NATIONAL INSTITUTES OF HEALTH

NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL

MINUTES OF MEETING

September 17, 2007

The 157th meeting of the National Advisory Allergy and Infectious Diseases Council (NAAIDC) was convened at 10:30 a.m. on Monday, September 17, 2007, in Conference Room E1/E2, Building 45, National Institutes of Health. Dr. Anthony S. Fauci, 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 11:40 a.m. and from 1:00 p.m. to 5:00 p.m. The meeting was closed to the public from 8:30 a.m. to 10:00 a.m. and from 11:40 a.m. to 12:00 p.m. for review and consideration of individual grant applications. Notice of the meeting was published in the *Federal Register.*

Council Members Present:

Dr. Barbara Baird
Dr. Robert Brooks
Dr. Stanley Chapman
Dr. Satya Dandekar
Dr. J. Brooks Jackson
Dr. Sharon Kiely
Dr. Martin Myers
Dr. Shelley Payne
Dr. Martin Rosenberg
Dr. Marc Rothenberg
Dr. Ruth Ruprecht
Dr. Gary Schoolnik
Dr. Nathan Thielman
Dr. David Wilkes

***Ex Officio* Members Present:**

Dr. Mitchell Cohen
Dr. Anthony Fauci
Major General Eric Schoomaker
Dr. Ronald Valdiserri

Council Members Absent:

Dr. Kathryn Edwards
Dr. Richard Insel
Dr. Megan Sykes
Dr. Gail Wertz

***Ad Hoc* Members:**

Dr. Terence Dermody
Dr. Hans Ochs
Dr. Jordan Orange

NIAID Senior Staff:

Dr. Hugh Auchincloss
Dr. Carl Dieffenbach
Dr. Carole Heilman
Dr. Marvin Kalt
Dr. Cliff Lane
Dr. Daniel Rotrosen

I. REVIEW OF GRANT APPLICATIONS

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

Funding Actions: The Council reviewed 2,360 research and training applications with primary assignment to NIAID for a requested amount of $520,670,197 in first-year direct costs and recommended approval of 418 applications for $64,220,543 in first-year direct costs. Three Method to Extend Research in Time (MERIT) awards were recommended for approval.

II. REMARKS OF THE DIRECTOR, NIAID - Anthony S. Fauci, M.D.

Dr. Fauci opened the Council session by welcoming visitors to the meeting and noting that Drs. Edwards, Insel, Sykes, and Wertz, a retiring member, would be absent. He introduced three *ad hoc* Council members: Dr. Terence Dermody, Vanderbilt University School of Medicine; Dr. Hans Ochs, University of Washington School of Medicine; and Dr. Jordan Orange, Children's Hospital of Philadelphia.

Dr. Fauci acknowledged the contributions of four other retiring members, Dr. Stanley Chapman, Dr. Ruth Ruprecht, Dr. Nathan Thielman, and Dr. Brooks Jackson, and presented them with plaques.

Since Dr. Kathryn Zoon could not attend the Council meeting, she provided a written report about the Division of Intramural Research to the Council members.

Consideration of Minutes of Previous Meeting

The minutes of the May 21, 2007, meeting were considered and approved as written.

Staff and Organizational Changes

Since the last Council meeting, two staff members in the Division of Microbiology and Infectious Diseases have been promoted to new positions. Dr. Irene Glowinski is now the deputy director of the Division, and Dr. Richard Johnson is the new chief of the Office of Regulatory Affairs.

Several other staff and organizational changes have taken place since the last Council meeting. In the Division of AIDS, Judy Brooks is the new chief of Policy Training in the Quality Assurance Branch, and Dr. Lisa Dawson is the new chief of the Human Subjects Protection Branch.

Gwen Shinko has been selected as chief of the Office of Administrative Services, Intramural Administrative Management Branch. In the Office of Workforce Effectiveness and Resources, Lisa Douek joined NIAID as chief of the Workforce Retention and Development Branch. Judy Quasney has been appointed director, Office of Research Operations within the Office of Management Operations.

Tributes and Awards

Dr. Fauci remembered two friends and colleagues who recently passed away, Dr. Stephen Straus and Anthony Itteilag. Both made significant contributions to the Institute and will be missed.

Several NIAID scientists were recognized for recent honors they have received. Dr. Tom Nutman received the Physician Researcher of the Year award from the Physicians Professional Advisory

Committee to the Surgeon General. Three NIAID intramural scientists were named NIH senior investigators: Bernard Moss, Robert Purcell, and William Paul.

Budget Update

The President's FY 2008 budget request for NIH is $28.8 billion, a 0.8 percent increase over the FY 2007 budget. NIAID's allocation is approximately $4.6 billion, an increase of $210 million over FY 2007. Of the $210 million, $201 million is slated for the Global Fund to fight AIDS, TB, and malaria. After accounting for the Global Fund increase, the actual increase for the Institute is $9 million or 0.2 percent.

The House and Senate have prepared appropriations bills for FY 2008 which propose similar budgets. A significant amount of the proposed increase would go to the NIH Office of the Director to support the Common Fund which is used to support NIH Roadmap initiatives. Both bills contain provisions that the administration finds objectionable, and the President says he will veto them.

Until the FY 2008 appropriations bills are signed, NIAID will be operating under a continuing resolution.

Legislative Update

In May, Dr. Fauci testified before the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies regarding the FY 2008 NIH budget. At the beginning of June before the same Subcommittee, Dr. Fauci and CDC Director Dr. Julie Gerberding testified about the burden of tuberculosis and other drug resistant infections.

Later in June, Dr. Zerhouni and Dr. Fauci met with House Speaker Nancy Pelosi to update her on various aspects of NIH research.

Dr. Fauci met with First Lady Laura Bush twice: the first time to participate in a round table discussion about voluntary HIV testing and the second to brief her and her staff on HIV/AIDS, malaria, and other diseases of global health importance.

Dr. Fauci thanked NIAID staff for their assistance with congressional briefings. Dr. Lee Hall participated in a briefing on "Malaria: Strategies for Prevention," and Dr. Roland Levandowski participated in a briefing on pandemic influenza.

Other Information Items

NIAID is updating its strategic plan. The plan sets broad strategic goals grouped into four major themes: infectious diseases, non-AIDS, including emerging and reemerging diseases and biodefense; HIV/AIDS; allergy, immunology, and immune-mediated disease; and essential foundations for the future. The final document should be available at the next Council meeting.

Dr. Fauci gave an overview of NIAID's involvement in the global health research arena giving examples of what the Institute has done, the mechanisms that have been used, and accomplishments. For more information on NIAID's global research activities, see the Global Research portal on NIAID's Web site.

Two HIV/AIDS meetings took place over the summer, and at each meeting Dr. Fauci gave a presentation entitled "Much Accomplished, Much to Do." The talks outlined the accomplishments with regard to

pathogenesis, treatment and vaccine, and prevention but also acknowledged that there is still much left to do.

Dr. Fauci reported on the status of influenza vaccine research, malaria vaccine research, food allergy research, and the biodefense strategic plan.

III. GUEST SPEAKER – Marvin R. Kalt, Ph.D., Director, Division of Extramural Activities, NIAID – Trans-NIH Initiatives to Strengthen Peer Review

Before Dr. Kalt began his presentation, he called on Dr. Gary Schoolnik to make a statement for the Council. On behalf of the Council, Dr. Schoolnik recognized Dr. Fauci for his outstanding contributions to science and public service and congratulated him for winning the Lasker Medical Award and the National Medal of Science.

Dr. Kalt explained that one of the topics that came out of last year's NIH Leadership Forum was to devise a trans-NIH initiative for strengthening the peer review process. The process should be one that maintains equity and transparency in the peer review process. Both internal and external strategies are being considered and coordinated at the same time. One group is focusing on inputs and ideas from the extramural community, and another group is seeking input from NIH staff. The inputs and ideas from the two committees will eventually be integrated.

A study is underway to look for the best options to improve the peer review process. The four phases of the study are diagnostic, pilot design and choice of pilot, implementing the pilot in May 2008, and evaluation and feedback. For the diagnostic phase, NIH distributed a request for information and received over 2,200 responses. Dr. Kalt discussed the emerging themes from the responses received.

For more information on the process, see the Enhancing Peer Review at NIH Web site.

IV. REPORT OF THE DIVISION OF ALLERGY, IMMUNOLOGY AND TRANSPLANTATION COUNCIL SUBCOMMITTEE - Daniel Rotrosen, M.D., Director

Dr. Rotrosen presented the following new staff members, scientific and division activities:

STAFFING/ORGANIZATIONAL CHANGES

Ms. Julian Poyser, R.N., M.P.A., M.S.: Ms. Poyser joined the Asthma, Allergy and Inflammation Branch in April 2007 as a Project Manager. She received her bachelor's degree in nursing and a master in Public Health Administration from the State University of New York (SUNY) at Brockport. She went on to attain a masters of science in Family Nurse Practitioner from the University of Rochester, NY. Ms. Poyser started her career in research in 2000, working at Johns Hopkins University as a Nurse Practitioner/Research Coordinator.

Joseph M. Kaminski, M.D.: Dr. Kaminski joined the division in June 2007 as a Medical Officer in the Office of Product Development, Radiation Countermeasures Research and Emergency Preparedness Branch. Dr. Kaminski received his medical degree from the Medical College of Georgia (MCG). He completed his residency training at Vanderbilt University and is board certified by the American Board of Radiology. Prior to his arrival at DAIT, Dr. Kaminski served as a principle basic research investigator and clinician at MCG.

Katherine Thompson, R.N.P, M.S.N, C.C.R.P.: Ms. Thompson joined the Asthma, Allergy, and Inflammation Branch in July 2007 as a Project Manager. She received her bachelor's degree in nursing from College of Notre Dame of Maryland and her master's degree in nursing from Johns Hopkins University School of Nursing. Ms Thompson has held several positions at Johns Hopkins University including nurse manager in the Asthma Allergy and Clinical Immunology Division and most recently as Clinical Nurse Specialist Research Manager in the Division of Pulmonary and Critical Care Medicine.

Wendy Gao, B.S.N., M.S.: Ms. Gao joined the Clinical Immunology Branch in July 2007 as a Project Manager. She received her bachelor's degree in nursing from University of Minnesota and her master's degree in computer science from University of Northern Virginia. Ms. Gao started her career in research in 1998 at MD Anderson Cancer Center. Since then, she held several positions as Research Nurse Specialist/Study Coordinator at the Clinical Center under intramural programs at NCI and NIAID.

SCIENTIFIC INITIATIVES

Exploratory Investigations in Food Allergy (R21) (RFA-AI-07-032): To support high impact, innovative exploratory/developmental investigations to determine the mechanisms and risk factors associated with IgE-mediated food allergy and related co-morbid conditions. The studies will focus on ex vivo studies with human specimens and on studies with current or new animal models of food allergy. This initiative is being co-funded by NIAID, the U.S. Environmental Protection Agency, the Food Allergy Project and the Food Allergy and Anaphylaxis Network.

Statistical and Data Coordinating Center (SDCC): NIAID Immune Tolerance Network and Asthma and Allergic Diseases Cooperative Research Center (RFP-NIH-NIAID-DAIT-08-10): Provides for the establishment and management of a Statistical and Data Coordinating Center to support the National Institute of Allergy and Infectious Diseases sponsored clinical research programs in allergy/asthma, autoimmune, and transplant-related diseases.

DIVISION ACTIVITIES

2007 Annual Centers for Medical Countermeasures against Radiation (CMCR) Meeting: On June 18-19, 2007, NIAID sponsored a two day meeting to bring together investigators from the eight NIAID-funded Centers to provide a forum for the CMCR researchers to present data from the second year of the program (originally funded September, 2005). Other goals included fostering continued, synergistic interactions among the Centers, and facilitating relationships between the Centers and relevant government and commercial laboratories. In addition to the CMCR attendees, participants included NIAID and NCI staff, and representatives from several military and government agencies, such as DTRA, FDA, DHS, and DHHS.

Cytogenetic Biodosimetry Workshop: Held on July 5-6, 2007 at the Armed Forces Radiobiology Research Institute (AFRRI) in Bethesda, MD, this workshop sought to validate the dicentric assay for triage radiation dose assessment applications for mass casualties, in light of the data obtained from the NIAID/AFRRI sponsored inter-laboratory comparison study involving several cytogenetic biodosimetry laboratories. NIAID, through an existing interagency agreement, funded this meeting, and program staff gave the opening remarks.

NIAID Symposium: Results of the Inner City Asthma Consortium (ICAC)'s Asthma Control and Evaluation (ACE) Trial: On May 23, 2007 at the American Thoracic Society International Meeting in San Francisco, CA, NIAID sponsored a session entitled "Results of the Inner City Asthma Consortium (ICAC)'s Asthma Control and Evaluation (ACE) Trial." The most recent findings from the ongoing Inner City Asthma Consortium sponsored by the National Institute of Allergy and Infectious Diseases were presented. ACE is a randomized double-bind, controlled trial evaluating the role of a biomarker (eNO) in the management of inner-city asthma as contrasted to guideline driven asthma care. The relationship between the clinical and phenotypic characteristics of the participants and exhaled nitric oxide (eNO) and impact of eNO-guided therapy on asthma clinical outcomes in the ACE trial was presented. The use of a computerized algorithm to guide the selection of drug therapy was also described.

NIAID-EAACI Symposium: T cell homing and memory in the development of allergic diseases: On June 12, 2007 at the European Academy of Allergy and Clinical Immunology (EAACI) meeting in Goteborg, Sweden, NIAID hosted a symposium entitled "T cell homing and memory in the development of allergic diseases." Four experts in the field presented lectures on the development of T memory cells and their function, including the mechanisms of chemokine-mediated T cell accumulation during allergic airway disease.

School of Allergy and Hypersensitivity: DAIT has joined the American Academy of Allergy, Asthma and Immunology and the Clinical Immunology Society in co-organizing the 2nd School of Allergy and Hypersensitivity, which took place between September 7 and 10, 2007. The School included 10 faculty members and two groups of trainees, 15 post-doctoral fellows and 10 individuals who have junior faculty appointments at academic institutions. Each participant presented a research project (under development, ongoing or completed), followed by discussion. The focus of the School was to mentor young clinician scientists and clinical investigators in study design and data analysis, as well as to provide information on funding mechanisms and grant writing strategies. Two DAIT Program Officers participated as faculty.

Thymic Atrophy with Aging Workshop: On June 5-6, 2007, NIAID co-sponsored a workshop with the National Institute on Aging (NIA) to highlight the current state of research in thymic atrophy and identify gaps in our understanding and opportunities for future work. Major discussion topics included: age-related changes in hematopoiesis; regulation of lymphocyte differentiation in the thymus; molecular and cellular mechanisms of thymic involution; and strategies to enhance thymopoiesis and induce T cell recovery.

Annual Meeting and Educational Activities for the Modeling Immunity for Biodefense Contracts: On June 8, 2007 the second annual meeting of this contract program was held at Mount Sinai School of Medicine where the principal investigators and relevant staff described their recent program accomplishments in the areas of immunology, bioinformatics, computer simulations of immune responses, and education, and discussed future plans and collaborations among the contractors. An annual symposium and modeling summer school are major components of the Modeling Immunity for Biodefense program. This year's symposium, Emerging Science of Emerging Pathogens: From Atoms to the World was held at Mount Sinai on June 7 where presentations focused on modeling tools to study host-pathogen interactions, host immune responses, pathogenesis, and pathogen spread. The Immune Modeling Summer School was hosted by the University of Pittsburgh and Carnegie Mellon University, Pittsburgh, PA from June 17-22, 2007 to introduce experimental techniques and computational modeling of immunity to graduate students, post doctoral fellows, and faculty. Topics included: database development and management, ordinary differential equations and agent-based modeling, flow cytometry, imaging techniques, and a mini symposium on modeling *Mycobacterium tuberculosis* infection.

West Nile Virus - Research Advances in Immunology, Virology, and Genetics: On June 13-14 DAIT and the Division of Microbiology and Infectious Diseases, NIAID convened a workshop to discuss research advances in the immunology, virology, and genetics of West Nile virus. The participants included immunologists, epidemiologists, virologists, geneticists, structural biologists, and physicians; and the topics presented included: clinical manifestations of West Nile virus; host immunity and virus-host interactions; molecular determinants of antigenicity and virulence; virus neutralization and immune epitope discovery; novel therapeutic and diagnostic methods for West Nile infection; and epidemiology, ecology, and vector-virus transmission of West Nile virus in the Americas. The workshop participants also discussed research and knowledge gaps; and methods to foster collaborative projects to advance both basic research and clinical approaches for interventions.

Mycobacterium tuberculosis (TB) Epitope Workshop: On June 26, 2007, DAIT sponsored a workshop to determine the importance of the curated and analyzed TB immune epitope information contained within the Immune Epitope Database and Analysis Resource (IEDB, www.immuneepitope.org); and how this information can be applied to the control and treatment of mycobacterial infections. Participants conducted a critical review of the TB epitope data and meta-analysis report generated by the IEDB staff, including: evaluation of the biological significance of the meta-analysis; discussion of the criteria for development of a list of validated immune epitopes of potential clinical and research importance; identification of data missing from the analysis; and determination of gaps and opportunities to advance our understanding of adaptive immune responses to TB infection.

Development of Reagents for TLRs and Other Innate Immune Receptors: On June 28-29, 2007, the NIAID sponsored a workshop on the "Development of Reagents for Toll-Like Receptors (TLRs) and other Innate Immune Receptors". A panel of researchers was assembled to present research findings and to discuss existing and developing experimental methodologies, reagents, resources, and other research tools to facilitate studies of innate immune receptors and foster a better understanding of the innate immune system.

How to Get Your First NIH Grant Funded: On June 9, 2007 an hour-long training session on NIH grants for new applicants was presented by Branch staff at the annual meeting of the Federation of Clinical Immunology Societies in San Diego, California. Three prominent academic mentors also took part in a round-table discussion on achieving success in peer review of a grant application. The 50 attendees were presented with a CD containing slide sets on "Writing a Successful NIH Grant" and "NIH Grant Submission Process: Electronic or Paper?" as well as downloads from the NIAID Web site "All About Grants" for their subsequent self-instruction. The session was well received, and several other professors attending the FOCiS meeting asked for the informational CD to share with their fellows and students.

DIVISION ADVISORY COUNCIL PRESENTATION

NIAID Overview of the Primary Immunodeficiency Diseases Program

The following programmatic presentation was given by division staff and guest*:* Josiah Wedgwood, M.D., Ph.D., Chief, Immunodeficiency and Immunopathology Section, Clinical Immunology Branch discussed an **Overview of the Primary Immunodeficiency Diseases Consortium**; and Hans Ochs, M.D., Professor of Pediatrics, Jeffrey Modell Chair of Pediatric Immunology Research, University of Washington presented a discussion on **USIDnet-Supported Research in Primary Immunodeficiency Diseases; and** Jordan Orange, M.D., Ph.D., Assistant Professor of Pediatrics, Children's Hospital of Philadelphia presented **Human NEMO Mutation and Immunodeficiency.**

CONCEPT REVIEW

All concepts were presented and approved.

Mechanisms, Diagnosis and Treatment of Radiation Injury from a Nuclear Accident or Terrorist Attack: Basic, applied, and translational research will be supported through this initiative to generate new countermeasures from academic and commercial research groups. Countermeasures may include novel biodosimetry devices, radioprotectant drugs, drugs or therapies that mitigate the effects of radiation when given soon after exposure, and drugs or therapies that treat radiation-induced tissue damage.

Studies of Immunosenescence and Other Late Effects of Acute Radiation Exposure in Atomic Bomb Survivors: This program will focus on determining the effects of radiation and aging on the immune and other organ systems and the contribution of such effects to disease development in persons exposed to an atomic bomb explosion. In the first phase of the project, research will be conducted to better understand the mechanisms of radiation and aging and how these factors impact immune aging, to determine how immune dysfunction results in a persistent inflammatory state, and the resulting diseases and infections that may occur with immunosenescence in those who survived an Atomic bomb explosion. Specimens obtained from atomic bomb survivors will be used and correlative basic science studies will be performed in animal models to elucidate the underlying mechanisms of radiation-induced immunosenescence. Subsequent phases of the project may entail research on the delayed manifestations of acute radiation exposure in other organ systems.

Immune Mechanisms of Viral Control: This program will support single (U01) or multiple (U19) project cooperative agreement grants to discover and define the immune mechanisms that generate effective responses to viral infection and vaccination and provide potential new targets for future vaccine and therapeutic drug development. In the context of defining new immune mechanisms relevant to NIAID Category A, B, or C viral diseases in humans, areas of research interest include, but are not limited to:

- Innate immunity.
- The interface between innate and adaptive immunity.
- T and B cell memory.
- Mucosal immunity.
- Immunity in populations with altered immune status.

Antibody Epitopes and Mechanisms of Protection: This program will support the identification of linear and conformational B cell epitopes, coupled with basic studies to understand protective immunity mediated by antibodies. Investigators may utilize recent technological advances for epitope discovery, such as genome-wide scanning, structural genomics and proteomics, phage-display libraries, and combinatorial synthetic peptide library screens; or develop new or improved technologies, including computer-based B cell epitope prediction algorithms, for the identification of novel B cell epitopes. Epitope discovery methods must be accompanied by basic studies in appropriate animal models or using human cells to validate the epitope as a target of antibody-mediated protective immunity and to understand the mechanisms by which the antibodies induce immune protection. Supported investigators will be required to attend an annual program review meeting at NIH and submit their epitope information to the Immune Epitope Database and Analysis Resource (www.immuneEPITOPE.org).

Large Scale T Cell Epitope Discovery Program: This program will consist of identification of immunodominant and subdominant T cell epitopes, which bind class I, class II, or non-classical MHC/HLA molecules. Epitope discovery methods must be accompanied by validation studies in

appropriate animal models or using human cells to confirm the contribution of the epitopes to the generation of protective immunity. Investigators supported under this program will be required to attend an annual progress review meeting at NIH and to submit their epitope data to the Immune Epitope Database (www.immuneEPITOPE.org).

Innate Immune Receptors and Adjuvant Discovery: This program will support the discovery and development of potential new vaccine adjuvants for NIAID Category A, B, and C priority pathogens. Successful proposals are required to:

- Utilize high throughput screening with multiplexed readouts to discover and analyze agonists of mammalian innate immune receptors, focusing on the basic mechanisms of action;
- Evaluate the cellular responses activated through receptor/ligand binding;
- Identify and optimize lead compounds; and
- Pursue the most promising lead compounds through pre-clinical testing.

There have been recent successes in identifying agonists of a few well characterized Toll-Like Receptors and it is anticipated that more such agonists may be discovered under this new solicitation.

Population Genetics Analysis Program: Immunity to Vaccines/Infections: This program will support studies on the association of genetic polymorphisms with host immune responsiveness to infections and vaccination. The focus will be on NIAID Category A-C agents of bioterrorism and emerging/reemerging infectious diseases. Human specimens for these studies will be obtained from patients with a history of natural infections; individuals currently enrolled in vaccine trials; and/or previously vaccinated high-risk groups, such as military, laboratory, and health care personnel. Genomic information from mouse model systems will be used to facilitate identification of relevant human immune response genes. Particular emphasis will be placed on studies identifying host immune factors that play a role in controlling, protecting, or predisposing to an infection; exacerbating disease; determining resistance to treatments; or that might serve as targets for passive immunotherapy. Interdisciplinary teams that combine diverse scientific expertise (e.g., microbiology, immunology, genetics, mathematics, computer science) will be encouraged.

Autoimmunity Centers of Excellence: This initiative will renew NIAID's successful Autoimmunity Centers of Excellence (ACEs), a cooperative network of integrated basic, pre-clinical, and clinical research centers that:

- Conduct single site and multi-site cooperative clinical trials and studies of mechanisms of action of tolerance induction and new immune modulation interventions in multiple autoimmune diseases;
- Accelerate early translation of basic findings into clinical application;
- Facilitate the utilization of clinical materials for basic research studies;
- Enhance the exchange of information between basic scientists and clinicians and among various specialists involved in treating autoimmune diseases; and
- Promote a collaborative approach to clinical and basic research among multiple institutions in various geographic areas.

Each Center will include multidisciplinary, interactive research projects focused on elucidation of the basic mechanisms of autoimmunity; understanding of self tolerance and/or immune modulation in autoimmune disease; and an integrated clinical component for piloting new and novel immunotherapies for autoimmune diseases. The inclusion of basic or clinical central cores and an integrated clinical network facilitates basic investigation, clinical studies/trials, and the translation of basic research findings into the clinic.

Cooperative Centers for Translational Research on Human Immunity and Biodefense: This program will support a centralized research infrastructure to develop, standardize, and apply appropriate reagents, assays, and technologies to the study of human immunity. The Centers will facilitate translation from animal studies to human studies, and translation from basic research to clinical applications. In addition, novel research projects will be supported to investigate the molecular control of immunoregulation in the human, and to identify immunotherapeutic targets relevant to the prevention of disease caused by, or control of, NIAID Category A-C pathogens and their toxins. An education program for basic and clinical fellows/visiting scientists is also included. One component of the program will support small, exploratory pilot projects. Each Center will focus on a particular area of human immunity, such as innate immune mechanisms of protection or long-term immune memory, and will provide specialized expertise in the area and develop new methods for use by the Centers' network and the scientific research community.

V. REPORT OF THE DIVISION OF MIRCROBIOLOGY AND INFECTIOUS DISEASES COUNCIL SUBCOMMITTEE - Carole Heilman, Ph.D., Director

Dr. Carole Heilman, Director of the Division of Microbiology and Infectious Diseases (DMID), chaired the Microbiology and Infectious Diseases Subcommittee meeting. Dr. Heilman introduced Dr. Terence Dermody, who joined the meeting as an *ad hoc* member of the Subcommittee. Dr. Dermody is the Director of the Elizabeth B. Lamb Center for Pediatric Research at Vanderbilt University School of Medicine. Dr. Dermody is a long-time DMID grantee and was recently recognized with a Merit award. He is a world-recognized leader in the field of viral pathogenesis. She then referred to the Branch Chiefs/Acting Branch Chiefs in attendance to introduce their respective new hires.

Dr. Heilman presented a brief overview of recent Departmental and NIAID biodefense guidance documents and strategic plans to provide context for several of the research concepts presented later during the meeting. She noted that Homeland Security Presidential Directive -18 was introduced earlier in the year and that it encourages a broader approach to biodefense research. This directive dovetails with the Department's Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan for Chemical, Biological, Radiological and Nuclear Threats. Moreover, she reported that the Institute recently updated the NIAID Strategic Plan for Biodefense Research, which embraces the goals set forth by both HSPD-18 and the PHEMCE Strategy and Implementation Plan for Chemical, Biological, Radiological and Nuclear Threats. She briefly discussed some of the new research approaches DMID has begun to undertake consistent with these planning documents.

Dr. Heilman also distributed the recently updated Jordan Report, noting that DMID has updated this comprehensive vaccine report documenting the state of the science several times over the past 25 years; it continues to be an invaluable resource for the scientific community.

There were several concepts presented for the Subcommittee's consideration:

Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases

Subcommittee members voiced support for the evaluation process currently underway for the RCE program, but expressed concern that results of this exercise were not available for consideration prior to concept clearance, nor were more extensive details about scientific outcomes stemming from the program. It was noted that early results from the evaluation process have been received by program staff

and will help inform the development of the new initiative. In particular, new elements will be included in the recompetition of this program, such as an expanded focus to include emerging infectious diseases beyond Category A-C pathogens, a required evaluation component, and greater focus on themes to promote synergy and collaboration. The Subcommittee unanimously approved the initiative.

Cooperative Research Partnerships for Biodefense

Subcommittee members supported the Partnerships initiative, acknowledging the benefit and importance of engaging academia and industry in the Biodefense product development enterprise. The members were encouraged by the emphasis shift towards development of broad spectrum countermeasures/platforms in order to be consistent with the updated NIAID Strategic Plan. Some members noted that the Partnership program complements ongoing product development efforts within NIAID as well as with those of other federal agencies. There was agreement that the Partnerships program provides a worthwhile mechanism to support the translational research critical to development of new countermeasures against Category A-C pathogens. The Subcommittee unanimously approved the initiative.

Application of Platform Technologies for the Development of Therapeutic Agents

Subcommittee members supported this concept by acknowledging the need for translational science to advance the development of promising products for biodefense. The subcommittee recognized the need to encourage innovation in drug development by supporting the development of drugs with broad spectrum activity, and the evaluation of broad spectrum technologies and platforms with the potential to provide overarching advances in the drug development process. The subcommittee also acknowledged the risk involved in evaluating untested technologies and platforms. The Subcommittee unanimously approved the initiative.

Genomic Sequencing Centers for Infectious Diseases

Subcommittee members enthusiastically supported this initiative, and acknowledged the importance of providing microbial sequence data to the scientific community as it provides a valuable research resource for scientists engaged in basic and applied infectious diseases research. It was also emphasized that the continuing decrease in sequencing costs, coupled with new and emerging technologies, will allow for new opportunities to increase the examination of genetic variation across populations and communities of human pathogens, and also across the human genome. The Subcommittee supported the continued rapid data release to international public databases as a critical element of this concept. The Subcommittee unanimously approved the initiative.

Bioinformatics Resource Centers

The Subcommittee members enthusiastically received this initiative. There was strong agreement among the subcommittee members that these database resources are essential to allowing the scientific community easy access to the abundance of genomics data generated by other NIAID genomics projects. The Subcommittee unanimously approved the initiative.

VI. JOINT MEETING OF THE AIDS SUBCOMMITTEE, NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL AND AIDS RESEARCH ADVISORY COMMITTEE – Carl Dieffenbach, Ph.D., Acting Director, DAIDS

Dr. El-Sadr called the meeting to order. The minutes of the previous meeting were approved by unanimous voice vote.

Director's Report – *C. Dieffenbach, Acting Director*

Dr. Carl Dieffenbach, Acting Director, Division of Acquired Immunodeficiency Syndrome (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID), welcomed ARAC members and introduced invited guests: Anna Forbes, Global Campaign for Microbicides; Polly Harrison, Alliance for Microbicide Development; Sharon Hillier, Microbicide Trials Network; Sean Philpott, Global Campaign for Microbicides; and Joseph Romano International Partnership for Microbicides – who were asked to participate in the microbicide discussion later in the meeting. Dr. Dieffenbach announced two staff appointments: Judith Brooks was named Chief of Policy Training, Quality Assurance Branch, and Liza Dawson, Chief of the Human Subject Protections Branch. In addition, given Sandra Lehrman's departure for a new position at Merck & Co., Inc., Jeff Nadler has agreed to serve as Acting Director of the Therapeutics Research Branch.

Dr. Dieffenbach also announced the establishment of a fourth scientific program, the Prevention Sciences Program (PSP), which will encompass a dedicated Microbicide Research Branch and a Prevention Research Branch. Dr. Sheryl Zwerski has agreed to serve as Acting Director of PSP, which will have an extensive portfolio of grants and contracts covering basic research, observational studies and clinical trials to evaluate prevention strategies and agents. It will also provide oversight of two of NIAID's HIV-AIDS clinical trials networks, namely the HIV Prevention Trials Network and the Microbicides Trials Network.

Dr. Dieffenbach went on to review the President's FY2008 budget request, which includes $28.8 billion for NIH, an increase of 0.8 percent from FY2007. The NIAID allocation is $4.6 billion, an increase of $210 million (or 4.8 percent) from 2007. However, $201 million of that increase is slated for the Global Fund to Fight AIDS, Tuberculosis and Malaria; the remaining $9 million increase represents only a 0.2 percent increase from 2007. The House version of the budget includes a nearly 3.0 percent increase for NIH, 60 percent of which would go to the Office of the Director to support the Roadmap initiatives; NIAID and other institutes would receive a 1.5 percent increase. The Senate version includes another $250 million over the amount in the House bill, with NIAID and other institutes receiving a 2.3 percent budget increase. Both bills exceed the President's request, and the Senate bill also includes language authorizing stem cell research; there is little optimism that the differences will be ironed out quickly. Thus, it appears that NIAID will begin FY2008 under a continuing resolution.

A recent scientific finding highlights the potential impact of DAIDS research on both the state of the science and public health. Results from the Children with HIV Early Antiretroviral Therapy or "CHER" study were reported in July at the 2007 International AIDS Society Conference on HIV Pathogenesis in Sydney, Australia. CHER, a Phase 3, randomized clinical trial, showed that when infants begin treatment before three months of age, they do better than infants whose treatment was delayed. These results will likely impact the standard of care in many parts of the world, and highlight the importance of diagnosing HIV infections within the first six to 12 weeks of life.

Dr. Dieffenbach also noted that the PAVE 100 vaccine trial will begin enrolling participants at the end of September. *(Note: Since this report was given, a review of interim data by the Data and Safety*

Monitoring Board from the HVTN 502 or STEP Study found that the vaccine being tested could not be shown to prevent HIV infection or affect the course of the disease in those who become infected with HIV. Thus, immunizations were halted in the study and a related study. As a result, the initiation of PAVE 100 will be postponed until late 2007 or early 2008 to allow time to review /discuss these data and determine what (if any) change in the study design may be needed.) PAVE 100 is a Phase 2B, test-of-concept study of the Vaccine Research Center's (VRC's) six-plasmid DNA vaccine boosted by VRC's multiclade HIV-1 recombinant adenovirus (Ad) vector. The objectives are to further evaluate the safety of the vaccine and to assess its ability to prevent infection and (among those who become infected) to modulate viral load. This study is collaboration among NIAID and the Centers for Disease Control, HIV Vaccine Trials Network, International AIDS Vaccine Initiative, and U.S. Military HIV Research Program. At sites in the Americas, Eastern Africa and Southern Africa, the study will recruit 8,500 volunteers who are at high risk for infection due to sexual exposure.

Finally, Dr. Dieffenbach acknowledged three ARAC members who would be rotating off the committee after this meeting – Brooks Jackson, Nathan Thielman and Ruth Ruprecht – and thanked them for their numerous contributions over the past three years.

Working Group Updates

AIDS Vaccine Research Subcommittee – *Jim Bradac*
Dr. Bradac reported that the *AIDS Vaccine Research Subcommittee* (AVRS) had met on May 22 in Bethesda and on August 20 in conjunction with the AIDS Vaccine 2007 conference in Seattle. Four new members joined the AVRS: Kevin Fisher, Jeffrey Lifson, Louis Picker, and Bruce Walker. The major agenda item in May was the annual report from the Center for HIV-AIDS Vaccine Immunology (CHAVI), which includes 94 investigators at 51 institutions, including 12 clinical sites. CHAVI investigators have successfully organized themselves into discovery teams supported by core laboratories, and publications are already beginning to appear reporting their discoveries.

The subcommittee also heard from the HIV Vaccine Research and Design Program (HIVRAD), which was established by DAIDS in 1999 to support research in areas such as animal models, immunogen structure, mechanisms of action, and vector development. HIVRAD awards 5 year grants at $1 to $2 million/yr, and usually makes one or two awards each year. To date, a total of 18 grants have been awarded; 4 have been completed, 12 are currently active, and 2 new grants were made in FY2007. Eight of the 12 active grantees made presentations to the AVRS. AVRS concluded that:

- HIVRAD is achieving its programmatic goals, pursuing promising research in important scientific areas.
- It would be useful to bring HIVRAD grantees together in a more regular fashion, possibly in conjunction with AVRS or in a theme-based workshop, to encourage further scientific interaction.

AVRS had previously recommended that large-scale vaccine trials should go forward only if the "take rate" is greater than those of other in-class products that are being tested, and that (with regard to PAVE 100 in particular) a "go/no-go" decision should be based on preliminary data from the "triad" of harmonized Phase 1 and 2 trials currently underway. At the Seattle meeting in August, AVRS received updates suggesting that preexisting immunity to Adenovirus type 5 may not be as big a problem as previously feared, and that the take rate necessary to proceed with PAVE 100 most likely will be achieved. The August meeting also included a workshop on assays for monitoring T-cell immune responses in which it became clear that the assays currently being used may not correlate with functional T cell responses. The AVRS recommended that investigators continue to use the validated assays

currently in use for monitoring vaccine trials while making a strong effort to identify new validated assays that measure functional responses.

The next meeting of AVRS will be in conjunction with the ARAC meeting in January 2008.

Strategic Working Group – *David Margolis*

Dr. David Margolis reported on the *Strategic Working Group's* (SWG) June 27-28 meeting, at which it adopted guiding and operating principles; considered one new initiative in the Microbicide Trial Network (MTN); and reviewed the HPTN's revised domestic research agenda. The SWG also heard a presentation from the two Community Partners representatives regarding their goals and emerging challenges.

The MTN study that was reviewed is known as VOICE – Vaginal and Oral Interventions to Control the Epidemic (VOICE), a Phase 2B safety and effectiveness study comparing Tenofovir 1-percent gel, TDF tablet and FTC-TDF tablet for prevention of HIV infection in women. VOICE will be a five-arm, randomized trial involving 4,200 women at 10 sites in South Africa, Malawi, Uganda, Zambia and Zimbabwe. The SWG's strong support for VOICE is reflected in the following statements:

- A key strength of the design is the unique head-to-head comparison of topical versus oral agents;
- The sample size is very defensible;
- MTN investigators have demonstrated that they have the site capacity and incidence to conduct the study; and
- Behavioral assessments are a critical component of the study, specifically the impact of pre-exposure prophylaxis on disinhibition.

The SWG also heard a presentation on the proposed agenda for the HIV Prevention Trials Network (HPTN). The goal of HPTN is to generate epidemiological data about target populations, risk characteristics and high-incidence areas where NIH-funded research is appropriate. The SWG found that the presentation lacked a sense of priorities, costs and timelines on specific protocols. It further recommended that NIAID establish a priority-setting mechanism so to ensure that the agenda is driven by the highest scientific priorities. Other recommendations included the following:

- The HPTN should be a mechanism for performing larger, multicenter prevention studies analogous to Phase 2 and 3 studies in drug development;
- The HPTN needs to identify one or more studies that is derived from these considerations and that addresses the highest priority areas of prevention science. This should be done quickly, ideally along with the larger plan in November being developed in conjunction with the Trans-NIH Working Group.
- There is a need for perspective and a sense of balance between studies performed internationally and those performed domestically.

The SWG also began a discussion of acute HIV infection that will be continued at its next meeting, in November. Other topics will include the HPTN domestic agenda, HPTN 060, and a strategic update on the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT).

Microbicide Development: The Pipeline and Early Clinical Trials

The Pipeline for Microbicide Development

Division of AIDS Overview – *Jim A. Turpin, Prevention Sciences Branch, DAIDS*

Dr. Jim A. Turpin explained that the purpose of the DAIDS Microbicide Development Program is to identify and support/facilitate the development of safe, effective and acceptable topical microbicides to prevent HIV-AIDS and other sexually transmitted infections (STIs). The goal is the quickest and most efficient selection of the best candidates and, just as importantly, the quickest and most efficient elimination of inappropriate candidates. Activities to achieve this goal fall in three areas of emphasis: basic biomedical; non-clinical product development; and clinical evaluation.

Experience has shown that it is difficult to build a basic research portfolio for microbicides based on investigator-initiated grants (R01, R21, R03, and SBIR/STTR), so most microbicide development flows from targeted research supported by the Microbicide Innovation Program (MIP) and the Integrated Preclinical/Clinical Program for HIV Topical Microbicides (IPCP-HTM). The MIP has issued 24 grants in the first two rounds, with the ultimate goal of achieving a steady state of approximately ten new R21 awards each year and four to six continuing R33 awards. To move promising candidates and strategies from discovery through preclinical development, IPCP-HTM requires applicants to have a partner from industry or the private sector; this program is in year 2.5 of a four-year plan to achieve a steady state of eight to ten active awards. The MIP and IPCP-HTM already support research on a wide range of compounds, targets and strategies; future directions will include not only additional targets and delivery systems but also biomarkers for safety, efficacy and acceptability and strategies based on innate and/or adaptive immunity.

In addition to these grant mechanisms, DAIDS also provides two types of contract support: focused support for microbicide product development; and gap-filling resources. The HIV Microbicide Design and Development Teams (MDDT) are an example of focused support for product development. The MDDT require that the lead applicant be from an industrial source, and that the product advance to at least one Phase 1 clinical trial within the five-year term of award. Examples of gap-filling resources include support contracts to provide *in vitro* evaluation, developmental support, and nonhuman primate (NHP) efficacy and safety testing for promising candidates. Decisions about providing this type of support are made by the Microbicide Evaluation Group, which evaluates and prioritizes requests for assistance based on rigorous criteria, such as:

- Known anti-HIV or anti-STI activity;
- Target compatibility with microbicide use;
- Ongoing or proposed clinical activity;
- Stage of development;
- Significance to the microbicide field (i.e., new target or approach); and
- How the request fits with the overall microbicide effort.

Minimal requirements must be met for each step in this process. Dr. Turpin noted that many requests are rejected because the applicant cannot provide a sufficient quantity of purified compound, has not identified the mechanism of action, or has neglected to conduct preliminary safety testing such as the rabbit vagina irritation test.

Criteria for Microbicide Candidates – *Joseph Romano, International Partnership for Microbicides*

Dr. Joseph Romano described the decision criteria used by the International Partnership for Microbicides (IPM), a non-profit product development partnership established in 2002 to accelerate the development and availability of a safe and effective microbicide for use by women in developing countries. To ensure eventual availability, IPM insists on answers to questions about the drug *product,* as well as the drug *substance:*

- What is the mechanism of action (MOA)? (The earlier the better.)
- What are the results of lab and animal tests? (Pharmacokinetics, efficacy, safety.)
- What are the results of primary and secondary toxicology tests? (Genotoxicity, reproductive toxicity, immunotoxicity, etc.)
- What are the expected cost and availability? (Intellectual property, synthesis, manufacturability, costs.)
- Who are the sponsors and their partners?

There is a battery of assays and tests for answering each of these and other questions, but those answers should be in hand before a decision is made to support clinical testing. "No-gos" include late MOA, genotoxicity, formulation problems, instability, poor pharmacokinetics, and intellectual property issues. Even when a candidate enters clinical testing, it may be eliminated due to human safety concerns, demonstrated acceptability, and such nonclinical "killers" as formulation, manufacturability, cost, and sponsorship. One example is the Dapivirine intravaginal ring (IVR) – preclinical testing suggested that the *substance* was potent, safe and well-tolerated, but there were unknowns about the *product's* acceptability, safety, and environmental impacts. Initial tests in human volunteers have demonstrated both acceptability and safety, and multiple clinical trials are underway or scheduled into 2008. The product is still a "go," but may yet fall victim to problems of manufacturing or funding.

Dr. Romano noted that many pharmaceutical and biotechnology companies are partnering with IPM to facilitate microbicide development through licensing, codevelopment, and the provision of funding or resources for product development. He sees a synergistic role for NIH in expanding the pipeline and IPM is working with NIH to facilitate the development of candidate microbicides. NIH, through its grant and contract-based support of basic microbicide discovery and preclinical development is an important partner in providing the basis for other entities, such as IPM, to act as drug developers and facilitate product advancement.

Discussion

Discussants – Anna Forbes and Sean Philpott, from the Global Campaign for Microbicides, and Polly Harrison from the Alliance for Microbicide Development – pointed to the desirability of integrating decision-making structures at different points in the pipeline. They acknowledged and commended DAIDS and IPM for already meeting on a semiannual basis to discuss areas of overlap and potential "go/no-go" criteria. They also called on DAIDS and IPM to bring other players to the table, particularly those in the community. It was noted that microbicide development and prevention campaigns in general,

cannot succeed if they fail to engage civil society. For example, it will be important to introduce successful microbicides in a controlled way, to avoid the introduction of counterfeit drugs that will subvert the overall prevention effort. These and other sociocultural issues need to be addressed early in the development process. Discussants also raised the issue of cost and the need to know more about how low "low cost" has to be in order to be acceptable in various countries.

At present, there are about 67 microbicide candidates, some of which may not be viable. They agreed that it is important to eliminate failures quickly. Some trials have been stopped for statistical or safety reasons and we need to determine if there is more to be learned from these failures, such as from cellulose sulfate. It will not be until 2015 before the microbicides being tested begin to enter the market. Discussants also recommended that we consider whether or not we have an adequate pipeline to ensure that more and stronger candidates will continue to emerge in the future.

There was a general feeling that the current NIH mechanisms are stimulating scientific interest. The first MIP solicitation led to a five-fold increase in R01 applications, showing the stimulus effect of targeted grants, but it's not clear how well translational research will fare in peer review. It's extremely interdisciplinary, which review panels like, but a lot of the work that needs to be accomplished to move a product from concept through preclinical testing is difficult to do in the context of any of the existing structures of funding support.

The key gaps are in preclinical testing and manufacturing, an area where the Integrated Preclinical/Clinical Program-HIV Topical Microbicide and the Microbicide Design and Development Teams, have successfully attracted commercial partners. The NIH Office of AIDS Research is organizing a Microbicide Research Working Group that to look across the pipeline to see what can be done in a rational manner.

Early Clinical Trials: Criteria for Advancing Candidate Microbicides into Phase I – *Sharon Hillier and Ian McGowan, Microbicides Trials Network*

Drs. Hillier and McGowan, Microbicide Trials Network (MTN), described the criteria used by the MTN for advancing candidates to Phase 1 clinical trials. The Pharmaceutical Manufacturers Association has estimated that out of every 10,000 molecules screened for activity, 250 will be approved for full preclinical testing, 5 will enter Phase 1 clinical trials, and only one will result in an approved drug. Of the candidates that fall by the wayside, 30 percent fail because of lack of efficacy and 40 percent because of safety concerns.

The MTN currently has about 300 molecules in preclinical testing and hopes to move 5 candidates into Phase 1 in the next 5 years. Early leading candidates – nonoxynol-9, Savvy (C31G), cellulose sulfate – which are nonspecific microbicides or spermicides that had never undergone rigorous preclinical or clinical testing. Current candidates in the microbicide pipeline include BufferGel, lactobacillus, PRO2000, VivaGel (SPL7013), PMPA (tenofovir), UC781, dapivirine (TMC120), and CCR5 antagonists, which are undergoing more rigorous study.

When the HPTN 035 trial was launched several years ago, investigators selected BufferGel and PRO2000 as their active agents because of their proven *in vitro* activity, combined with favorable data from animal models (especially toxicity in rabbits) and the ready availability of the products. Today there would be far more attention to anti-HIV activity, using a wider range of assays based on diverse cell types, strains and clades, as well as toxicity against lactobacillus and microflora in vaginal tissues. The MTN comparative assessment core is designed to meet the need for this more intense study and meets this need by addressing 3 areas of candidate microbicide activity: *in vitro* activity, formulation, and *ex vivo* activity; only if the results of all three are acceptable does the candidate advance to human tissue for study of penetration and permeability.

In summary, it was noted that a few promising molecules are already available, but most of them will need further work before moving to Phase 1. The MTN has the capability to do comparative assessment, but they will continue to need assistance. Because of heavy attrition, there is a need to constantly bring new candidates into the pipeline. Even when effective and safe, formulation and scale-up to clinical trials remains a major challenge and expense. For this reason, it is vital to identify and encourage industry partners.

Discussion

Discussants noted that there is need for additional research on biomarkers, especially for safety. Also, there may be a need for more extensive and realistic safety testing prior to Phase 1, including more exhaustive and sensitive mucosal safety assays. There were questions about microbicide testing in adolescents and Dr. Hillier her previous work in girls as young as 14 years of age. The group voiced their concern that many of the models don't reflect how the products will actually be used in Phase 3 or on the market. It was also suggested that a broader focus on other sexually transmitted infections (STIs) might advance the field, generally, although the MTN already tests for effects against other STIs as secondary outcomes.

Concept Review

Master Contract for Non-Clinical Microbicide Development – *Jim A. Turpin, Microbicide Research Branch*

Dr. Turpin described the proposed *Master Contract for Non-Clinical Microbicide Development*, which is a five-year contract (using the N01 mechanism). Its objective is twofold: (1) to provide gap-filling resources that will advance promising candidates into clinical trials and (2) to develop infrastructure and research methodologies as a platform for future harmonization of testing efforts. The first part of the contract, gap-filling resources, will include general microbiology, pharmacokinetics, toxicology, manufacturing, formulation, and IND application development. Gap-filling activities are currently conducted using supplemental funds to the Vaccine Research Program Preclinical Master Contract, which expires in September 2009. The second part of the contract will replace select elements of the Microbicide Quality Assurance Program, which expires in September 2008. This contract will provide the Microbicide Research Branch a base of support for these activities. The first year costs are projected at $2.8 million, with lower costs in the following four years and an option to extend the contract for an additional two years. The written proposal includes responses to the comments of four ARAC members who were among the reviewers.

There were no questions or discussion, and the chair commented that most members had already expressed their approval for this concept in earlier discussions. The concept for this initiative was unanimously approved by a show of hands; written ballots were also collected.

The next meeting of ARAC will be in January 2008. Various potential areas for discussion at the upcoming meeting were raised. Members indicated that they would like to discuss the general topic of adolescents – some 60 percent of new infections occur in adolescents, who need various prevention interventions and my need specific mechanisms that will increase their cooperation in studies and programs in order to improve their outcomes. Other members suggested the topic of how to integrate prevention studies and how to design prevention studies in the future.

VII. ADJOURNMENT

The meeting of the Council was adjourned at 5:10 p.m., on Monday, September 17, 2007.

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

_____-s-_____ **__11/08/2007_____**

Anthony S. Fauci, M.D.
Chairman, National Advisory Allergy
and Infectious Diseases Council
Director, National Institute of Allergy
and Infectious Diseases

Date

_____-s-_____ **__11/05/2007_____**

Marvin R. Kalt, Ph.D.
Executive Secretary
National Advisory Allergy and Infectious
Diseases Council
Director, Division of Extramural Activities
National Institute of Allergy and Infectious
Diseases

Date

These minutes will be formally considered by the Council at its next meeting; any corrections or notations will be incorporated in the minutes at the meeting.