NATIONAL INSTITUTES OF HEALTH

NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL

MINUTES OF MEETING

September 18, 2006

The 154th meeting of the National Advisory Allergy and Infectious Diseases Council (NAAIDC) was convened at 10:30 a.m. on Monday, September 18, 2006, 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 10:15 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. Stanley Chapman
Dr. Charles Davis
Dr. Kathryn Edwards
Dr. J. Brooks Jackson
Ms. Anne Munoz-Furlong
Dr. Martin Myers
Rev. Raymond O'Brien
Dr. Shelley Payne
Dr. Anjana Rao
Dr. Martin Rosenberg
Dr. Ruth Ruprecht
Dr. Gary Schoolnik
Dr. Megan Sykes
Dr. Nathan Thielman
Dr. Gail Wertz

***Ex Officio* Members Present:**

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

**Council Members Absent:**

Dr. Anthony D'Alessandro
Dr. Richard Insel

***Ex Officio* Members Absent:**

Dr. Lawrence Deyton

***Ad Hoc* Members:**

Dr. William Busse
Dr. George Drusano

**NIAID Senior Staff:**

Dr. Hugh Auchincloss
Dr. John McGowan
Dr. Carole Heilman
Dr. Cliff Lane
Dr. Daniel Rotrosen
Dr. Paula Strickland
Dr. Ed Tramont

## 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 2,092 research and training applications with primary assignment to NIAID for a requested amount of $450,442,483 in first-year direct costs and recommended approval of 582 applications for $100,110,303 in first-year direct costs. Thirteen 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. Insel and D'Alessandro, a retiring member, would be absent. He introduced two *ad hoc* Council members: Dr. William Busse, University of Wisconsin School of Medicine, and Dr. George Drusano, Ordway Research Institute.

Dr. Fauci acknowledged the contributions of four other retiring members, Dr. Charles Davis, Ms. Anne Munoz-Furlong, Father Raymond O'Brien, and Dr. Anjana Rao and presented them with plaques.

A written report from the Division of Intramural Research Board of Scientific Counselors review of intramural laboratories was distributed to the Council members.

### Consideration of Minutes of Previous Meeting

The minutes of the May 22, 2006, meeting were considered and approved as written.

### Staff and Organizational Changes

Several staff and organizational changes have taken place since the last Council meeting. In the Division of AIDS two new leadership positions have been created. Dr. Carl Dieffenbach will serve as interim principal deputy director, and Dr. Jonathan Kagan has been appointed deputy director for program development.

In the Division of Allergy, Immunology, and Transplantation, Dr. Nancy Bridges was named chief of the Transplantation Immunobiology Branch. Dr. Gennady Platoff has joined the Institute as the chemical, biological, radiological, and nuclear scientific advisor for the Office of Biodefense Research.

Gray Handley is the new associate director for international research affairs and acting director, Office of Global Research. Dr. Y'Drissa Sow has been appointed director, NIAID Research Support Office in Bamako, Mali.

In the Division of Intramural Research, Lisa Coronado is the new associate director for scientific management.

**Budget Update**

Until the FY 2007 budget is signed, NIAID is operating under a continuing resolution. Dr. Fauci compared NIH's FY 2006 budget with the proposed FY 2007 President's budget, House mark, and Senate mark. The Senate proposes a slight increase to all ICs in contrast to the President's budget and the House mark that propose a reduction for many ICs. NIAID continues to fare better than most other ICs whose budgets are flat or falling. NIH's Office of the Director would receive a substantial increase to be used largely for Roadmap activities and for the NIH Advanced Development Fund which supports advanced development of medical countermeasures for biodefense and emerging infectious diseases.

**Legislative Update**

Congress continues to express interest in reauthorization of NIH. Provisions that are being considered for the reauthorization bill would affect funding and management authorities and emphasize trans-NIH research activities.

In June, Representative Michael Burgess and his staff visited NIAID laboratories and were briefed on our pandemic and interpandemic influenza activities. In August, Senator Max Baucus visited the NIAID Rocky Mountain Laboratories in Hamilton, Montana. Dr. Marshall Bloom hosted the Senator as he toured the laboratories and received a demonstration of BSL-4 procedures.

**Other Information Items**

The NIAID Influenza Blue Ribbon Panel met on September 11 through 12, 2006. The group reviewed the current NIAID influenza portfolio and previously identified areas of scientific opportunity, and identified additional scientific opportunities and approaches to guide NIAID's future influenza research agenda. Dr. Fauci reported on some of the influenza research that the Institute has been participating in and gave an update on the status of influenza vaccine research.

This year commemorates 25 years since the recognition of AIDS as a distinct disease. OAR and NIAID sponsored a ceremony at the NIH Clinical Center which reviewed the progress and future challenges of AIDS research.

Dr. Fauci announced the leadership for the newly restructured HIV/AIDS Clinical Trials Network. The network has six components that will focus on safe and effective treatments and prevention strategies, including HIV vaccines.

## III. GUEST SPEAKER – Clifford Lane, M.D., Director, Division of Clinical Research, NIAID

The Division of Clinical Research (DCR) was established in 2006. Dr. Cliff Lane gave background information about how the newest division in NIAID, DCR, came to be and its role in the Institute. The Division is not focused on doing research, but on trying to facilitate high quality, state-of-the-art clinical research within NIAID. DCR is responsible for overseeing and managing certain elements of the Institute's intramural clinical research infrastructure; developing, coordinating, and implementing NIAID clinical research policy; regulatory monitoring and compliance for a subset of work within intramural; and statistical consulting and capacity building.

Dr. Lane gave an overview of the organizational structure of the Division and the role of each component. He also mentioned that a new facility is under construction that will be part of the national interagency biodefense campus. The facility will have BSL-2, -3, and -4 capabilities.

## 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

**Jonah Odim, MD, PhD, MBA** Dr. Odim joined the Transplantation Immunobiology Branch in June 2006, as a Medical Officer. He received his undergraduate degree from Amherst, his medical degree from Yale, completed a general surgery residency at University of Chicago, and trained in cardiovascular and thoracic surgery at McGill, where he also received his PhD. Prior to joining the Division, he held clinical positions in cardiothoracic surgery at Children's Hospital (Boston), University of Manitoba, and UCLA.

**Nancy Bridges, MD** Dr. Bridges was recently appointed Chief of the Transplantation Immunology Branch. Since 2002, she served as Chief of the Clinical Transplantation Section. Prior to joining DAIT, Dr. Bridges was an Associate Professor at the University of Pennsylvania School of Medicine and Medical Director of Thoracic Organ Transplantation, and Medical Director for Pulmonary Hypertension at Children's Hospital of Philadelphia; subsequent to that she was a Professor and Associate Division Chief at Mt Sinai Medical Center, in New York City. She is Board Certified in Pediatrics and Pediatric Cardiology, and has been certified as a Heart Transplant Physician and as a Lung Transplant Physician by the United Network for Organ Sharing. Dr. Bridges has been involved in the care of children with end-stage cardiovascular disease and those receiving thoracic organ transplants for the past 13 years.

**Laura Wilson, BSc, PhD** Dr. Wilson joined the Basic Immunology Branch as a Health Specialist, in August 2006. She received both her Bachelor's degree, in inorganic chemistry and microbiology, and her PhD at the University of Manitoba. Using an experimental model of the hygiene hypothesis, her doctoral research focused on the inverse correlation between intracellular bacterial infection and the development of allergic disease. Dr. Wilson also studied the role of dendritic and natural killer T cells in *Chlamydia* immunopathology and protective immunity.

### SCIENTIFIC INITIATIVES

**Allergen and T-Cell Reagent Resources for the Study of Allergic Diseases** (RFP-BAA-NIH-NIAID-DAIT-07-34): This Broad Agency Announcement solicits proposals to identify novel allergens using innovative purification methods, and to generate a set of defined peptides that regulate the function of allergen-specific effector and regulatory T cells.

**Systems Approach to Immunity and Inflammation** (BAA-NIH-NIAID-DAIT-07-35): This Broad Agency Announcement solicits proposals to develop an "encyclopedia" of innate and adaptive immune responses to infection, vaccination, or immunotherapy, with a focus on NIAID Category A-C priority pathogens. Development of the "encyclopedia" will be based on genome-wide screens of mutant mice for identification of key regulatory immune response genes.

**Non-Human Primate Islet/Kidney Transplantation Tolerance (NHPCSG) (U01, U19)** (RFA-AI-06-018): This Request for Applications, co-sponsored by the NIAID and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), solicits applications for research projects studying non-human primate models of islet and/or kidney transplantation tolerance. The goals of the NHPCSG are to: (1) evaluate preclinical safety and efficacy of existing and newly developed candidate immune tolerance induction regimens; and (2) elucidate the mechanisms underlying the induction, maintenance, and/or loss of tolerance in non-human primate models of islet, kidney, heart, and lung transplantation.

## DIVISION ACTIVITIES

**Centers for Medical Countermeasures (CMCR) Workshop on the Food and Drug Administration (FDA) Pre-Market Regulatory Process: Applications to Technologies for Radiation Biodosimetry after a Large-Scale, Radiological Incident**: On March 27, NIAID sponsored a workshop for CMCR Principal Investigators (PIs) on the FDA requirements for the development and approval of biodosimetry devices for radiation triage and treatment, as well as Clinical Laboratory Improvement Amendment (CLIA) approval and certification procedures. In addition to the CMCR PIs, participants included staff from the FDA and Centers for Medicare and Medicaid Services (CMS). Topics discussed included data analysis, the CLIA program, and pre-IDE processing. CMCR PIs made presentations on their biodosimetry devices. Slide presentations given by the FDA can be accessed at: http://www3.niaid.nih.gov/research/topics/radnuc/FDA_corner.htm

**Centers for Medical Countermeasures against Radiation (CMCR) 2006 Annual Meeting**: On June 7-8, NIAID sponsored a forum for CMCR investigators to present their research progress since September 2005. The forum also presented opportunities to establish collaborative efforts among the CMCRs, as well as with government and industry laboratories. Presentation topics included: Identification and Development of Countermeasures - early and late radiation effects countermeasures development, cell-based therapies, and high throughput screening; Mechanisms of Radiation-Induced Damage & Repair, Biodosimetry - biomarker and method validation and device design; and updates on Training and Education/Pilot Projects.

**Centers for Medical Countermeasures (CMCR) Workshop on the Food and Drug Administration (FDA) Pre-Market Regulatory Process: Applications to Radiation Countermeasures After a Large-Scale, Radiological Incident**: On June 9, NIAID sponsored a workshop for CMCR PIs on the FDA requirements for the development and approval of drugs and biologics that can be used following a radiological incident. The workshop also served as an introduction to the role that NIAID plays in the regulatory advancement of candidate countermeasures. Slide presentations given by the FDA and NIAID can be accessed online at: http://www3.niaid.nih.gov/research/topics/radnuc/FDA corner.htm.

**2nd International Conference on Biodosimetry and 7th International Symposium on EPR Dosimetry and Applications**: NIAID participation in this conference included:

- Co-Sponsored a meeting with Uniformed Services University of the Health Sciences
- NIAID Program Staff Keynote Presentation - "Overview of Biodosimetry Projects in the NIH Radiation/Nuclear Countermeasures Program"

**Antibody Epitope Prediction Tools Evaluation Workshop**: On September 7-8, the NIAID convened a workshop to evaluate the capabilities of currently available antibody epitope prediction tools. Antibodies are proteins produced by a host in response to infection or vaccination, and are critical components of

immune protection against infections. Antibodies can also contribute to the pathogenesis of immune-mediated diseases. An epitope is the region of an infectious agent that is recognized by the antibody, and allows the antibody to help neutralize the infection. Although antibody structures have been known for years, the mechanisms that govern epitope identification are largely unknown. The ability to predict antibody epitopes could lead to improved vaccines or immune-based therapies for infectious and immune-mediated diseases. This workshop brought together tool developers and users to provide critical feedback regarding the value of currently available antibody epitope prediction tools and to recommend common metrics and datasets for tool evaluation. This workshop was organized by DAIT staff and investigators from the NIAID-supported Immune Epitope Database and Analysis Program contract (IEDB: www.immuneepitope.org). As part of the IEDB project, the contractor was tasked with development of an Analysis Resource, which includes algorithms to predict antibody epitopes. Recommendations from this workshop will be posted on the IEDB and NIAID websites.

**Genomics, Proteomics, and Genetics for Transplantation: Status, Challenges and Evolving Technology**: On May 17-18, the NIAID co-sponsored a workshop, entitled "Genomics, Proteomics, and Genetics for Transplantation: Status, Challenges and Evolving Technology." The experts in genomics, proteomics, and bioinformatics came together with transplant physicians and surgeons to discuss the applications of emerging technologies for gene expression profiling, proteomics, and genetics. The major topics of discussions were: 1) how to best advance our understanding of basic and clinical challenges in transplantation biology and therapy; and 2) exploring how different technologies will contribute to the identification and application of biomarkers for transplantation outcomes including the efficacy of immunosuppression.

## DIVISION ADVISORY COUNCIL PRESENTATION

### NIAID Overview on the Inner City Asthma Consortium

The following program was presented by division staff and guest: Matthew Fenton, Ph.D., Chief, Asthma, Allergy and Inflammation Branch discussed an overview of **DAIT's Inner City Asthma Consortium**; and William Busse, M.D., Professor and Chair, Department of Medicine, University of Wisconsin School of Medicine; Madison, WI presented a **Report on the Inner City Asthma Consortium.**

## CONCEPT REVIEW

All concepts were presented and approved.

Asthma and Allergic Diseases Cooperative Research Centers: This program will support integrated basic and clinical research centers to conduct studies on the immunologic mechanisms underlying the onset and progression of asthma and allergic diseases. The overarching goal of the program is to improve the diagnosis and treatment of asthma and allergic diseases, and provide a rational foundation for the development of effective prevention strategies.

**Clinical Trials in Organ Transplantation in Children:** This initiative is to support clinical trials with associated mechanistic studies, as well as epidemiologic studies, in pediatric heart, lung, kidney, liver, and/or small intestine transplantation. This initiative is an expansion of RFA AI-02-004, "Cooperative Clinical Trials in Pediatric Transplantation," which was limited to kidney transplantation.

**National Swine Research and Resource Center:** This initiative is to continue to co-sponsor the National Swine Research and Resource Center (NSRRC) established by the National Center for Research Resources in 2003 for depositing, maintaining, preserving, and distributing swine models for studies of human diseases.

**Data Coordinating Center for the Immune Tolerance Network:** The Data Coordinating Center for the Immune Tolerance Network (ITN) will provide statistical, data management, safety monitoring, medical writing, and administrative support for 25 to 30 ITN clinical and non-clinical studies. These studies will focus in the areas of asthma and allergic diseases, autoimmune diseases, and rejection of transplanted solid organs, tissues, and/or cells.

**Immune Mechanisms of Viral Control:** This initiative is to establish a synergistic network of research teams focused on basic immunological parameters of pandemic influenza infection and vaccination, as well as other relevant viruses, leading to practical approaches to prevent and treat pandemic influenza outbreaks, including methods to a) induce tissue-specific immunity and b) control virus-induced inflammation and immunopathology.

**Innate Immune Receptors and Adjuvant Development:** This initiative is to advance to phase I clinical trials the best candidate compounds that stimulate the innate immune response through Toll-Like Receptors and demonstrate strong adjuvant properties in animal models. These candidate compounds will be utilized as adjuvants in the development of novel vaccines for human use against NIAID Category A, B, and C pathogens. Knowledge gained from these studies will also likely benefit non-biodefense related vaccine adjuvant development. The results will bring new adjuvants for human use closer to FDA approval and to human application.

**Primary Immunodeficiency Disease Consortium:** This initiative is to establish a primary immunodeficiency disease consortium to address emerging opportunities and accelerate research in the field, develop and implement collaborations and sharing of resources, provide mentoring for new investigators, maintain and expand the Primary Immunodeficiency Diseases Registry, and maintain and expand the Primary Immunodeficiency Diseases Repository.

## V. JOINT MEETING OF THE AIDS SUBCOMMITTEE, NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL AND AIDS RESEARCH ADVISORY COMMITTEE - Ed Tramont, M.D., Director, DAIDS

Dr. Holmes welcomed ARAC members, NIAID staff, and invited guests to the ARAC meeting and asked the ARAC members to approve the summary from the May 22, 2006 meeting. Hearing no objection, the summary was approved.

### Director's Report

Dr. Tramont also welcomed ARAC participants and began his report by announcing the first step in the reorganization of the Office of the Director (OD). He established a new leadership position, Deputy

Director, Program Development; Dr. Jonathan Kagan has agreed to serve in this position. Dr. Kagan will focus on knowledge management, program development, and coordination of activities with external stakeholders. A second senior leadership position was also established, Principal Deputy Director. Carl W. Dieffenbach, Ph.D. has agreed to serve in this capacity, acting as second in command, on an interim basis. Dr. Dieffenbach will provide oversight to the Office of Program Operations and Scientific Information and to the Office for Policy in Clinical Research Operations. He will also retain his position as Director of the Basic Sciences Program.

Dr. Tramont also introduced two new staff members: Dr. Jeffrey Nadler who recently joined the Division as Deputy Director of the Therapeutics Research Program and Dr. Katherine Kripke, who joined DAIDS as Assistant Director of the Vaccine Research Program.

Dr. Tramont then reviewed the budget, acknowledging that the payline is down to the 10 the percentile. He reviewed the House and Senate marks to the FY 2007 President's request; the House requested $28.5 billion for the NIH, a reduction of $99 million compared to the FY 2006 budget, while Senate budget provided $28.8 billion, an increase of $200 million compared to the FY 2006 budget. In both the House and Senate budget, NIAID fares relatively well. Because the budget will not go to the conference committee until after the November elections, it appears we will begin FY 2007 under a Continuing Resolution.

Dr. Tramont also reviewed highlights of the selected scientific advances published over the past year. He also mentioned that the Division will be releasing a Request for Proposal to solicit a contract in support of DAIDS activities, which are currently being performed through an Interagency Agreement between NIAID and the US Army Medical Research and Material Command (USAMRMC).

In closing Dr. Tramont recognized and thanked outgoing ARAC members Phyllis Kanki, Charles Davis, Reverend O'Brien, and King Holmes for the time and energy they devoted to the committee. He presented a special plaque to Dr. Holmes for his outstanding leadership and vision as chair of the ARAC, particularly as the Division went through the challenging and complex restructuring of the clinical trials networks.

**Update on Trends in AIDS Funding –** *C. Dieffenbach, Ph.D.*

Dr. Dieffenbach reviewed AIDS funding since 1982, which until approximately 3 or 4 years ago had grown substantially. As a result of level funding over the past few years, the Office of AIDS Research (OAR) had adjusted funding allocations to ensure that high priority research areas such as HIV vaccines, receive adequate funds. Thus between 2005 and 2007 even during a level budget overall, there has been growth in the budget for HIV vaccine research. The payline for NIAID from 1999-2004 was in the 20$^{th}$ or 22$^{nd}$ percentile; since it has decreased slightly since and, in 2007 will be half of what it was at the 10$^{th}$ percentile. For NIAID, the number of applications (RO1s only) from new investigators has remained relatively constant since 2004, as has their overall success. For established investigators, there's been an increase in the number of applications, and a similar relatively flat level of funding, which is to be expected due to the declining payline. For DAIDS there has been a steady increase in the number of RO1 applications and the number of RO1s funded over the last four years has remained relatively constant. However, with the payline going to the 10$^{th}$ percentile in 2007, it is unlikely that that trend can continue.

During the discussion, members sought clarification of success rate vs. percent funded, how the payline is established and how it could be increased, and what other opportunities exist for new investigators.

Dr. Dieffenbach further explained that the total R01's to be funded are set at the NIH level; if an initiative is cancelled or not approved at ARAC the savings does not necessarily roll into the investigator-initiated pool. In addition, an increase in the payline for AIDS at NIAID would only occur if the payline for non-AIDS, non-biodefense activities also increases. Finally, Dr. Dieffenbach noted that there are a number of new programs at NIH for new investigators, information from which will help shape future programs. For now, NIAID has elected to increase the payline for new investigators by two percent.

**Concept Review: Microbicide Innovation Program –** *J. Turpin, Ph.D.*

Dr. Turpin presented the concept for the renewal of the Microbicide Innovation Program (MIP), which is designed to strengthen and maintain an innovative microbicide pipeline while facilitating the design, development, and transition of technologies and methodologies to advance the field as a whole. The initiative would be for 5 years, coupling the innovation grant (R21) mechanism, and the R33 mechanism; first year costs are $3.3 million. The goal of this initiative is to build the microbicide field and the basic science required to help respond to future microbicide research needs. The specific areas of focus will be on gap filling (e.g., emerging technologies and complex prevention strategies), combination products (targeting HIV and STIs to HIV acquisition and synergism leading to reduced dose/frequency of application); unique/underexplored chemical class or mechanism of action; and new technological and methodological approaches.

For the first MIP, there were initially 53 submissions, and with 15 awards proposed. Three awards will go to NICHD, one will go to NIMH, and 11 come to NIAID. Of these, there were six investigators new to microbicides.

Drs. Holmes and Ruprecht served as reviewers for this concept. Dr. Holmes used several key questions to assess the concept: is this an area that needs stimulation; are there good scientific opportunities; are there enough investigator initiated proposals to support this; and is this the right mechanism. Dr. Holmes felt that the concept met all these criteria, and that the use of the milestone approach is important. In discussion it was noted that the R21/R33 mechanism has been used by NCI with good success. Dr. Ruprecht also felt the concept had a great deal of merit, as did other ARAC members, and recommended approval. ARAC members voted to approve the concept for this initiative.

**Concept Review: Non-human Primate Models to Evaluate Therapeutic Strategies and Topical Microbicides –** *Frosso Voulgaropoulou, Ph.D.*

This contract is designed to support the evaluation of therapeutic and topical microbicide interventions using the SIV/macaque and SHIV/macaque animal models. The first year costs of this 5 year contract are approximately $5.4 million dollars. The goal of the program is to facilitate the development of vaginal and rectal microbicides to prevent mucosal transmission of HIV and to advance therapeutic approaches to complement or even replace HAART regimens in HIV-infected individuals. This program also aims to support the development of better and improved non-human primate animal models for HIV/AIDS that better mimic HIV infection and transmission. The reviewers – Drs. Ruprecht and Margolis – both thought the concept was meritorious. Dr. Ruprecht suggested the use of R5 SHIV strains as challenge virus as well as the use of the repeated low dose model for topical microbicide studies. Dr. Margolis urged the establishment of contract resources to support testing of therapeutics or microbicide interventions in improved mouse models when these models become available.

In discussion, ARAC members questioned how these proposals are reviewed, the relationship to the National Center for Research Resources (NCRR) and statistical support of the studies. It was explained

that the studies proposed to be conducted using contract resources are reviewed internally by a panel of DAIDS staff with appropriate expertise. The contract solicitation on the other hand, is peer reviewed at an NIAID study section meeting and only applicants with access to non-human primate facilities qualify for such solicitation. The NCRR is not involved in the program, as it supports facilities, not studies. Finally, it was explained that statistical support of the studies supported by the contract is provided through a subcontract. With no further discussion, the ARAC committee voted to approve the concept.

**Standardization and Harmonization of NIAID Clinical Research Policies and Procedures –** *C. Lane, M.D.*

NIAID has established the NIAID Clinical Research Subcommittee (NCRS) of the NIAID Executive Committee to look for opportunities for harmonization of policies and an exchange of best practices across NIAID divisions. The membership for this subcommittee involves key representatives from all NIAID divisions and relevant offices that have a direct engagement with clinical research. Examples of issues being addressed by the subcommittee include one from the Division of AIDS dealing with the subject of investigator liability and indemnification, the development of a protocol template, clinical trials agreements, DSMB policies, and the development of a Global Studies Database. In addition, there is a clinical research seminar series that will address different issues, such as handling of an IND and monitoring issues.

In its deliberations, the NCRS decided not to establish a centralized office for regulatory oversight, but rather to establish and enforce common policies. A working group of the NCRS was established in response to the report from the "Sullivan Committee to focus on regulatory issues. (The Sullivan Committee was convened in 2005 and charged with reviewing the regulatory processes within the Division of AIDS (DAIDS) and identifying areas for improvement.) Chaired by Dr. Auchincloss, this working group has made specific recommendations related to the structure needed for DAIDS to accomplish its regulatory functions and the need for additional personnel. The working group also considered whether the organizational structure designed for DAIDS should fit all the divisions; due to the different volume of clinical research activity, different funding mechanisms used, and different use of clinical and regulatory contractual services, it concluded that it would be inappropriate to use the same structure for each division. Nonetheless, the group identified universal principles that should be addressed within each division, e.g., every division should have an identified employee reporting directly to the Division Director, who would be charged with the responsibility of ensuring that NIAID-sponsored clinical trials are "conducted in compliance with all applicable regulations and requirements for the safety of the patient and the integrity of the trial."

In discussion, ARAC members asked for clarification about the relationship with the Office for Human Research Protection (OHRP), which is now in the office of the Secretary, Department of Health and Human Services, the decentralized nature of NIAID's regulatory approach, and other agency involvement particularly with regard to international regulations. Dr. Lane clarified that OHRP sets the overall guidance for NIH, and all NIAID policies are developed within that context. In order to give each division the flexibility to implement NIAID policies according to its own needs, the subcommittee intentionally chose a decentralized approach with stronger, centralized oversight. That said, it was agreed that the impact on investigators involved with more than one division should be taken into consideration. Dr. Lane emphasized the need for Secretary Sullivan's and Leavitt's support for an interagency meeting to discuss national and international regulations and in closing, clarified, the use of the terms being used. Standards are a set of statements of what is expected; policies are ways in which we would achieve those standards. The divisions would then be held accountable to the policies generated.

**Interim Reports of the HIV/AIDS Clinical Trials Restructuring Network Leadership Awards –** *J. Kagan, Ph.D.*

Dr. Kagan reviewed the funding for the leadership of the HIV/AIDS clinical trials networks and goals of the restructuring effort, which were primarily to achieve greater efficiency, increase collaboration among the networks, increase integration of treatment and prevention research, and ensure flexibility to respond to changing research priorities and opportunities and performance. He then provided a status report on the units for the HIV/AIDS clinical trials networks: 121 clinical trials unit (CTU) applications and 662 clinical research site (CRS) applications were received. When taking into account the multiple areas of research they proposed, there were 2094 reviewable units. Unit and site selection will be based on: scientific peer review, relevance to leadership groups' agendas, special populations, past performance, pluripotentcy, and available budget. The units and sites will be funded differently than in the past. They will receive 1) core funds, which are stable over the funding period, to support basic operations and a minimum level of protocol activity, 2) a protocol implementation fund (PIF), which can vary over the funding period, to support protocol-specific work, and 3) funds from the PIF reserve, which are set aside for high priority/high impact, and/or high cost studies. It is anticipated that CTU/CRS awards will be made by the end of calendar year 2006 (November or December 2006).

Discussion focused on clarification of how the budgets are developed and the PIF funds, and the need for stable funding at the units and sites for staffing purposes.

**Strategic and Operational Oversight and Coordination of the HIV/AIDS Clinical Trials Networks** – *J. Kublin, M.D.*

Dr. Kublin reviewed the roles and responsibilities of two leadership groups that have been formed as well as the role and priorities of the HIV/AIDS Network Coordination Office (HANC). The AIDS Clinical Trials Network Strategic Working Group (SWG) was established to provide insight on the coordinated efforts of the clinical trials networks, and on critical issues that cut across all six networks, including priority setting and specific scientific plans, progress and opportunities. The SWG will serve as a working group of the ARAC and will be comprised of representatives from each network, Community Partners, CHAVI and the Adolescent Trials Network, partner NIH institutes and centers, OAR, ARAC, HANC, NIAID and DAIDS and external experts designated by NIAID. Meeting 2-3 times a year, the agenda for this group will be driven by potential high impact/high resource studies and other issues surrounding network scientific research priorities and network coordination. Deliberations and findings will be shared with the NIAID and DAIDS through the ARAC.

The AIDS Clinical Trials Network Leadership Operations Group was also established so that the Principal Investigators of each network, the chair of Community Partners and the leadership coordinator of HANC could work toward implementing and advancing optimal collaborative research, consider crucial operational and scientific questions and develop recommendations for improving efficiency. This group will meet several times per month most frequently by conference call.

The HIV/AIDS Network Coordination Office (HANC) was established in October 2004 to help the networks begin identifying opportunities for coordination, increased communication, and streamlining processes. In this new award period, the HANC office will play a key role in facilitating coordination, collaboration and communication among the networks and research partners. Dr. Kublin reviewed the numerous cross-network committees and working groups that are receiving HANC support; they span the areas of cross network training, laboratory, community, statistical and data management, and evaluation.

Discussion addressed collaborative efforts with other research partners and efforts to include them in some of the cross-network committees and support for HANC, which is estimated to be between $800,000 and $1.2M in year 1.

Dr. Holmes reflected on the various challenges that the committee has addressed during his 5 years on the ARAC: a flat budget, impressive growth of the clinical trials networks, growth of feasibility and acceptability research, and regulatory and policy constraints that has affected investigator initiated research. He cautioned the ARAC to remain focused on what is really "value added" when evaluating new initiatives and activities, and for the Division to have restraint on the number of directed initiatives it puts forth. The Committee and meeting participants all applauded his outstanding leadership as chair of the committee.

## VI. 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. George Drusano, who joined the meeting as an *ad hoc* member of the Subcommittee. Dr. Drusano is an infectious diseases physician based at Ordway Research Institute in Albany, New York. She then referred to the Branch Chiefs/Acting Branch Chiefs in attendance to introduce their respective new hires.

Dr. Heilman noted that there were several concepts to present to the Subcommittee today for approval, and that most of them fell in the therapeutics realm. Given that focus, she informed the Subcommittee that she felt it would be beneficial to provide them with an overview of DMID's therapeutics program, which has grown significantly in recent years. She acknowledged the role Council member Marty Rosenberg has played in recent years, advising NIAID on therapeutic issues, and then introduced Dr. Michael Kurilla, Associate Director for BioDefense Product Development, who provided an overview of how DMID's therapeutics program has evolved in recent years. In his presentation, Dr. Kurilla spoke about the problems of resistance and stagnation with regard to new antimicrobial development, and then described recent and current DMID efforts to enhance the Institute's response to these issues. In particular, he noted several NIAID-sponsored meetings focused on these topics, and described recent scientific efforts to enhance DMID's antimicrobial drug development infrastructure.

The Subcommittee then considered four concepts:
Development of Therapeutic Agents for Selected Biodefense Pathogens – this initiative is designed to advance promising candidate therapeutics for select high priority biodefense viral and bacterial pathogens, with a special emphasis on therapeutics with broad spectrum activity or that address antimicrobial resistance. The concept was approved by the Subcommittee.

Pharmacological Approaches to Combating Antimicrobial Resistance – through this initiative, academic or industry scientists will be encouraged to submit creative proposals for research on existing antimicrobial regimens using *in vitro* and animal models that are based on human pharmacokinetics with the expectation that these studies will lead to a better understanding of the contribution of PK/PD correlates to the development and/or avoidance of drug resistance. These studies are also expected to result in improved animal models of infection and drug treatment, and are expected to inform the discovery and development process for new drug candidates. The Subcommittee approved the concept.

Phase I Clinical Trial Unit for Therapeutics Against Infectious Diseases – the goal of this initiative is to provide a DMID clinical resource with the capability and expertise to undertake Phase I clinical trials for

drugs. Under this initiative Phase I clinical trials of promising candidate therapeutics will be conducted. In collaboration with program staff, the contractor will be responsible for design and implementation, conduct and completion of all clinical trials. The Subcommittee approved the concept.

Indo-U.S. Vaccine Action Program (VAP) Small Research Grant Program – the goal of this initiative is to encourage collaborative research on issues relevant to the ongoing Indo-U.S. Vaccine Action Program, which supports a broad spectrum of activities relating to immunization. The Subcommittee approved the concept.

## VII. ADJOURNMENT

The meeting of the Council was adjourned at 5:00 p.m., on Monday, September 18, 2006.

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

**_____*-s-*_____** **__12/01/2006_____**
Anthony S. Fauci, M.D. Date
Chairman, National Advisory Allergy
and Infectious Diseases Council
Director, National Institute of Allergy
and Infectious Diseases

**_____*-s-*_____** **___11/28/2006 ___**
Paula Strickland, Ph.D. Date
Executive Secretary
National Advisory Allergy and Infectious
Diseases Council
Acting Director, Division of Extramural Activities
National Institute of Allergy and Infectious
Diseases

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.