylaxis (PrEP) before and during pregnancy in the follow-up phase of a global study among cisgender women. The analysis of outcomes from more than 300 pregnancies and infants were presented in July at the 2024 International AIDS Conference in Munich.

NIAID Strategic Plan FY 2025-2029

NIAID is currently updating the strategic plan for FY 2025-2029 to guide NIAID's priorities over the next 5 years. There are five research priorities: 1) advance foundational research on the immune system, host-pathogen interactions, and pathogen biology; 2) apply foundational knowledge of the complex interactions between microbes and the immune system to develop and test medical countermeasures against known infectious diseases (non-HIV/AIDS); 3) apply knowledge of HIV/AIDS to reduce HIV incidence through the development of safe and effective prevention, treatment, and cure strategies; 4) apply knowledge of basic immunology to develop and enhance intervention strategies for asthma, allergic, and immune-mediated diseases, and transplantation; and 5) support innovative research efforts to prepare for and respond to nationally or internationally significant biological incidents affecting public health.

Later in this meeting, we will hear more from Dr. Nicholas Bushar on the NIAID strategic plan, summarizing feedback in response to the Request for Information (RFI) earlier this year.

DAIDS FY 2026 Concept Presented – ARAC Approval Requested

One proposed FY 2026 DAIDS research grant concept was presented for ARAC approval.

Translational Approaches to Developing New TB Meningitis (TBM) Drug Regimens in People Living with and without HIV
Robert Mahon, Ph.D., DAIDS, Therapeutics Research Program

The objective of this new grant/cooperative agreement concept is to advance research to develop novel treatment strategies that address TB meningitis (TBM)-specific needs, as well as to ensure recent successes in pulmonary TB treatment are appropriately adapted to advance TBM treatment in people living with and without HIV. TBM is largely the result of a dysregulated immune response. Thus, the initiative will also support research to elucidate the role of inflammation and the effect of inflammatory

damage on drug penetration of the blood-brain barrier and therapeutically target key inflammatory pathways to improve treatment outcomes.

This initiative will support the establishment of a collaborative network of integrated, multidisciplinary research teams that will utilize a combination of laboratory and computational methods with animal and human samples to improve our ability to diagnose and treat TBM. It is expected that the network will include a combination of expertise in clinical research including pediatrics, animal models, computational modeling, diagnostics, pharmacology, and data and statistical management. Applications are expected to include individual preclinical, clinical (though no clinical trials), and translational projects and will require the inclusion of at least one component involving the study of TBM in the context of HIV.

Ballot Voting Outcome

The TBM concept was unanimously approved by the voting members of the Committee.

NIH Office of AIDS Research Advisory Council (OARAC) Briefing
Anne M. Neilan, M.D., MPH

Dr. Neilan presented a report-out of the OARAC meeting held on June 20, 2024.

The agenda included a report from Acting OAR Director Dr. Finzi; updates on the NIH Strategic Plan for HIV and HIV-Related Research for 2026 to 2030; a presentation by White House Office of National AIDS Policy (ONAP) Director Francisco Ruiz; two presentations on Perinatal HIV Research and Response; as well as updates from the ARAC, the NIH HIV/AIDS Executive Committee (NAEC), and all of the HIV Clinical Practice Guidelines Groups.

In her updates, Dr. Finzi previewed the Fiscal Year 2026 NIH HIV/AIDS Professional Judgment (PJ) Budget. The PJ Budget estimates the amount of funding that would be needed to fully pursue the goals of the NIH HIV/AIDS research agenda above current funding levels and it is structured to align with the Strategic Goals. Dr. Finzi also highlighted several recent and upcoming OAR engagements.

OAR Senior Policy Advisor Dr. Rachel Anderson reported on the process to develop the NIH Strategic Plan for HIV and HIV-Related Research for 2026 to 2030, which is expected to launch during the summer of 2025. The new plan proposes a framework of three broad research goals and one capacity goal with corresponding objectives: Goal 1: Enhance discovery and advance HIV science through fundamental research; Goal 2: Advance the development and assessment of novel interventions for HIV prevention, treatment, and cure; Goal 3: Optimize public health impact of HIV discoveries through translation, dissemination, and implementation of research findings; and Goal 4: Build research workforce and infrastructure capacity to enhance sustainability of HIV scientific discovery.

In terms of next steps, three OAR task forces were formed in the summer of 2024 based on functional science areas - basic and preclinical research, clinical and intervention research, and BSSR. The task forces will be charged with developing recommendations for funding priorities that will be shared at the next OARAC meeting in October.

Mr. Francisco Ruiz, named ONAP Director in April 2024, discussed how ONAP's values—equity, accountability, innovation, inclusivity, accessibility, adaptability, and collaboration—serve as a platform and direction for the Office's efforts to implement the *National HIV/AIDS Strategy for the United States 2022–2025*. Mr. Ruiz highlighted ONAP's 2024 priorities—to center science and modernize policies to ensure they are based on current scientific knowledge; to accelerate progress in the federal HIV response; and to advance equity and access.

Mr. Ruiz ended his remarks with a call to action, encouraging OARAC members and meeting attendees to recommit to efforts to end the HIV epidemic.

Presentations followed on issues related to perinatal HIV research and response. The OARAC meeting closed with updates from the ARAC provided by Dr. Elaine Abrams, from the NIH AIDS Executive Committee (NAEC), as well as updates from the HIV Clinical Guidelines Working Groups of OARAC which develop the HIV clinical practice guidelines that inform clinical practice in the United States and around the world.

Update on the NIAID Strategic Plan: Responses to the Request for Information (RFI)
Nicholas Bushar, Ph.D.

The previous NIAID Strategic Plan was last updated in 2017, and so with changes in the global landscape of infectious diseases since then, as well as the introduction of a new NIAID Director, it is time to engage in forward-thinking for an update. The update to the NIAID Strategic Plan is both an organizational exercise and an opportunity to partner with the public and obtain input to create the plan moving forward. Through an RFI earlier this year, NIAID invited public feedback on NIAID's proposed priorities. The RFI was open for 90 days from February 26 through May 27. A total of 63 very thoughtful and well-articulated responses (about 200 pages worth) were received, the majority from individual researchers, and societies and advocacy organizations. Nearly half (30) of the responses included comments directly related to HIV/AIDS research.

NIAID has five Institute Priorities and the ARAC discussion for today will focus on Priority #3: Advance and apply knowledge of HIV/AIDS to end the HIV epidemic through the development of safe and effective prevention, treatment, and cure strategies. The objectives within Priority #3 are: advance HIV prevention strategies; develop and assess novel HIV treatment approaches; prevent and treat co-infections and comorbidities associated with HIV; and foster community involvement in all stages of research planning and implementation.

Dr. Bushar summarized the main four RFI topic areas, listed here, that we received and then the Committee engaged in discussion: 1) expanding HIV/AIDS research; 2) comorbidities and co-infections; 3) implementation science, behavioral and social research; and 4) health disparities, inclusion, women's health, and global health.

The RFI input will be incorporated into the plan where appropriate. The goal is to publish the NIAID Strategic Plan next year in the first quarter of 2025.

Renewal of the HIV Clinical Trials Networks
Carl Dieffenbach, Ph.D.

Dr. Dieffenbach provided a status report, including timeline, on the upcoming recompetition of the NIH HIV/AIDS Clinical Trials Networks for FY 2028. Every 7 years, NIH competitively reviews its HIV Network funding, addressing significant changes in research priorities. Three years remain in the current cycle; the next 7 years will begin in December 2027. With the upcoming FY 2028 renewal, the goal is to determine the future need, focus, and structure of the HIV clinical trials networks through 2034. We are currently focused on obtaining written feedback and analyzing the input from stakeholders (investigators, community, etc.), and community engagement such as webinars, blog posts on selected topics, and town halls. NIH staff has participated in all of the annual Network meetings this year.

The overall Network structure was described. We will maintain the four Network Leadership Groups, and the overarching theme of this renewal will be innovation and collaboration. This past cycle, the

groundbreaking studies, such as REPRIEVE, often sprouted from collaborations. Across all areas of HIV science, further progress will be expedited through collaboration to address the highest priority questions. We will enhance dialogue across the NIH on the research that is going to be really critical to help improve the health of people living with HIV.

We will plan for what can be accomplished prior to the end of the current grant cycle. We will assess what adjustments in structure and scientific direction should be made to accelerate the pace of discovery, and how we should build implementation research needs into our plans.

Dr. Dieffenbach detailed the challenges and future directions of the functional HIV research areas: HIV Prevention, HIV Vaccines, HIV Therapeutics, and HIV Cure.

The next ARAC meeting on January 27, 2025, will focus on the FY 2028 Network Recompetition. DAIDS leadership will present seven FY 2028 RFAs for ARAC concept approval: four Network Leadership and Operations Centers, Laboratory Center (LC), Statistical and Data Management Center (SDMC), and Clinical Trials Units (CTUs).

VII. Adjournment

The meeting of the Council adjourned at 4:10 p.m., on Monday, September 9, 2024.

We do hereby certify that, to the best of our knowledge, the foregoing minutes are accurate and complete.

_ S _ **11/18/2024**
Jeanne Marrazzo, M.D., M.P.H. Date
Chair, National Advisory Allergy
and Infectious Diseases Council
Director, National Institute of Allergy
and Infectious Diseases

_ S _ **11/18/2024**
Kelly Poe, Ph.D. Date
Executive Secretary
National Advisory Allergy and Infectious
Diseases Council
Director, Division of Extramural Activities
National Institute of Allergy and Infectious
Diseases

Council will formally consider these minutes at its next meeting; any corrections or notations will be incorporated in the minutes of that meeting.