DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL LIBRARY OF MEDICINE

MINUTES OF THE BOARD OF REGENTS
February 7-8, 2006

The 141st meeting of the Board of Regents was convened on February 7-8, 2006, at 9:00 a.m. in the Board Room, Building 38, National Library of Medicine (NLM), National Institutes of Health (NIH), in Bethesda, Maryland. The meeting was open to the public from 9:00 a.m. to 3:45 p.m., followed by a closed session for consideration of grant applications until 4:15 p.m. and then an open session from 4:15 p.m. to 4:45 p.m. On February 8, the meeting was reopened to the public from 9:00 a.m. until adjournment at 12:00 p.m.

MEMBERS PRESENT [Appendix A]**:**
Dr. Thomas Detre [Chair], University of Pittsburgh
Dr. Holly Buchanan, University of New Mexico
Dr. Ernest Carter, Howard University
Dr. Vasiliki Karlis, New York University, College of Dentistry

MEMBERS NOT PRESENT:
Mr. Richard Chabran, California Community Technology Policy Group
Dr. A. Wallace Conerly, University of Mississippi Medical Center
Honorable Newt Gingrich, The Gingrich Group

EX OFFICIO AND ALTERNATE MEMBERS PRESENT:
Ms. Eleanor Frierson, U.S. Department of Agriculture
MGEN Bruce Green, U.S. Department of the Air Force
Dr. Deanna Marcum, U.S. Library of Congress
Dr. Kenneth Moritsugu, Deputy Surgeon General, Public Health Service
Col. John Powers, U.S. Department of the Army
Dr. Dale Smith, Uniformed Services University of the Health Sciences
Dr. Sylvia Spengler, National Science Foundation
Capt. Robert Taft, U.S. Department of the Navy
Ms. Mary Ann Tatman, U.S. Department of Veterans Affairs

CONSULTANTS TO THE BOR PRESENT:
Dr. Tenley Albright, Whitehead Institute for Biomedical Research
Dr. Marion Ball, Johns Hopkins School of Nursing
Dr. James Gray, Microsoft Research
Dr. Clement McDonald, Regenstrief Institute, Inc.
Dr. Cynthia Morton, Brigham and Women's Hospital
Dr. William Stead, Vanderbilt University
Dr. H. Kenneth Walker, Emory University School of Medicine

SPEAKERS AND INVITED GUESTS PRESENT:
Dr. Jeremy Berg, Director, National Institute of General Medical Sciences, NIH
Dr. Yves Lussier, University of Chicago
Dr. Jeffrey Taubenberger, Armed Forces Institute of Pathology

MEMBERS OF THE PUBLIC PRESENT:
Ms. Mila Becker, American Society of Hematology
Mr. Vince Haley, American Enterprise Institute
Mrs. Mary Lindberg, Public
Ms. Alice Raanam, American Physiological Society
Ms. Eleanore Tupscott, American Society of Hematology
Mr. Thomas West, The Krasnow Institute

FEDERAL EMPLOYEES PRESENT:
Dr. Donald A.B. Lindberg, Director, NLM
Ms. Betsy Humphreys, Deputy Director, NLM
Dr. Donald King, Deputy Director for Research and Education, NLM
Dr. Michael Ackerman, High Performance Computing & Communication, NLM
Dr. Ken Addess, National Center for Biotechnology Information, NLM
Ms. Kristi Anderson, Uniformed Services University of the Health Sciences
Ms. Suzanne Aubuchon, Office of the Director, NLM
Ms. Joyce Backus, Division of Library Operations, NLM
Dr. Dennis Benson, National Center for Biotechnology Information, NLM
Dr. Joe Bischoff, National Center for Biotechnology Information, NLM
Ms. Susan Buyer, Office of Health Information Program Development, NLM
Dr. Milton Corn, Division of Extramural Programs, NLM
Mr. Todd Danielson, Executive Office, NLM
Mr. Andrew Diggs, Division of Extramural Programs, NLM
Dr. Mariana Dimitrov, Lister Hill Center, NLM
Dr. Robin Dupuis, Office of the Director, NIH
Ms. Gale Dutcher, Division of Specialized Information Services, NLM
Dr. Jerome Eastham, National Center for Biotechnology Information, NLM
Dr. Valerie Florance, Division of Extramural Programs, NLM
Dr. Charles Friedman, Division of Extramural Programs, NLM
Dr. Kin Wah Fung, Lister Hill Center, NLM
Dr. Martha Gaie, Lister Hill Center, NLM
Dr. E. Michael Gertz, National Center for Biotechnology Information, NLM
Mr. Alan Graeff, National Center for Biotechnology Information, NLM
Ms. Wendy Hadfield, Executive Office, NLM
Ms. Mary Hollerich, Division of Library Operations, NLM
Dr. Zoe Huang, Division of Extramural Programs, NLM
Ms. Christine Ireland, Division of Extramural Programs, NLM

Ms. Jiwon Kim, Division of Library Operations, NLM
Dr. Lawrence Kingsland, Lister Hill Center, NLM
Ms. Michelle Krever, Division of Extramural Programs, NLM
Mr. Sheldon Kotzin, Division of Library Operations, NLM
Dr. Iyer Lakshminarayan, National Center for Biotechnology Information, NLM
Dr. David Landsman, National Center for Biotechnology Information, NLM
Ms. Janet Laylor, Office of the Director, NLM
Dr. Daniel Le, Lister Hill Center, NLM
Ms. Susan Levine, Office of the Director, NLM
Dr. David Lipman, National Center for Biotechnology Information, NLM
Dr. Simon Liu, Office of Computer and Communications Systems, NLM
Dr. Robert Logan, Lister Hill Center, NLM
Ms. Becky Lyon, Division of Library Operations, NLM
Ms. Wei Ma, Office of Computer and Communications Systems, NLM
Dr. Song Mao, Lister Hill Center, NLM
Mr. James Marcetich, Division of Library Operations, NLM
Mr. Robert Mehnert, Office of Communication and Public Liaison, NLM
Mr. Dwight Mowery, Division of Extramural Programs, NLM
Mr. David Nash, Office of the Director, NLM
Dr. Aaron Navarro, Lister Hill Center, NLM
Dr. Stuart Nelson, Division of Library Operations, NLM
Ms. Jill Newmark, Division of Library Operations, NLM
Dr. James Ostell, National Center for Biotechnology Information, NLM
Dr. Arthur Petrosian, Division of Extramural Programs, NLM
Dr. Lon Phan, National Center for Biotechnology Information, NLM
Dr. Barbara Rapp, Division of Library Operations, NLM
Ms. Julia Royall, Office of Health Information Program Development, NLM
Dr. Michael Sappol, Division of Library Operations, NLM
Dr. Elliot Siegel, Office of Health Information Program Development, NLM
Dr. Hua-Chuan Sim, Division of Extramural Programs, NLM
Dr. Jack Snyder, Division of Specialized Information Services, NLM
Mr. Suresh Srinivasan, Lister Hill Center, NLM
Ms. Marti Szczur, Division of Specialized Information Services, NLM
Dr. Neil Thakur, Office of Extramural Research, NIH
Dr. George Thoma, Lister Hill Center, NLM
Ms. Patricia Tuohy, Division of Library Operations, NLM
Dr. Lowell Vizenor, Lister Hill Center, NLM
Dr. Fredrick Wood, Office of Health Information Program Development, NLM
Dr. Deborah Zarin, Lister Hill Center, NLM

I. OPENING REMARKS

Dr. Thomas Detre, Chair of the NLM Board of Regents, welcomed the Regents, alternates, consultants, and guests to the 141st meeting of the Board. He introduced three newly named members of the Board of Regents who are attending this meeting as guests: Dr. James N. Gray of the Microsoft Bay Area Research Center, San Francisco; Dr. Clement J. McDonald, Director of the Regenstrief Institute for Health Care, Indianapolis; and Dr. Cynthia C. Morton, Director of the Cytogenetics Division, Brigham and Women's Hospital, Boston.

II. REPORT FROM THE DEPUTY SURGEON GENERAL, HHS

Deputy Surgeon General Dr. Kenneth Moritsugu presented the Surgeon General's greetings and his regrets for missing the meeting. Dr. Moritsugu discussed the Public Health Service's response to the natural disaster in the Gulf region. More than 2,500 (of 6,000) Commissioned Corps officers have been deployed, the largest single deployment in the history of the Corps. On January 18, HHS Secretary Michael Leavitt announced his vision of the transformation of the Commissioned Corps—to improve its disaster response capability, to begin to increase the size of the Corps from 6,000 to 6,600, and to use "force management" to help determine the size, shape, and capabilities of the Corps. Dr. Moritsugu said that a new HHS Assistant Secretary for Health has been sworn in, Dr. John Agwunobi. The Surgeon General's "call to action to improve the health and wellness of persons with disabilities" was distributed to the Regents. Other activities under way: the release of a Surgeon General's call to action on correctional health and community health is near; the report of a workshop on child maltreatment and another on a healthy environment are both in the works; a workshop on women and mental health was recently held; and the PHS is currently working on calls to action on global health, health literacy, and preventing underage drinking. A workshop on deep vein thrombosis is planned for the near future. The PHS also continues to work with NIH Human Genome staff on the Family History Project.

III. CONSIDERATION OF MINUTES FROM PREVIOUS MEETING

The Regents approved without change the minutes from the September 2005 meeting.

IV. DATES FOR FUTURE BOARD OF REGENTS MEETINGS

The Board of Regents will meet next on May 9–10, 2006. The Board meeting next fall is September 19–20, 2006. The dates of February 6–7, 2007, were adopted for the following meeting.

V. REPORT OF THE NLM DIRECTOR

Dr. Lindberg announced that Dr. Charles Rice, an ex officio member of the Board, is being inaugurated today as President of the Uniformed Services University of the Health Sciences. He reported on the NLM budget situation—the FY 2006 level is $323,110,000, a $36,000 reduction from the FY 2005 level. He said that taking into account various "taps" the final figure will be roughly $321,000,000 for FY 2006. Rather than reduce each program by a certain percent to reach this figure, NLM has decided to eliminate (or put on hold) several entire programs. The Director said the Board of Regents should keep these budget constraints in mind when it reviews and considers NLM programs. Dr. Lindberg welcomed a new staff member: Mary Hollerich (Head, Collection Access Section, Public Services Division) and noted the departures of Ron Stewart (Deputy Executive Officer) and Mary Smith (NLM Contracts Office). Other new employees were later introduced by Dr. Donald King (Lister Hill Center): Dr. Mariana Dimitrov, Dr. Kim Wah Fung, Suresh Srinivasan, and Dr. Lowell Vizenor; by Dr. Milton Corn (Extramural Programs): Andrew Diggs and Dr. Zoe Huang; and by Dr. David Lipman (National Center for Biotechnology Information): Alan Graef, Dr. Ken Adess, Dr. Jerome Eastham, Dr. Lon Phan, and Dr. Eric Sayers.

In the area of legislation, Dr. Lindberg briefly noted that the American Center for CURES Act of 2005, introduced in the Senate, mentions NLM multiple times in connection with creating a clinical trials database and developing new computational methods for processing genomic data. The bill mandates that the NIH Director require NIH-funded peer-reviewed manuscripts to be deposited in PubMed Central within 6 months of publication. NLM is also directed to develop a multifaceted approach to increasing the number of persons trained in clinical bioinformatics. Finally, there is a section titled "National Library of Medicine Expansion of Facilities." Dr. Lindberg said that another bill, the "Wired for Health Care Quality Act," has the goal of standardizing electronic health information. He distributed to the Regents a copy of a letter sent to the EPA Administrator and signed by 51 members of the Congress asking the Administrator not to increase the level of discharges that would require reporting and not to decrease the reporting frequency from every year to every two years. If implemented, these actions would affect the contents of NLM's Toxic Release Inventory database. The NLM Director reported that the requirements for more space, especially for the staff of the National Center for Biotechnology Information, are becoming more critical. We are taking over more space in NIH's Natcher Building. On a related matter, he reported that the beautiful flowering crabapple trees that have been a distinguishing feature of the NLM for four decades are slowly dying and will be replaced this spring.

The new PubChem database, an important part of the NIH Roadmap Initiative, is being successfully managed by the NCBI and other NIH participants. He affirmed that the NIH is not competing with the American Chemical Society in mounting and supporting this database of small molecules. It currently contains 8.8 million records and 5.5 million molecular structures; 28 organizations have contributed the information. A Working Group convened by the NLM in

December, made up of chemical information producers, discussed that matter extensively and was reassured that PubChem represented no direct competition with the private sector. Dr. Lindberg briefly recounted the history of the development of ClinicalTrials.gov database, which has now grown to 26,000 trials. The primary reason for the recent dramatic growth of the database is the declaration by a group of influential journal editors that they would not consider manuscripts for publication in which the clinical trials had not been registered in ClinicalTrials.gov or other appropriate database. On another matter, the Director brought up the troubling issue of how NLM should deal with what turns out to be faulty, or even fabricated, data. He noted that as "interactive publications" become more widespread it may be easier to analyze the data provided in articles and to detect anomalies or fraud. Dr. Lindberg said that the four Long Range Planning Panels are each meeting twice and will produce a draft for the Board of Regents to consider at its next meeting in May. There are excellent people on the panels and the whole process is going quite well. He said that if any Regents wish to attend the meetings, they would be welcome.

Following Dr. Lindberg's presentation, there was a discussion about how many clinical trials there are altogether. Dr. Deborah Zarin said there really isn't any answer to the question—the definition of just what is a clinical trial is quite "fuzzy." Dr. Lindberg acknowledged that this is an uncertain area. For example, there are certainly many more clinical trials about devices than are registered in our database. Dr. James Gray noted the formidable problem of how to handle the "terabytes and petabytes" of outcomes data that result from clinical trials.

VI. COLLECTING PHENOTYPIC INFORMATION FROM MULTIPLE DATABASES FOR CORRELATION WITH GENOMICS

Dr. Yves Lussier of the University of Chicago Center for Biomedical Informatics, an NLM grantee, discussed his project on collecting phenotypic information (an organism's physical characteristics) with genomic information. There is great optimism that our understanding of diseases can be improved by integrating clinical and genomic data of a patient—identifying the molecular underpinning of medical problems. By developing better and faster diagnosis tools, we can likely reduce the time and cost of drug development and gain insights into personal health and individualized treatment. Dr. Lussier said that NLM has shown vision in supporting such research—about two-thirds of the databases he uses in his research are published by the NLM (examples are the UMLS and PubMed). He cited the nude mouse used in cancer research to illustrate his points. SNOMED is an example of how a vocabulary can be used to express complex phenotypes in a declarative representation system. He discussed Natural Language Processing and the difficulty of mapping from the Language Domain, with its words, phrases, parts of speech, syntactic and semantic structures, to the Conceptual Domain, with its biologically interesting entities, events, processes, and relations. He described PhenoGO, a new system that augments Gene Ontology (GO) annotations with such phenotypic information as cell type, tissue type, organ, or disease. Dr. Lussier showed how his lab also developed a Human Phenome Analyzer to employ a systems approach to diagnosis, understanding, and treatments of

human diseases. The next step is to extend his system into pharmacogenomics so as to be able to predict drug targets and side effects. His research team also plans to develop query engines for the diagnosis of rare disorders, conduct comparative studies of phenotypes with model organism databases, and develop novel cross-disciplinary analyses.

Following Dr. Lussier's presentation, Dr. Cynthia Morton said the complexity of the work Dr. Lussier described is mind-boggling and very exciting. In answer to a question from Dr. Deanna Marcum, Dr. Lussier briefly described the background and area of expertise of the members of his research team.

VII. FEDERAL HEALTH INFORMATION TECHNOLOGY DEVELOPMENTS

Betsy L. Humphreys, NLM Deputy Director, discussed Federal actions taken to promote the adoption of Electronic Health Records and the exchange of electronic health data to support health care and the public health. The NLM became involved in this subject through its Unified Medical Language System (begun in the 1980s) and its familiarity with vocabularies and coding systems. As Dr. Lussier reminded us, NLM has been providing grant support for work in this arena for more than 30 years. Although the VA, DOD, and Indian Health Service have been working on clinical information systems for decades, the pace of Federal activity to promote health data standards picked up with the passage of HIPAA in 1996 and continued with the Consolidated Health Informatics Electronic Government initiative in 2001. In 2003, NLM negotiated the U.S.-wide license for the SNOMED clinical vocabulary. The Medicare Modernization Act of 2003 mandated e-prescribing and a time-limited Commission on Systemic Interoperability, for which the NLM provided a home and which finished its work with the publication of its report, "Ending the Document Game," in October 2005. The Regents have heard about the Commission and its work at past meetings.

In April 2004, President Bush issued an Executive Order "...to provide leadership for the development and nationwide implementation of an interoperable health information technology infrastructure to improve the quality and efficiency of health care…." The Executive Order also established the National Coordinator for Health Information Technology in the HHS Office of the Secretary. In July 2004, the National Coordinator, Dr. David Brailer, and the HHS Secretary released a National Health IT framework, and, later, issued a "request for information" for ideas on how to foster and support a national health information network and Electronic Health Records. As a result, a number of Requests for Proposal were issued in 2005. HHS Secretary Leavitt last fall announced a new high-level advisory committee (which he chairs), called the American Health Information Community, to provide advice and try to reach a consensus about how to push for the adoption of electronic health records. Ms. Humphreys described the committee's public and private makeup.

In October 2005, the Office of the National Coordinator (ONC) awarded three contracts to establish a sustainable standards selection and harmonization process, to set up compliance

certification for Electronic Health Record software products, and to examine barriers to health IT adoption imposed by state privacy and security laws. NLM has one of the four federal seats on the board of the standards harmonization process. Ms. Humphreys then briefly described the Commission on Systemic Interoperability's recently released report (which is on the NLM Web site). HHS action is being taken on a number of the report's 14 recommendations. Returning to other recent events, Ms. Humphreys said that the first standards mandated under the Medicare Modernization Act of 2003 were published in November. The ONC has awarded four new contracts for prototypes for the National Health Information Network architecture. The contracts are to consortia that are headed by large commercial companies. In January 2006, the Interagency Health Information Technology Policy Council was formed, as was the HHS Health Information Technology Policy Council. NLM is represented on this latter council.

All these activities, she said, are designed to help drive the adoption of health IT systems—they will provide infrastructure that will be valuable to the technology industry and help them to develop products that meet the needs of consumers, providers, and the public health environment. The whole initiative is just getting under way. NLM is involved in the standards activities because of our extensive involvement in medical and health terminology and vocabulary work, dating back to the early years of the Unified Medical Language System. Ms. Humphreys briefly described NLM's current involvement with health IT standards, including its work in support of standard clinical vocabularies, collaboration with the FDA on "DailyMed" (to be discussed with the Regents tomorrow), support for aligning the Health Level Seven (HL7) messaging standard with standard vocabularies, and work with NIH to promote use of standards in clinical research. NLM has been partially supported in this work with funds from the Agency for Healthcare Research and Quality and the HHS Office of the Secretary. The ultimate goal, she said, is to have "computers that understand medical meaning," (in Dr. Lindberg's words back in 1985), to be able to be transmit the meaning, and for the meaning to be precise enough so that in some cases a computer can determine what action is needed depending on the data received. We are a long way from there, she said.

Following Ms. Humphreys' presentation, Dr. William Stead (who served on the Commission on Systemic Interoperability) said he believes interoperability can be achieved only if standards are "built into everything from the ground up." He said that the essence of the Commission's report is in the interlocking nature of its recommendations. Working on individual pieces of the overall effort, although important and necessary, may not be sufficient. There is more "noise" than substance that emanates from the confusion about what people mean when they talk about the "Electronic Health Record." Moreover, many people working in this area want to claim credit for all the benefits that are possible. Dr. Stead noted that Secretary Leavitt gave the Commission a good visual graphic—that we need one piece that, when added to the mixture, will crystallize everything around it. Within all the noise, Dr. Stead said, the role of the NLM consistently emerges as a key in the area of controlled terminology—including explicit representation of the semantic relationships among terms and the development of tools for using the controlled terms. We have to learn how to set aside a fraction of every health care dollar to support these

operational, on-going Library functions, he said.

Dr. James Gray said that the stakes in this issue are huge. The anecdotes in the Commission's report are compelling. There are points of light: some institutions do in fact have Electronic Health Records. Although we seem to be on the edge of something, "it" isn't happening. Maybe there are economic incentives that could be applied. It is not a technical problem, he said. Dr. Clement McDonald added that although there are a number of individual institutional Electronic Health Record systems, we have not built anything on a regional, much less a national scale.

VIII. PUBLIC ACCESS WORKING GROUP REPORT

Dr. Thomas Detre chaired the Public Access Working Group, with Dr. Deanna Marcum, co-chair. The 11-member Group (excluding chairs) was established last May to review the impact of the NIH "Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research." Dr. Detre reported to the Board on the Working Group's most recent meeting on November 15, 2005. The Group agreed that information deriving from research supported by the Federal Government should be shared as effectively as possible. The publishers believe that the best way to guarantee quality is through peer review. The article ultimately to be deposited and preserved should be the final version as published in the journal. There was also agreement (with two abstentions) that the policy should be mandatory on the part of the investigators. All agreed that the format and stylistic presentation of an archived manuscript should be close to the version as printed in the journal. Eight of the members agreed that there should be public access to articles within 6 months of publication, but that in some cases flexibility could allow the embargo period to be extended to 12 months. Dr. Detre read to the Board several comments from Dr. Newt Gingrich, who was unable to attend this meeting. Dr. Gingrich is in favor of making it a condition of receiving a Federal grant that the resulting research be made available online in a timely manner. The purpose of taxpayer funding of biomedical research, Dr. Gingrich wrote, is to accelerate the introduction of new health knowledge into the common good. The minutes of the two Public Access Working Group meetings (July and November 2005) are on the Web at www.nlm.nih.gov/od/bor/bor.html.

Following Dr. Detre's report, Dr. Gray suggested that NIH employees themselves should be strongly encouraged to submit the results of their research. He also raised a question about providing for unpublished manuscripts. Dr. David Lipman, Director of the National Center for Biotechnology Information (which runs the PubMed Central archive) said that it is interesting to note the experience of the Wellcome Trust in the U.K., which made manuscript submission mandatory as a condition of getting a grant. Wellcome has been able to work out special arrangements with a number of commercial publishers to facilitate the submission of manuscripts. Dr. Detre suggested that the Regents prepare a draft Board statement to be submitted to NIH Director Zerhouni. Dr. Lindberg said that if the Board outlines the major points to be included, NLM staff can help draft a statement that can be considered for action by the Board of Regents tomorrow. The Regents agreed with the proposed main points of a letter as

put forward by Dr. Detre. There was also agreement that the NIH should make it easier for scientists to understand what they must do to comply with the policy.

IX. INFLUENZA GENOME SEQUENCING PROJECT

Dr. David Lipman, Director of the National Center for Biotechnology Information, introduced Dr. Jeffrey K. Taubenberger of the Armed Forces Institute of Pathology, who has developed interesting techniques to learn more about influenza by reconstructing actual molecular makeup of the Spanish flu of 1918. He has also had an important role in the NIAID influenza sequencing effort. Dr. Taubenberger gave a brief overview of the influenza sequencing project that began about a year ago. Current concern is with avian flu (H5N1 strain), which has had several outbreaks in the last decade, in Hong Kong, Northern Europe, and Southeast and Central Asia. Although human infection has been limited, millions of chickens and other poultry have been slaughtered. He said there were three flu pandemics in the 20th century—the "Spanish" flu in 1918 (675,000 deaths in the U.S.), the 1957 "Asian" flu (70,000 deaths), and the 1968 "Hong Kong" flu (30,000 deaths). No one knows when or where the next pandemic will occur, but some are worried that the avian flu may evolve into a strain dangerous to humans. The scientific community is using some of the new tools of molecular biology and genomics to do large-scale genomic analysis of flu so we can understand its complex biology. Dr. Taubenberger described several of the features of the flu virus RNA that allow it to mutate into new strains. He said the big question was how the viruses, which are predominantly in waterfowl, are transferred to humans. It raises complex ecobiology questions involving wild animals and domestic animals (both birds and mammals) and humans.

Dr. Taubenberger described the NIAID-funded Influenza Genome Sequencing Project, which is a collaborative effort to increase the genome knowledge base of influenza so as to help researchers understand how flu viruses evolve, spread and cause disease. The project will reveal and make publicly available (through NCBI's GenBank) complete genetic blueprints of thousands of human and animal influenza viruses. The NLM is one of the collaborators. The Project will help specifically in a number of areas, including comparisons of receptor binding changes, comparisons between human and avian viruses, and comparisons between the 1918 influenza and the current H5N1 strain. Epidemic human influenza remains a big problem because of the race to make protective vaccines each year. The WHO global surveillance network, although it isn't complete, is a great accomplishment, Dr. Taubenberger said. The new genomic analysis should help to improve the process by which annual vaccines are developed.

Dr. Lipman said that the Influenza Genome Sequencing Project is an example of a new role that NLM is playing: not only is the Library the "receptacle at the end of the process" of scientific research (for example, Medline/PubMed for the literature and GenBank for factual genomic data), but now NLM is involved in the *planning* stages of research. Scientists ask how they should best structure experiments so that those who view and use the data resulting from them can do smoothly and efficiently. Dr. Lipman cited several examples of this, including PubChem

and the new flu project. He said that knowing genetic sequences can be enormously helpful in addressing medical problems, especially in the area of infectious diseases where there are relatively few genes to look at. He demonstrated his points by going on the Web and, with Dr. Taubenberger, showing the Regents how genetic information about the H5N1 virus could be called up and not only displayed, but computed upon. Following the presentations, Dr. Taubenberger answered questions from the Regents about the influenza virus, how it replicates, the barriers to its moving between species, and the death rates of its various forms. Dr. Kenneth Walker discussed the historical aspects of influenza epidemics, describing references to influenza beginning in the middle ages.

X. EXTRAMURAL PROGRAMS REPORT

Dr. Valerie Florance, Deputy Associate Director for Extramural Programs, presented to the Regents the guidelines for operating procedures. The procedures were affirmed unanimously by the Board. She opened the FY 2006 budget update by discussing the effect of budget constraints on success rates. The success rate is the percentage of applications received that are funded. The rate varies among the Library's dozen or so grant programs. During the NIH budget-doubling period, success rates of 20–25% were the norm. This ended in FY 2005, when the budget began to flatten. As a result, the success rate for NLM's grant programs is now averaging 10%. Dr. Florance said commitments for "out years" of previously awarded grants also affect the amount of money available for new grants. Thus the burden of a budget decrease falls disproportionately on the new grants waiting to be funded. The success rate for FY 2006 is expected to fall again. NLM is trying to ameliorate the situation by suspending several grant programs, so that others can have a higher success rate. Those suspended are: Integrated Advanced Information Management Systems Operations Grants; Biomedical Informatics Resource Grants; Internet Access to Digital Libraries Grants; Individual and Senior Biomedical Informatics Fellowships; Senior Informationist Fellowships; and Grants for Disaster Management.

Dr. Florance said that NLM is responding to the NIH Director's call for "high risk/ high payoff" projects by launching a new grant program called the Advanced Informatics for Biomedicine (AI BIO). A Request for Information was published by NLM in the NIH Guide asking for "Grand Challenges" in informatics—problems that might be difficult but that are approachable and that are relatively unexplored and untested. About 50 responses have been received from computer scientists, engineers, biomedical informaticians, computational biologists and others. NLM will draw upon these suggestions to develop a series of Requests for Applications (RFAs) on focused, high-priority aspects of informatics. Successful applicants will be funded with a set-aside portion of the existing research budget ($2 million initially). Review will be by a Special Emphasis Panel on a 4–5 month turn-around. Dr. Florance said that because this is a new program, the Board is being asked to approve the concept.

ACTION: The Board of Regents voted unanimously to approve the concept of the Advanced Informatics for Biomedicine (AI BIO) grant program.

Dr. Florance next discussed changes in the way NIH defines "principal investigator," so as to give credit for a grant to more than one investigator. At the present, co-investigators and collaborators have "no official status." She described how NIH is working on a system to credit multiple principal investigators, in cases where that is appropriate. The pilot begins June 1 with several different institutes, including NLM, taking the lead. NIH intends to move all grant programs to this new model in the next two years.

Dr. Florance also described the NLM Early Career Transitions Award Program (K22), which began in March 2003. It is for young scientists who are just embarking on their careers as informaticians. The program provides salary support and a small research fund. To date there have been 41 applicants; 14 awards have been made. Dr. Lussier, who presented to the Board this morning, was the first recipient of such a grant. Dr. Florance said that NLM was very pleased with the outcome of the program. A list of the awardees was presented. Dr. Florance also discussed the new "NIH Pathway to Independence Award," announced by Dr. Zerhouni in January 2006. All NIH components are participating in this program, which provides five years of career development support in two phases: Phase I (one or two years of mentored support for advanced fellows at a total cost of $90,00 per award) and Phase II (three years of support for independent research at a total cost of $249,000 per award). As of April 2006, this program will replace NLM's existing Early Career Transition Award.

MEETING CLOSED FOR THE REVIEW OF GRANT APPLICATIONS
February 7, 2006, 3:45 P.M. and reopened on February 7, 2006 at 4:15 P.M.

XI. BORROWING ARTIFACTS: ANATOMY OF A LOAN

Ms. Jiwon Kim, Exhibition Program Educator in the History of Medicine Division (HMD), introduced Jill Newmark, who is the registrar in NLM's exhibition program. Ms. Newmark works behind the scenes to bring artifacts to NLM, securely and safely. Ms. Kim said that the objects and artifacts come from many different places, and acquiring them for an exhibition poses interesting and complex challenges. Ms. Newmark described to the Board the long and sometimes tortuous process of borrowing historic fingerprints and several other artifacts from the Police Museum in Argentina. The curator of the exhibition selected the artifacts, and the registrar shepherded the loan through the process from the lender to the NLM, and then, after the exhibition, will ensure that the artifacts get returned to the lender. In the case of the historic fingerprints, the process took 30 months from selection by the curator to display in the current NLM exhibition, "Visible Proofs." The fingerprint in this case, dating from 1892, was the first case of a fingerprint being used in a criminal investigation to solve a murder. Ms. Newmark described the process and the extensive interaction with government agencies (U.S. and Argentinean) that culminated in the successful acquisition of the fingerprints and accompanying artifacts for display.

XII. VISIBLE PROOFS: FORENSIC VIEWS OF THE BODY

Following the presentation about borrowing artifacts, Dr. Michael Sappol, historian and curator of the Visible Proofs exhibition, discussed the content of the exhibition in some detail. There is tremendous interest today in forensic medicine—a number of top network television shows are on the subject. Although we did borrow some materials for the exhibition, the NLM has a very fine collection of historical material relating to the history of forensic medicine. There are extremely rare medical treatises and manuscripts on the subject from the 1600s on in the History of Medicine Division. Dr. Sappol said that NLM's is the first major exhibition he knows of on the broad history of the forensic sciences. A series of symposia at NLM are planned over the life of the exhibition that will shine a light on various aspects of this understudied subject. Dr. Sappol then briefly described some of the highlights of the exhibition.

Patricia Tuohy, Head of the NLM Exhibition Program, talked about NLM's broad program in exhibiting. For the last 10 years the History of Medicine Division has created a series of major exhibitions in the rotunda area of the Library. Each topic brings new personalities, new technologies, new contractors, new vendors—in short, a set of new challenges to be met. The staff began working on Visible Proofs three years ago: the first year was devoted to research and conceptual development and to identifying visual assets; the second year was the creative/design phase—to conceive of the ideas in a 3-dimensional space; the third year was for production, fabrication, and installation of the exhibition. Ms. Tuohy described how the HMD staff collaborated with private firms to accomplish the various tasks. The Regents were then conducted on a tour of Visible Proofs, which opens to the public on February 16.

XIII. REPORT FROM THE DIRECTOR, NIGMS

Dr. Jeremy M. Berg, Director of the National Institute of General Medical Sciences, gave the Board a progress report on the project, "Protein Structure Determination: From Myoglobin to Modeling The Human Proteome." The project has a substantial experimental component and also a substantial informatics component. He gave a brief historical survey of the subject, beginning with the discovery of x-rays (1895) to solving the structure of hemoglobin (1960), for which Perutz shared the Nobel Prize in 1962. The structure of sperm whale myoglobin was solved, which opened up an area which we continue to take advantage. Crystallography has always been heavily dependent on technology, so it has been at the cutting edge of computer technology. The calculations for myoglobin back in the 1960s took 12 hours to do on the fastest computer available. Dr. Berg presented diagrams showing how myoglobin and hemoglobin chains have similar structures. As protein structures were determined, a database, the Protein Data Bank, was founded in 1971 at Brookhaven National Laboratory. The databank, which has grown to over 35,000 structures, is supported by NSF, DOE, NIGMS, NLM, and other NIH components. Models based on homology, he said, can provide powerful insights. This led to a new concept, Structural Genomics. Any time you have the structure of any family member that is recognizable by sequence to other families, you can use that as a framework for building up

models. The recent doubling of the NIH budget made the Protein Structure Initiative (PSI) possible to test the hypothesis that high-throughput pipelines can be generated that produce well-determined structures of proteins that are representatives of protein families. To do this, nine high-throughput pilot centers that made heavy use of informatics were funded between 2000–2005. Dr. Berg gave a number of examples of the technology they developed and applied. By 2005, the centers had determined more than 1300 structures. The PSI structures are available on the Web through NLM's NCBI. In Phase 2 of the Protein Structure Initiative there have been four large-scale and six specialized centers funded. The difficult problem is how to model *unknown* protein structures, without knowledge of the structure of a homologous protein. Last year a potential breakthrough was announced with Rosetta, a program at the University of Washington, that utilizes many sources of information to predict protein structures. Dr. Berg concluded by saying that the Structural Genomics initiative is providing structures of great potential utility. As there is more explicit targeting the value of the structures will go up. Computational methods will increase in power driven by new insights and increases in computer power. The analysis of macromolecular complexes is an important frontier requiring combination of information from high-resolution structure determinations and other methods. Drug design is an area where the structures are potentially extremely valuable.

XIV. BOARD ACTION ON PUBLIC ACCESS

Dr. Detre presented to the Board a draft letter to the NIH Director summarizing the deliberations of the Public Access Working Group and the discussions yesterday by the Board of Regents. A small modification will be made in the letter to indicate that the Board is pleased that most of the publishers on the Working Group indicated an interest in depositing the final published version of articles in PubMed Central on behalf of NIH-funded authors. The text of the letter is in Appendix B.

XV. INDEXING 2015: AUTOMATION FOR ENHANCED PRODUCTIVITY OF INDEXING FOR MEDLINE

Sheldon Kotzin, Chief of the Bibliographic Services Division, introduced the topic of indexing journal articles, and the Library's long involvement in that activity. He noted how the Library's famous director, Dr. John Shaw Billings, began indexing journal articles in the 1870s—the *Index Medicus* was first published in 1879. Over the next century, the *Index Medicus* became an indispensable tool for researchers, physicians, and librarians. In 1971, the MEDLINE database was developed to provide online access to the indexed records. The number of records added each year has increased greatly in recent decades, and last year more than 600,000 articles were indexed. Mr. Kotzin said a million citations is quite likely in the next few years. There are currently 70 million searches a month on the MEDLINE data via the PubMed system. NLM tries to keep costs under control by using more efficient methods of processing MEDLINE input data—in 1997, 100% of data entry was done by manual keying. In 2004 there was no manual entry—80% of the journal input was submitted electronically by the publishers and 20% was

entered by optical scanning. The goal of the "Indexing 2015" initiative is to continue to find ways to make the indexing of MEDLINE citations and data entry more cost-effective, timely, productive, and efficient.

James Marcetich, head of the Indexing Section, described the indexing function as applying subject headings to each citation record in MEDLINE. The headings are from NLM's controlled thesaurus, called Medical Subject Headings. By applying consistent subject headings, NLM deals with the many variations of language used by authors in their articles, thus enhancing retrieval from the database. There are mapping programs built into the PubMed/MEDLINE system so that even if users don't use MeSH terminology, their searches find appropriate records. There is also a "find related records" feature built into PubMed that uses the MeSH headings, so if a user finds one relevant record, the system can be instructed to go out and look for more like that one. Mr. Marcetich showed a sample citation and described the various aspects of the indexing process. Other information included in an indexed citation includes GenBank and other molecular sequence databank accession numbers, ClinicalTrials.gov identifiers, funding information (including NIH grant numbers), translation of foreign language titles, links to letters, comments, errata, and retraction, and gene indexing. Mr. Marcetich described and then did a live demonstration for the Regents of the DCMS (Data Creation and Maintenance System), the Web-based online indexing system developed at NLM. The DCMS has greatly enhanced the productivity of NLM indexing in recent years. He also showed the Medical Text Indexer (MTI) program which suggests to the indexer potential MeSH headings. Most NLM indexing is done by contractors who work off-site; a small portion is done by in-house staff. About eight percent of the indexing is done by staff at four international centers. All indexers receive training at NLM and the rate of indexing averages four per hour, Mr. Marcetich said. He briefly reported on an indexing consistency study recently completed—the first in more than 20 years. NLM began the Indexing 2015 project last year. Its goal is to anticipate and prepare for indexing a million articles a year. The project is doing R&D on tools, technologies, and methods that can enhance the productivity, accuracy, timeliness, and cost-effectiveness of MEDLINE indexing. Mr. Marcetich mentioned several areas of the indexing process that are being looked at for enhancement: expanded Medical Text Indexer; a prototype WebMARS tool, created by Lister Hill Center staff, that highlights text words corresponding to check tags, randomized trials, other concepts; a Web-based indexer training program that is already in use; and improved equipment used by the indexers.

Dr. Holly Buchanan said that the NLM has long been in the forefront in applying technology to medical information. She asked about the longer-term prospect of indexing—what will we see in 2025? Mr. Marcetich said that he believes the greatest changes will be in the recording and manipulating of genomic information, including 3-dimensional structural information, as was discussed by Dr. Berg earlier. Dr. Lindberg asked whether there were certain types of journals where the automatic indexing aids worked better than others. Mr. Marcetich said that they were looking into that question, however, the real variation was from article to article.

XVI. DAILYMED

Dr. Stuart Nelson, Head of the Medical Subject Headings Section, Library Operations, described DailyMed, a new Web site developed by NLM, which provides medication information derived from product labels. This is information primarily for prescribers and dispensers, the wording of which is negotiated by the manufacturer and the FDA. The old method of distributing this information is in the multi-fold, small-print inserts included in the boxes containing medicinal products. NLM has signed an agreement with the FDA to help devise a new electronic method of distributing this label information. After the FDA approves of an electronic submission from a manufacturer, it is sent to the NLM where it is put online both for viewing and download in DailyMed. The first such submission was in November 2005; we expect within a year to have all of the labels available. Dr. Nelson demonstrated the Web site to the Regents (http://dailymed.nlm.nih.gov/). He said that RxNorm names would be linked tightly with DailyMed records so that, as soon as the FDA approves a drug, we will have an RxNorm name for it. Dr. Nelson said that there would be a permanent archive of labels, so that there will always be a record at any point in time. Dr. Nelson acknowledged that the Agency for Healthcare Research and Quality has helped to support the DailyMed.

XVII. NOMINATING COMMITTEE FOR BOR CHAIR

Dr. Detre named a committee to nominate a chairman for 2006–2007. The committee, consisting of Mary Ann Tatman (chair), Dr. Charles Rice, and Dr. Deanna Marcum, will report at the next Board meeting.

XVIII. A SPECIAL ANNOUNCEMENT

Dr. David J. Lipman, Director of the National Center for Biotechnology Information, noted the recent public announcement of a group of related projects—a “harmonic convergence.” Across NIH there is the realization of the power of consolidating information from valuable clinical trials and enhancing data from those trials with high-density genotype information. This will be made available in a coordinated fashion to researchers through a database at NLM. Dr. Lipman said that the National Heart, Lung, and Blood Institute is announcing that information from the Framingham (Mass.) heart study will be made available in a database that NCBI has been building. Furthermore, there is an announcement by the NIH and Pfizer that the company is investing $20 million to take five case-controlled clinical studies to have the phenotype clinical information consolidated within an NCBI database, access to which would be controlled, and have all of the participants genotyped with high-throughput methods. The goal is to determine the genetic basis of more common diseases. The third part of the “harmonic convergence” is the $40 million Genes and Environment Initiative announced today by HHS Secretary Leavitt. This initiative, announced by the National Human Genome Research Institute, will support studies to try to identify the genetic and environmental underpinning of common diseases. The consolidation of all this information in an NCBI electronic resource intended for scientists will

be of immense value to scientists and may lead to important insights.

XIX. REPORT FROM THE PLANNING SUBCOMMITTEE

Dr. William Stead provided the Board with an update on the status of the four Long Range Planning panels. (Each panel is meeting twice.) The Regents will receive drafts of the panel reports before the May meeting and additional time has been allotted at that meeting for discussion. There is a special challenge in dealing with cross-cutting issues, Dr. Stead noted. He said examples of such issues are nurturing the science of biomedical informatics, training, and ethics. NLM staff will amalgamate the individual draft panel reports and the Board deliberations into an integrated planning report that the Board will review at its September meeting.

XX. REPORT FROM THE SUBCOMMITTEE ON OUTREACH AND PUBLIC INFORMATION

Dr. Vasiliki Karlis, substituting for Dr. Conerly, reported on yesterday morning's meeting of the Subcommittee on Outreach and Public Information. Dr. Karlis congratulated the NLM staff for the outreach items, updates, press releases, etc., that they regularly provide by email and on the Web. The Subcommittee heard about the progress of the discussions of the Long Range planning panel that includes outreach. There was a presentation about the new NLM exhibition, Visible Proofs, and the publicity surrounding it. The Subcommittee received an update on NLM's Environmental Health Information Outreach Program. Dr. Marian Ball told the Subcommittee about a radio broadcast, "The Business of Government," which included an extensive interview with Dr. Lindberg about the NLM. The program, which is sponsored by IBM, will be broadcast on February 18. Dr. Ball distributed to the Regents information about the program.

XXI. CLINICALTRIALS.GOV - VISIONARIES VIDEO

The Board viewed a 15-minute video presentation about ClinicalTrials.gov. This database was created by the Library in 2000, on behalf of the NIH and the FDA. ClinicalTrials.gov was the recipient of a prestigious award from the Ash Institute for Democratic Governance and Innovation of the Kennedy School of Government at Harvard University. The video, a part of the "Visionaries" series on PBS, was made as a result of ClinicalTrials.gov receiving the award.

XXII. ADJOURNMENT

The meeting was adjourned at 12:00 p.m.

ACTIONS TAKEN BY THE BOARD OF REGENTS:

- Approval of the September 20-21, 2005 Board of Regents Minutes
- Approval of February 6-7, 2007 Meeting Dates
- Issued Letter to the NIH Director on Public Access Policy Recommendations
- Approval of Board Grant Operating Procedures for 2006
- Approval of Advanced Informatics for Biomedicine Grant Program
- Approval of EP Subcommittee Recommendations and En Bloc Grant Concurrence
- Creation of Nominating Committee for New Board of Regents Chair

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

Donald A.B. Lindberg, M.D.
Director, National Library of Medicine

Thomas Detre, M.D.
Chair, NLM Board of Regents