NATIONAL INSTITUTES OF HEALTH

NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL

MINUTES OF MEETING

May 22, 2006

The 153rd meeting of the National Advisory Allergy and Infectious Diseases Council (NAAIDC) was convened at 10:15 a.m. on Monday, May 22, 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 Chairman.

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. Charles Davis
Dr. Richard Insel
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. Megan Sykes
Dr. Nathan Thielman
Dr. Gail Wertz

***Ex Officio* Members Present:**

Dr. Anthony Fauci
Major General Eric Schoomaker
Dr. Elias Zerhouni

Council Members Absent:

Dr. Stanley Chapman
Dr. Anthony D'Alessandro
Dr. Kathryn Edwards
Dr. Gary Schoolnik

***Ex Officio* Members Absent:**

Dr. Mitchell Cohen
Dr. Lawrence Deyton

***Ad Hoc* Members:**

Dr. William Bertrand
Dr. Alexandre Sette

NIAID Senior Staff:

Dr. Hugh Auchincloss
Dr. John McGowan
Dr. Irene Glowinski
Dr. Cliff Lane
Dr. Daniel Rotrosen
Dr. Ed Tramont
Dr. Kathryn Zoon

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 3,903 research and training applications with primary assignment to NIAID for a requested amount of $1,535,506,850 in first-year direct costs and recommended approval of 1,021 applications for $630,659,189 in first-year direct costs. Five 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. Chapman, D'Alessandro, Edwards, and Schoolnik would be absent. Also, two *ex officio* members, Drs. Mitch Cohen and Lawrence Deyton were unable to attend. He introduced two *ad hoc* Council members: Dr. Alexandre Sette, La Jolla Institute for Allergy and Immunology, and Dr. William Bertrand, Center for International Development and Technology Transfer at Tulane.

A written report about the Vaccine Research Center was distributed to the Council members.

Consideration of Minutes of Previous Meeting

The minutes of the January 30, 2006, meeting were considered and approved as written.

Staff and Organizational Changes

NIAID reorganized in April 2006. The new structure includes three deputy directors: a principal deputy director, Dr. Hugh Auchincloss; a deputy director for science management, Dr. John McGowan; and a deputy director for clinical research and special projects, Dr. Cliff Lane. Dr. Lane is also director of the new Division of Clinical Research.

Several staff changes have taken place since the last Council meeting. In the Division of Intramural Research (DIR), Dr. Thomas Quinn is the new associate director for international research, and Dr. Jeffrey Taubenberger is now senior investigator in the Laboratory of Infectious Diseases. Dr. Philip Murphy is the new chief of the Laboratory of Molecular Immunology.

In the Division of AIDS, Dr. Alan Fix was named chief of the Vaccine Clinical Research Branch in the Vaccine and Prevention Research Program. Dr. Joanne Rhoads is the new associate director for clinical research in the Division of Microbiology and Infectious Diseases.

Due to a restructuring, NIAID's Office of Acquisitions has four new branch chiefs: Ms. Barbara Shadrick, Microbiology and Infectious Diseases Research Contracts Branch B; Ms. Olga Acosta-Polston, Acquisition Management and Policy Branch; Ms. Sharon Kraft, Microbiology and Infectious Diseases Research Contracts Branch A; and Ms. Shelly Goergen, Allergy, Immunology, and Transplantation Research Contracts Branch.

Dr. Fauci announced that in March of 2006 in Mali, Drs. Bob Gwadz, Lou Miller, and Cliff Lane received the Malian National Medal of Honor Rank of Knight, Drs. Gwadz and Miller for their work on malaria vaccines and Dr. Lane for his research on HIV/AIDS.

Budget Update

The President's FY 2007 budget request, the first step in the appropriations process, asks for a $4.4 billion budget for NIAID, 0.3 percent more than this fiscal year. NIAID continues to fare better than other ICs and NIH, whose budgets are either flat or falling. NIH's Office of the Director would receive almost $140 million more monies mainly for advanced product development of biodefense countermeasures and the Roadmap.

Recent increases for NIAID reflect growth in AIDS and biodefense and a slightly greater proportion of the recent doubling than the NIH mean. NIAID's proposed increase for 2007 is targeted to pandemic influenza, HIV/AIDS vaccines, and our contribution to the NIH Genes and Environment Initiative, which will explore the relative contributions of genes and the environment to major public health disorders.

Legislative Update

In March, Dr. Fauci testified at a congressional hearing on avian influenza, focusing on a human pandemic and research to improve our ability to respond to an influenza pandemic and seasonal flu.

Dr. Fauci accompanied Dr. Zerhouni to the 2007 House and Senate appropriation hearings. Other briefings addressed emerging and re-emerging infectious diseases in global health and avian influenza. Drs. Christine Sizemore and Lee Hall briefed the Senate Committee on Health, Education, Labor, and Pensions on neglected diseases. Dr. Karen Lacourciere briefed Representative Wayne Gilchrist on the scientific and public health challenges of preparing for seasonal and pandemic influenza.

Other Information Items

As a follow-up to his presentation at September 2005 Council, Dr. Fauci gave an update on the Working Group on Regulatory Activities in DAIDS – the "Sullivan Committee." The group conducted its evaluation between September 2005 and April 2006 and recently delivered its final report.

It did not find safety issues but found that rapid increases in DAIDS staff as well as in complexity and international efforts have led to operating inefficiencies. Recommendations include revising the organizational structure and authority for developing regulatory policies and resolving challenges common to U.S. sponsors and those in resource-poor countries. The Institute is responding by standardizing clinical trials processes and assessing DAIDS' organizational structure.

The C.W. Bill Young Center for Biodefense and Emerging Infectious Diseases was dedicated on May 2, 2006. The building has BSL-2 and BSL-3 laboratories, animal care areas, offices, and, conference rooms, including one dedicated to former NIAID Deputy Director John LaMontagne. Research in the facility will focus on respiratory viruses and bacteria, insect-borne viruses, immunology, and vaccines.

Dr. Fauci gave a brief update on the potential for an influenza pandemic. In February NIAID began a series of meetings called Influenza Research Summit. Two additional meetings are planned. The second will involve outside experts, and the third will be an interagency symposium. The effort will result in a report to guide future research. Dr. Fauci presented preliminary results of a pre-pandemic H5N1 vaccine study along with major challenges faced in developing a vaccine.

III. NIH at the Crossroads: Myths, Realities, and Strategies for the Future – Elias A. Zerhouni, M.D., Director, NIH

Dr. Zerhouni described the current period at NIH as a "perfect storm." Many factors are influencing the NIH budget including federal deficits, defense and homeland security needs, Katrina, pandemic flu, post-doubling effects, a focus on physical science, and biomedical research inflation of three to five percent.

There is concern in the scientific community about success rates and what's driving them, including 1) emphasis on applied science at the expense of basic science, 2) NIH's shift toward solicited research, and 3) the expense of the NIH director's Roadmap. Dr. Zerhouni used data to address each issue.

He discussed the three drivers of success rates. The main driver is the building of new research capacity throughout the U.S. and the increase in tenure track faculty as the NIH budget doubled. When the budget leveled, the number of applicants continued to increase as new buildings were ready and new faculty started applying for funding.

The second issue is that our appropriations have fallen below our inflation rate. The number of grant applications has increased, but purchasing power has decreased. The third issue is our outyear commitments. Funds for new grants come from grants that are ending and any increases.

Dr. Zerhouni's primary message was that NIH is transforming medicine through discovery. We need to convey a unified message and increase communications about the positive impact of NIH at local, regional, and national levels. The NIH budget should not be seen as a cost but an investment.

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

Lisa Siquel, CCRC, CCRA, and CCRP - Ms. Siquel joined the Transplantation Immunobiology Branch in February 2006 as a Health Specialist. She received her Bachelor's degree in psychology from University of California Los Angeles, and has several professional certifications in clinical research. Prior to joining the Division, she was a Senior Clinical Research Associate for a contract research organization, in Bethesda, Maryland.

Richard Legg - Mr. Legg joined the Office of Regulatory Affairs in April 2006 as a Program Specialist. He received his Bachelor's degree in healthcare management from Southern Illinois University. Prior to joining the Division, he worked at Walter Reed Army Medical Center.

Tina Sledge, RN, BSN - Ms. Sledge joined the Transplantation Immunobiology Branch in January 2006 as a Nurse Consultant. She received her Bachelor's degree in nursing from the University of Kentucky. Prior to joining the Division, she was a nurse clinician working with cardiothoracic surgery patients and transplant research coordinators at the University of Kentucky.

Lynda Chiodetti, PhD - Dr. Chiodetti was recently appointed Chief of the Molecular and Structural Immunology Section, in the Basic Immunology Branch. Since 2004, she served as a Program Officer in the Basic Immunology Branch. Dr. Chiodetti received her doctorate degree from the George Washington

University. Prior to joining the Division, Dr. Chiodetti was an investigator for the NIAID intramural research program, where her research focused on T cell activation and tolerance.

SCIENTIFIC INITIATIVES

Collaborative Network for Clinical Research on Immune Tolerance (RFP-NIH-NIAID-DAIT-07-033): The purpose of this RFP is to re-compete the "Collaborative Network for Clinical Research on Immune Tolerance," an international collaborative research effort to conduct clinical evaluation and mechanisms of action of new therapies to induce immune tolerance and improve treatments for autoimmune diseases, allergic diseases, and immune-mediated graft rejection.

Radionuclide Decorporation Agents for Radiation/Nuclear Emergencies: Project BioShield (R01) (RFA-AI-06-030): This is a funding opportunity announcement (FOA) to accelerate the development of safe and effective products to remove radionuclides from the body (decorporation) following nuclear contamination from any source. Specifically, candidate products will demonstrate an increase in efficiency and rate of radionuclide elimination from the body after contamination due to ingestion, inhalation or transdermal absorption.

DIVISION ACTIVITIES

Expert Panel on Food Allergy Research: On March 13-14, 2006, on behalf of the Secretary of Health and Human Services and at the request of Congress, the NIAID convened an expert panel on food allergy research. The panel reviewed basic and clinical research efforts related to food allergies and developed recommendations to the Secretary for enhancing and coordinating food allergy research. It is anticipated that the panel's recommendations will be forwarded to the Secretary this summer.

American Association of Immunologists (AAI) Annual Meeting: NIAID activities at the annual AAI meeting held May 12-16, in Boston, included:

- Twenty-second annual "Symposium on Contemporary Topics in Immunology," cosponsored by the NIAID and the AAI
- "The Humanized Mouse: Past, Present and Future" symposium, co-sponsored by the NIAID, NCI, NIDDK, and AAI
- "Bewitched, Bothered and Bewildered: Strategies for Engineering B Cell Reactivity in HIV Vaccination" workshop, co-sponsored by the NIAID, AAI, and NIH Office of AIDS Research
- Focus group meeting to discuss NIAID/NIH policies and issues of concern to basic and clinical research extramural investigators.

Innate Immune Receptors and Adjuvant Discovery Program All-Hands Meeting: On March 8, 2006, DAIT sponsored a workshop to review the progress of five contracts awarded under the NIAID RFP, "Innate Immune Receptors and Adjuvant Discovery." This meeting provided an opportunity for the principal investigators to present their results to date, review problems that had arisen during the high-throughput screening phase and network with each other as well as with program staff from NIAID and other interested government agencies. The purpose of this program is to support the discovery and development of novel adjuvants for vaccines against NIAID Category A-C priority pathogens.

Immune Ontology Workshop: On March 21-22, 2006, the DAIT Office of Biomedical Informatics and the Basic Immunology Branch sponsored a workshop on Immune Ontology. An ontology is a formal way of representing knowledge to provide a computational framework for assimilating biomedical content, integrating existing data and knowledge resources, and improving knowledge sharing. DAIT currently

supports several large programs that require extensive database development or the use of databases. This workshop brought together experts in ontology development and DAIT-supported investigators to discuss: standards and compatibility in different ontology frameworks; new and ongoing research and projects using or developing an immune-based ontology; and ideas, technologies, and approaches for formalizing immune ontology development.

Systems Approach to Innate Immunity, Inflammation, and Sepsis- Third Annual Meeting: The purpose of this project is to develop a comprehensive picture of the innate immune response to sepsis and other infectious diseases, including those caused by NIAID Category A-C Priority Pathogens. The team, headed by Drs. Richard Ulevitch (Scripps Research Institute) and Alan Aderem (Institute for Systems Biology, ISB), is focusing on the signaling pathways involved in innate immune cell activation and the subsequent induction of adaptive immunity. The team has been very productive over the past three years, and accomplishments include: 1) the production of monoclonal antibodies (mAbs) and cell lines expressing human and murine innate immune molecules. Eight mAbs have been sent to the NIAID Biodefense and Emerging Infections Research Resources Repository (BEI Resources) for public distribution (http://www.beiresources.org/); 2) forward genetics for the detection of novel immunological genes, using ENU mutagenesis: approximately 83,556 germ line mutant mice have been generated. A total of 67 mutations have been mapped to chromosomal intervals, and the molecular defect has been identified in 53 instances. Thirty of the mutations result in immunological phenotypes. Sixteen of these mice have been sent to the Mutant Mouse Regional Resource Centers for public distribution; and 3) proteomic identification of the TLR4 stimulated macrophage secretome. More than 200 proteins were identified by proteomics methods, approximately 160 proteins were not previously identified in the context of macrophage biology. Additional information, datasets generated as part of this program, and data analysis software used in this program are available at: http://www.innateimmunity-systemsbiology.org/

Modeling Immunity for Biodefense Centers Annual Meeting: DAIT organized the first annual meeting for four Immune Modeling Centers, funded in September 2005. The Centers, located at Duke University, Mount Sinai School of Medicine, University of Pittsburgh, and University of Rochester, are funded to develop mathematical modeling packages, validated in experimental systems, which provide tools for modeling of host immune responses to infection and vaccines. The investigators presented their research progress and engaged in further discussions for resource and data sharing among the centers. To foster additional collaborations, DAIT staff invited investigators from two large government funded programs to present their findings and resources to the Immune Modeling Center investigators. These programs were the Models of Infectious Disease Agent Study (MIDAS), funded by the National Institute of General Medical Sciences, NIH, and TeraGrid, funded by the National Science Foundation. The main goal of the MIDAS network is to develop computational models of the interactions between infectious agents and their hosts, disease spread, prediction systems, and response strategies. The models will be useful to policymakers, public health workers, and other researchers who want to better understand and respond to emerging infectious diseases. TeraGrid is a national, distributed cyber infrastructure for open scientific research. Through high-performance network connections, TeraGrid integrates high-performance computers, data resources and tools, and high-end experimental facilities around the country, with over 40 teraflops of computing power, nearly 2 petabytes of rotating storage, and specialized data analysis and visualization resources in production.

DAIT's Food Allergy Research Program and DAIT's Research Resources: Tetramer Facility and the Immune Epitope Discovery Program

Ad hoc Council members and division staff presented an interesting and stimulating discussion on DAIT's Food Allergy Research Program and DAIT's Research Resources: Tetramer Facility and the Immune Epitope Discovery Program. Moderator and discussant Marshall Plaut, M.D., Chief, Allergic Mechanisms Section, Division of Allergy, Immunology and Transplantation opened the discussion with an overview of the Report on the Food Allergy Expert Panel Meeting; and Hugh Sampson, M.D. Chief, Pediatric Allergy and Immunology, Mount Sinai School of Medicine presented the perspective of the Consortium of Food Allergy Research and Future Directions. Alison Deckhut Augustine, Ph.D., Chief, Immunoregulation Section, also moderator and discussant presented an Update on the Immune Epitope Discovery Program and the NIH Tetramer Facility Contract. Alessandro Sette, Dr. Sc. Biol., Head, Division of Vaccine Discovery and Director, Center for Emerging Diseases and Biodefense, La Jolla Institute for Allergy and Immunology ended the session with a discussion on the Immune Epitope Database and Analysis Program.

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. Tramont formally welcomed Dr. Debbi Birx, Division Director, Global AIDS Program, of the Centers for Disease Control and Prevention (CDC), who recently became an ex officio member of the ARAC representing the CDC. Dr. Tramont also announced the recent appointment of Dr. Alan Fix as Chief, Vaccine Clinical Research Branch, in the Vaccine Research Program at DAIDS.

Dr. Tramont noted that the total NIH budget, adjusted for inflation, has decreased in the past two years, although the NIAID budget has experienced a slight increase. In FY 2007 biodefense research will account for the largest fraction of NIAID funding—slightly more than the amount allocated for HIV/AIDS research and slightly more than all other NIAID funding. Within NIAID, significant increases in FY 2007 funding include $8 million for pandemic influenza, $2 million for HIV/AIDS, and $2 million for the genes-and-environment initiative.

The applications for both the leadership and clinical trial units of the HIV/AIDS clinical trials networks have undergone the standard NIH scientific peer review. The awards for the network leadership are on schedule to be made at the end of June 2006. This summer and early fall NIAID will work to fully establish the networks -- reviewing the results of the CTU reviews, and aligning CTUs with respective network(s). It is anticipated that awards for the CTUs will be made by the end of calendar year 2006.

Dr. Tramont reviewed the history of the strategic development of DAIDS' comprehensive vaccine program, including the Vaccine Research Program and the HIV Vaccine Trials Network (HVTN) as well as collaborative efforts with NIAID's Vaccine Research Center (VRC), US Military HIV Research Program (USMHRP), Partners for AIDS Vaccine Evaluation (PAVE) and newer initiatives such as NVITALS, (NIAIDS Vaccine Immunogenicity T Cell Antibody Laboratory) and the Center for HIV/AIDS Vaccine Immunology (CHAVI).

Update: AIDS Vaccine Research Working Group – *James Bradac, Ph.D.*

Dr. Bradac reviewed current membership of the AVRWG as well as the agendas of the past four meetings. The AVRWG has four new members, Drs. Nina Russell, R. Paul Johnson, Juliana McElrath,

and Margaret Liu, and a new chairman, Dr. Scott Hammer. Dr. Timothy Mastro and Col. Nelson Michael are new ex officio members.

In January 2005, the AVRWG held a persistent-vector workshop, featuring research presentations and program updates. The May meeting, which focused on HIV-1 envelope immunogens to induce broadly neutralizing antibodies, culminated in an agreement that this area of research should be a high priority. At the AVRWG's September 2005 meeting grand challenge grants were discussed along with the Global HIV/AIDS Vaccine Enterprise and the CHAVI. The most recent meeting, January 10-11, 2006, focused on mucosal immunology and the preservation of mucosal CD4 cells as a determinant of vaccine and therapeutic efficacy and a discussion of the Merck IIb trial (HVTN 503) in South Africa.

The next meeting of the AVRWG will take place on May 25-26, 2006 and will be a workshop on strategies to elicit and analyze mucosal immune response to HIV and SIV. The AVRWG will also convene in Amsterdam in August 2006, in conjunction with the International AIDS Vaccine Conference.

Concept Review: Basic and Epidemiological Research – *Carl Dieffenbach, Ph.D.*

Dr. Dieffenbach presented two concepts for initiatives for consideration by the ARAC: the Women's HIV Interdisciplinary Network II (WHIN II) and the Women's Interagency HIV Study IV (WIHS IV).

The WHIN I was initiated by the National Institute of Child Health and Human Development (NICHD) in 2000 with the objective of expanding knowledge of the pathogenesis of HIV-1 infection in women. It was developed under a cooperative agreement with three sites and, has made numerous scientific contributions in the areas of viral factors and HIV transmission; mucosal immunology and virology; host factors and immunology.

It is proposed that NIAID provide partial support for WHIN II -- $1.5 million of the $6 million total first year cost. NIAID would also provide oversight and management of the initiative in collaboration with NICHD. The collaboration is designed to enhance the breadth of the research agenda. Dr. Dieffenbach further explained that the Request for Applications (RFA) for WHIN II would not be issued until after a review of WHIN, which is being organized by the Office of AIDS Research (OAR), is complete. It is anticipated that four applications would be awarded in 2008.

The ARAC reviewers agreed on the importance of the WHIN; it has been scientifically productive and holds promise for future discoveries. The reviewers encouraged the continued emphasis of WHIN on pathogenesis research and the development of linkages with other networks and gender specific HIV/AIDS research programs.

The WIHS is supported by the NIAID, NICHD, the National Cancer Institute (NCI), and the National Institute on Drug Abuse (NIDA) and is conducted as a cooperative agreement in six urban areas, with an additional data center in Maryland. Expansion of the WIHS was completed in 2000 in an effort to have a cohort that would support a better understanding of the long-term clinical history of HIV in the era of highly effective antiretroviral therapy. WIHS III will continue to conduct studies that increase our understanding of the long-term clinical effects of HIV, including HIV-related outcomes and other disease manifestations, and studies that elucidate the interaction between HIV and other infection in an era of treated HIV disease. The total first-year cost for the WIHS will be $23 million, $18 million of which would be from NIAID.

The ARAC reviewers noted the productivity of the WIHS and discussed whether the cohort should be further increased using targeted enrollment at high-performance sites and/or adding an additional in the southern part of the U.S.

In discussion, the ARAC members sought to understand the differences between the WHIN and the WIHS. It was explained that the WIHS is an epidemiological cohort study that banks specimens and has a large number of enrolled participants. In contrast, the WHIN is more of a mechanism that will exploit existing cohorts and data, working in parallel with other research programs. Some ARAC members wondered whether funds for these cooperative-agreement projects should instead be given to R01 programs. Others stressed the importance of these network projects and their ability to incorporate work from R01s.

The ARAC members discussed the possibility of adding a southern site to the WIHS study. They recognized the uniqueness of southern populations, for example, differences in access to care because of more rural settings. They also wondered whether the study would benefit from cohorts in developing countries.

Dr. Holmes asked the ARAC members to vote on the renewal of WHIN and WIHS. The committee approved the concept for the WIHS initiative with the modification that consideration is given to the relative benefits of increasing enrollment of women at high performing sites vs. inclusion of a new rural (southern) site.

For the WHIN, the committee also voted approval of the concept for this initiative with several modifications:
1) RFA development should incorporate the recommendations from the external review being convened by the NIH Office of AIDS Research
2) The network's primary focus should be on the pathogenesis and mechanisms of HIV infection in women (not health care utilization or behavioral issues)
3) Increased linkages/collaboration be sought with the many groups (e.g. clinical research networks and cohorts) working on gender issues and HIV, particularly those with an international scope.

Concept Review: Vaccine Research – *James Bradac, Ph.D.*

Dr. Bradac described the HIV Database and Analysis Unit, the history of which dates to 1987, when the NIAID created an interagency agreement with the Department of Energy (DOE) to create the database at the Los Alamos National Laboratory (LANL). The objective of the Unit is to provide a centralized resource for the compilation and analysis of genetic sequences, immunological epitopes, and associated data for HIV-1 and related lentiviruses. It currently features four databases: the HIV Genetic Sequence Database, the Immunology Database, the Drug Resistance Database, and the Nonhuman Primate Vaccine Trials Database. Based on the collected data, the NIAID distributes printed and online compendia of genetic sequences and immunology information to the research community each year.

The Genetic Sequence Database contains sequence alignments, online tutorials, a FAQ section, reviews, links, and tools. The HIV Immunology Database features data extracted from the HIV immunology literature. The Nonhuman Primate database contains publications on HIV/SIV vaccine studies in the nonhuman primate model. The Resistance Database is a compilation of mutations in the HIV genome that confer resistance to anti-HIV drugs. All four databases can be accessed through http://hiv-web.lanl.gov.

LANL has been successful in recompeting for the HIV Database and Analysis Unit three times since its inception. Dr. Bradac presented to ARAC Program's desire to renew the database for a seven-year period as a noncompetitive Interagency Agreement with the DOE.

Reviewers characterized the Unit as being highly effective and praised it for tracking the needs of the field. They raised the possibility of adding information on standardized virus neutralization panels when they become available and adding information about host genetic polymorphisms that associate with HIV pathogenesis.

The ARAC voted to approve the concept for this interagency agreement for the HIV Database and Analysis Unit at a first-year cost of $2.2 million.

Concept Review: Prevention Research – *Roberta Black, Ph.D.*

Dr. Black described the NIAID's Integrated Preclinical/Clinical Program for HIV Topical Microbicides, which has the following objectives:

- To stimulate a strong, diverse base in preclinical discovery and development
- To support translation from preclinical studies to exploratory clinical studies
- To facilitate the introduction of new methods and expertise in the field.

The program promotes the development of safe, effective, and acceptable microbicides, using hypothesis-driven studies and private-sector involvement. It produced the first report of combination microbicide efficacy in nonhuman primates and supported the validation of the protein-based R5 microbicide PSC-RANTES. It has also helped to elucidate the role of dendritic cells in transmission. The program emphasizes safety testing, encouraging the use of technologies such as the new noninvasive imaging technology known as optical coherence tomography.

ARAC reviewers were supportive of the program, but noted a lack of support for development of candidate microbicides for HIV-infected individuals. In discussion several issues were raised, including the need to more rapidly eliminate less than optimal candidates, by conducting safety evaluations, in particular, genotoxicity testing, earlier in the development process; the need for greater participation from the pharmaceutical industry; increased advancement of products to clinical testing; better understanding of optimal formulations and behavioral factors; identification of surrogate markers; and better preclinical models for toxicity, activity, and efficacy.

The ARAC voted to approve the concept for the Integrated Preclinical/Clinical Program for HIV Topical Microbicides initiative at a first-year total cost of $3 million.

Concept Review: Program Operations and Scientific Information
– *Matthew Murguia*

Mr. Murguia described the operations of the DAIDS Research Support Services, which is a comprehensive and flexible mechanism for supporting research management activities. Tasks of the Support Services contract include travel support (e.g., transportation, lodging, honoraria) meeting and conference support (e.g., facilities, invitations, materials, writer services, graphic design, Web development), and program support (e.g., teleconferences, publishing, document storage and distribution, evaluation).

The ARAC members voted to approve the concept for the Research Support Services contract initiative at a first-year total cost of $1 million.

Concept Review: Vaccine Research – *Peggy Johnston, Ph.D.*

Dr. Johnston described development of the new Global HIV/AIDS Vaccine Enterprise (GHAVE) Secretariat. The GHAVE is a virtual consortium of independent organizations that seeks to accelerate the development of a preventive HIV vaccine by coordinating efforts at a global level, facilitating the use of common tools and technologies, and ensuring access to resources. Endorsed by the G8, the GHAVE will stimulate the development of HIV vaccine manufacturing capacity, establish standardized preclinical and clinical laboratory assessment, optimize interactions among regulatory authorities, and encourage engagement by scientists from developing countries.

The Secretariat for the GHAVE will perform scientific stewardship (e.g., updating a scientific strategic plan), manage communication and knowledge, and develop policies (e.g., about financing, intellectual properties, and regulations). Dr. Johnston presented a proposal to create a high funding ceiling (up to $22.5 million for a 7-year contract period) to help support the scientific activities of the Secretariat, which would allow funding to be adjusted upwards if its operations are successful and the NIAID budget grows. In discussion, the ARAC members debated the wisdom of establishing such a high ceiling and how the success of the Secretariat could be measured.

The ARAC voted to approve the concept for the GHAVE Secretariat contract initiative at $1 million for the first two years, with a report back to ARAC after that time. Pending contractor progress, the contract would continue at a level budget, with a maximum ceiling of up to $14 million over the 7 years of the award to permit some growth if the NIAID budget for HIV vaccines grows. (Note: In consideration of the Institute's budget limitations, NIAID leadership made a decision to hold the contract ceiling to $7 million over 7 years).

Future Business

The ARAC members cited the need to maintain, or protect, the support for investigator-initiated research. This important issue should be considered along with Dr. Zerhouni's efforts to increase the support for new investigators. Dr. Johnston noted that the NIAID has a dual mission of (1) addressing infectious diseases through, for example, basic research and (2) addressing threats and countermeasures. Dr. Holmes proposed that the ARAC discuss these issues at the next meeting and include a report on trends in the number of investigator-initiated research proposals funded and total level of funding for them.

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), was unable to chair the May 22 NAAID Microbiology and Infectious Diseases Subcommittee meeting due to travel obligations; Dr. Irene Glowinski, Director of DMID's Office of Scientific Coordination and Program Operations, chaired the meeting in her stead. Dr. Glowinski introduced Dr. William Bertrand, a former member of DMID's Subcommittee, who joined today's meeting as an *ad hoc* member of the Subcommittee. Dr. Bertrand is a Professor at Tulane University's School of Public Health and Tropical Medicine. She then introduced Dr. Joanne Rhoads, who recently joined DMID as the Associate Director for Clinical Research. Dr. Glowinski then referred to the Branch Chiefs/Acting Branch Chiefs in attendance to introduce their own respective new hires.

Noting DMID's efforts to keep the Subcommittee informed about the activities of our large research portfolios and programs, Dr. Glowinski reported that Dr. Clare Schmitt, a program officer with the Enteric and Hepatic Diseases Branch, would be providing a status report on the Food and Waterborne Diseases Integrated Research Network (FWD-IRN) later in the day. She then introduced Dr. Polly Sager, DMID's Assistant Director for International Research in Infectious Diseases, who presented a brief overview on DMID's international training and resource support activities. Dr. Glowinski noted that this topic came up at our last Council meeting. Specifically, the Subcommittee was interested in learning more about the types of support DMID offers international researchers.

In response, Dr. Sager provided a brief overview of DMID's international research portfolio, and briefly outlined related NIH and NIAID responsibilities, particularly for research involving human subjects. She also described the resources we have available to support investigators, e.g., training foreign investigators on how to write NIH grants and conduct clinical research.

Following Dr. Sager's presentation, Dr. Schmitt updated the Subcommittee on activities and advances stemming from the *Food and Waterborne Diseases Integrated Research Network*, which DMID awarded in 2003. This program, comprised of seven contracts, supports multidisciplinary research and the development of products to rapidly identify, prevent, and treat food and waterborne diseases. Efforts under this program are also focused on developing resources, reagents and tools, e.g., animal models, for the scientific community to use.

The Subcommittee then considered three concepts:

Development of Animal Models and Assays for Plague Vaccines -- This initiative is for a new award and will allow NIAID to develop and validate animal models and assays for plague vaccines based on F1 and V antigens. The initiative will be part of a joint effort with the Joint Vaccine Acquisition Program of the Department of Defense to develop and support a plague vaccine through licensure. The Subcommittee commented that they thought this initiative was an example of good use of Government funds, prevents duplication of funds, and promotes data sharing. The Subcommittee unanimously approved the initiative.

Statistical and Data Coordinating Center (SDCC) for Clinical Research in Infectious Diseases – This initiative is a renewal of an existing contract. Based on past events, i.e. biodefense and public health needs of emerging and re-emerging diseases such as pandemic influenza, the new award will be expanded to allow for additional statistical and data management support. The subcommittee acknowledged that the contract is important to the work of the DMID and expressed full support for its renewal. The Subcommittee unanimously approved the initiative.

Cooperative Research Partnerships for Biodefense –This initiative is a continuation of a program to support discovery/design and development of countermeasures (vaccines, therapeutics, adjuvants and diagnostics) against NIAID Category A, B, and C Priority Pathogens. The Subcommittee agreed that this Cooperative Research program is important to achieving the goals of the NIAID Biodefense Program. The Subcommittee unanimously approved the initiative.

VII. ADJOURNMENT

The meeting of the Council was adjourned at 5:40 p.m., on Monday, May 22, 2006.

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

_____-s-_____ **__8-3-2006_____**
Anthony S. Fauci, M.D. Date
Chairman, National Advisory Allergy
and Infectious Diseases Council
Director, National Institute of Allergy
and Infectious Diseases

_____-s-_____ **_8-1-2006_____**
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.