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

MINUTES OF THE BOARD OF REGENTS
February 10-11, 2015

The 168th meeting of the Board of Regents was convened on February 10, 2015, 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 4:15 p.m., followed by a closed session for consideration of grant applications until 4:45 p.m. On February 11th, the meeting was reopened to the public from 9:00 a.m. until adjournment at 11:45 a.m.

MEMBERS PRESENT [Appendix A]**:**
Dr. David Fleming, University of Missouri School of Medicine
Dr. Robert Greenes, Arizona State University
Dr. Henry Lewis, American University of Health Sciences
Dr. Trudy MacKay [Chair], North Carolina State University
Ms. Sandra Martin, Wayne State University
Dr. Ralph Roskies, University of Pittsburgh
Dr. Esther Sternberg, University of Arizona
Ms. Gail Yokote, University of California, Davis

MEMBERS NOT PRESENT:
Mr. Eric Dishman, Intel Corporation

EX OFFICIO AND ALTERNATE MEMBERS PRESENT:
Mr. Christopher Cole, National Agricultural Library
RADM Scott Giberson, Office of the Surgeon General, PHS
Ms. Kathryn Mendenhall, Library of Congress
Col. Cathy Nace, United States Army
BGEN Charles Potter, United States Air Force
Dr. Dale Smith, Uniformed Services University of the Health Sciences

CONSULTANTS TO THE BOR PRESENT:
Dr. Marion Ball, Johns Hopkins School of Nursing
Dr. Holly Buchanan, University of New Mexico
Dr. H. Kenneth Walker, Emory University School of Medicine

SPEAKERS AND INVITED GUESTS PRESENT:
Dr. George Hripcsak, Columbia University
Dr. Kathy Hudson, Deputy Director for Science, Outreach and Policy, NIH

MEMBERS OF THE PUBLIC PRESENT:
Mr. John Harrington, Contractor to Lister Hill Center
Ms. Lynne Holden, Friends of the National Library of Medicine
Mr. Gerard Kuhn
Ms. Amy Lindberg
Mrs. Mary Lindberg
Mr. George Lundberg
Ms. Lesley Marcherilli, Friends of the National Library of Medicine
Dr. Barbara Redman, Friends of the National Library of Medicine
Dr. Elliot Siegel, Consultant
Mr. Thomas West, Krasnow Institute

FEDERAL EMPLOYEES PRESENT:
Dr. Donald A.B. Lindberg, Director, NLM
Ms. Betsy Humphreys, Deputy Director, NLM
Dr. Michael Ackerman, Lister Hill Center, NLM
Ms. Anne Altemus, Lister Hill Center, NLM
Ms. Queen Alike, Division of Specialized Information Services, NLM
Dr. Sameer Antani, Lister Hill Center, NLM
Ms. Stacey Arnesen, Division of Specialized Information Services, NLM
Ms. Dianne Babski, Division of Library Operations, NLM
Ms. Joyce Backus, Division of Library Operations, NLM
Ms. Hilda Bastian, National Center for Biotechnology Information, NLM
Dr. Dennis Benson, National Center for Biotechnology Information, NLM
Dr. Tony Chu, Office of Health Information Programs Development, NLM
Ms. Kathleen Cravedi, Office of Communications and Public Liaison, NLM
Ms. Francesca Crawford, Division of Extramural Programs, NLM
Mr. Ivor D'Souza, Office of Computer and Communications Systems, NLM
Dr. Kathel Dunn, Division of Library Operations, NLM
Ms. Gale Dutcher, Division of Specialized Information Services, NLM
Dr. Valerie Florance, Division of Extramural Programs, NLM
Dr. Dan Gerendasy, Office of Health Information Programs Development, NLM
Dr. Michael Huerta, Office of Health Information Programs Development, NLM
Ms. Christine Ireland, Division of Extramural Programs, NLM
Dr. Alla Kesselman, Division of Specialized Information Services, NLM
Mr. Paul Kiehl, Office of the Director, NLM
Mr. Ken Koyle, Division of Library Operations, NLM
Dr. David Lipman, National Center for Biotechnology Information, NLM
Dr. Robert Logan, Office of Communications and Public Liaison, NLM
Ms. Lisa Lang, National Information Center for Health Services Research and Health Care Technology, NLM
Ms. Mary Ann Leonard, Office of Communications and Public Liaison, NLM
Dr. Clement McDonald, Lister Hill Center, NLM
Mr. Dwight Mowery, Division of Extramural Programs, NLM
Mr. David Nash, Office of the Director, NLM
Dr. Steven Phillips, Division of Specialized Information Services, NLM

Dr. Barbara Rapp, Office of Health Information Programs Development, NLM
Dr. Jeffrey Reznick, Division of Library Operations, NLM
Mr. Jerry Sheehan, Office of the Director, NLM
Dr. Hua-Chuan Sim, Division of Extramural Programs, NLM
Dr. George Thoma, Lister Hill Center, NLM
Dr. Alan VanBiervliet, Division of Extramural Programs, NLM
Dr. Fred Wood, Office of Health Information Programs Development, NLM
Dr. Deborah Zarin, National Center for Biotechnology Information, NLM

I. OPENING REMARKS

Dr. Trudy MacKay, NLM Board of Regents Chair, welcomed the Regents, new Regents, alternates, and guests to the 168th meeting of the Board. She then commended Dr. Donald Lindberg, Director of the National Library of Medicine, on his more than thirty years of service to the NLM. She said this meeting would be his 91st and last official meeting as the NLM Director, noting he would be leaving the Library at the end of March. The Board unanimously adopted a resolution commending him on his leadership. She then introduced RADM Scott Giberson, Office of the Surgeon General (OSG).

II. REPORT FROM THE OFFICE OF THE SURGEON GENERAL, PHS

RADM Scott Giberson briefed the Board about the new Surgeon General Vivek Murthy, MD, who joined the OSG in December. He said they also have a new Acting Assistant Secretary for Health, Dr. Karen DeSalvo, who is outstanding in the public health area.

The new Surgeon General wants to modernize the OSG's approach to public health and utilize new social media tools to translate information into action.

The OSG has Calls for Action surrounding both prescription drug abuse and support for walking and walkable communities. One of the most visible actions underway in the OSG has been the response to the Ebola crisis in West Africa. RADM Giberson said he had the privilege to go to Africa and help create a hospital for US workers. Over two hundred folks from the Public Health Service were deployed on the West African mission. OSG partners are the CDC and DOD. The OSG is also working with the NIH in the development and operation of clinical trials. He said that they have an exit strategy for the April or May.

Dr. Clem McDonald asked if they were in the actual care units and if they use powered respirators or just masks? RADM Giberson replied that some use the powered respirators but most use the masks. Ms. Humphreys asked about vaccinations for measles and mumps and he responded that there would be a need to do this as well.

III. SEPTEMBER 2014 MINUTES AND FUTURE MEETINGS

The Regents approved without change the minutes from the September 9-10, 2014 meeting. The 2016 winter meeting will take place on February 9-10, 2016.

IV. REPORT FROM THE NLM DIRECTOR

Dr. Lindberg said that NLM has a 2015 budget, but an apportionment has not yet taken place. The 2016 President's budget is now available.

NLM's budget is $328 million plus $70 million in other forms. NLM found the funds to support NCBI expansion for much of its history, but more recently it has required broad NIH support to keep pace with the explosion of data. NIH agrees that the funds should be in its base budget, but the request of the NIH to the Congress has not been approved. The President's 2016 budget is again asking that funds be added to the NLM appropriation for this purpose.

One of NLM's major contractors went bankrupt at the end of the last fiscal year, resulting in a great deal of work to avoid the loss of funds due to the bankruptcy.

Dr. Lindberg asked Ms. Humphreys to introduce new personnel in NLM's OD. She introduced Ms. Dora Deegbe who was appointed as the Senior Administrative Officer in August 2014. She came to NLM in 1999 as a Library Technician in the National Information Center for Health Services Research and Health Care Technology and most recently as an Administrative Officer in the Division of Library Operations. Ms. Humphreys also introduced Ms. Valerie Whipple who was appointed as Deputy Director of the NLM Office of Acquisitions and Consolidated Operations Acquisitions Center on November 16, 2014. Ms. Whipple comes to the NLM from the Nuclear Regulatory Commission where she headed their Corporate Support Team. She

Dr. Lindberg introduced Mr. Thor Sigfusson who has been appointed to the position of General Engineer in the NLM Office of Administration. Mr. Sigfusson joins NLM from the Office of Facilities and Property Management in the National Institute of Standards and Technology (NIST), US Department of Commerce.

Dr. Lindberg then called on Joyce Backus to introduce a new addition to Library Operations. Ms. Backus introduced Ms. Jennifer Diffin who came to NLM in September 2014 as the head of the Library Technology Services Section of the Technical Services Division. She was previously the Assistant Director for Systems and Access Services, University of Maryland University College.

Dr. Clem McDonald introduced new Lister Hill National Center for Biomedical Communications (LHNCBC) Fellows: Dr. Ferdinand Dhombres is a practicing physician in obstetrics and gynecology at Armand Trousseau University Hospital (Paris, France) with a specialization in Fetal Medicine. His mentor is Olivier Bodenreider, MD, PhD; Dr. Kyungsook Gartrell received her doctorate degree in nursing informatics from the University of Maryland School of Nursing. Her mentor is James Cimino, MD; Dr. Bryan Hendrickson received his Master's Degrees in biomedical informatics and health sector management from Arizona State University. His mentors are Drs. Clem McDonald and Paul Fontelo.

Dr. Lindberg said that ClinicalTrials.gov reached an important transition point in November 2014 when the HHS issued a Notice of Proposed Rulemaking to clarify and extend requirements set out in the FDA Amendments Act of 2007, and NIH issued a proposed policy that would

require registration and results submission of all NIH-funded trials to complement the NPRM. ClinicalTrials.gov will require an infusion of NIH resources, an increase in staffing, and a shift in the way that NLM assists those submitting results, and closer interaction with NIH to monitor compliance. In response to these anticipated changes, NLM has transferred ClinicalTrials.gov, and its staff from the LHNCBC to the NCBI. This change will enable ClinicalTrials.gov to take advantage of NCBI's experience with monitoring and reporting compliance of NIH-funded researchers with the NIH public access policy. Dr. Lindberg asked Dr. Zarin to clarify the changes that were occurring. She stated that NIH would be giving NLM funds to secure staff required to assist in the implementation of the anticipated changes.

Dr. Lindberg noted that a legislative summary can be found in Tab D of the Board book. The Congress established a public access requirement for all agencies and bureaus within the DOL and DHHS that have research and development expenditures in excess of $100,000,000 per year. They have to develop policies to provide for free public access to peer reviewed publications. In HHS, this applies to AHRQ, CDC, and FDA. The Congress passed and the President enacted – a series of laws to improve U.S. cybersecurity provisions.

Tab F, said Lindberg, details how the NLM will not reconfigure the geographic boundaries of the eight regions. Based on input received from a RFI, the NLM will change the specific funding mechanism for the 2016-2021 RML funding cycle. The previous funding mechanism was a contract. Going forward they will be cooperative agreement grants.

Tab G describes NLM's use of the NIH Pathways hiring program for recent graduates. Through this mechanism, NLM hired nineteen recent graduates. After a year of successful service, they can convert from temporary to permanent status.

Lindberg updated the Board on the NIH Big Data to Knowledge (BD2K). It has moved into its implementation phase. It has been pushed by NSF and will involve grants to universities and others to facilitate the use of big data. An award has been made to support the design and formation of a Data Discovery Index. To accelerate this effort, grant supplements were made to 8 existing NIH grantees including two NLM grantees, Dr. George Hripcsak and Dr. Trevor Cohen. Nine awards were made to support Learning Resources for Big Data, nine awards were made for K01 Career Transition awards to Postdoctoral fellows managed by the NIEHS, and twelve awards were made for Centers of Excellence. In December 2014, a RFI was issued by NLM on behalf of BD2K, requesting information from extramural stakeholders in the areas of data management and data science. NLM received 20 responses.

Dr. Roskies summarized BD2K, directed by Phil Bourne, with NLM staff, including Betsy Humphreys, Jerry Sheehan and Mike Huerta, himself and others. They launched the Centers for Excellence with $32 million from the Common Fund and then will transition to IC budgets later. They will develop standards, software and indexing and other mechanisms. For FY2015, they committed $60 million to active awards. NLM should and is paying attention to this. We should look to opportunities to supplement what NLM is trying to do. Clem McDonald and Betsy Humphreys agreed that the BD2K effort is interested in pushing standards but their approaches are not necessarily in line with NLM.

Dr. Lindberg reported on the Pill Image Recognition Challenge underway in the OHPCC. Its goal is to recognize and identify prescription solid form pharmaceuticals (pills) from smart phone pictures sent to NLM through an NLM Pill Recognition APP. The 3D Informatics Program proposes a challenge to the computer graphics and computer vision communities. They will be invited to submit to NLM algorithms and their executable implementations on user-generated virtual machines on flash drives. NLM will use the responses to test, evaluate, and refine the parts of the challenge. Responses from this first phase are due in April. The actual Challenge will take place this fall and winter.

Next, Dr. Lindberg noted the recent celebration of the 20th anniversary of the Visible Human Project, recommended by the Board in the 1980s as part of its long-range plan. Now, two decades after the launch, nearly 4,000 people and institutions worldwide have licensed the data, free of charge, to study or create all kinds of things – from art to prosthetics, educational materials to surgical simulators.

Another recognition coming up, said Dr. Lindberg, is a program to mark NLM's acquisition of Marshall Nirenberg's Nobel Prize and certificate, through a generous donation from Dr. Myrna Weissman on Tuesday, March 17, 2015. The program will also announce a new NLM *Turning the Pages* of the Nirenberg genetic code charts, also a part of *Profiles in Science*.

Lastly, Dr. Lindberg updated the Board on the Native Voices traveling exhibition. He noted that the exhibition has finished phase one – an initial tour of Alaska, Hawaii, and North American sites. He presented a video overview of that tour.

V. ADVISORY COMMITTEE TO THE NIH DIRECTOR WORKING GROUP ON THE NATIONAL LIBRARY OF MEDICINE

Dr. Trudy MacKay called on Betsy Humphreys to discuss the role of the Advisory Committee to the NIH Director (ACD) Working Group on the NLM, and its charge.

Ms. Humphreys explained that NIH Director Dr. Francis Collins had formed a working group to consider the future of NLM as background for the recruitment of Dr Lindberg's successor. The working group will collect input over the next several months and present a set of recommendations to the full advisory committee to the director in June.

Ms. Humphreys introduced Lyric Jorgensen who is providing staff support for the working group. The working group is going to issue a request for information (RFI) at the end of this week from anyone who has an interest in the work of the NLM. There will be a 30-day comment period. The committee will meet at NLM, on March 2 where they will learn about the NLM and its current status from Dr. Lindberg, myself and NLM staff. Ms. Jorgensen said that the ACD is scheduled to meet on June 10 and 11. The ACD working group's final report will be ready by the end of May so it can be discussed at the June meeting. Today, we should talk about ways the board can provide input to this process.

Ms. Humphreys explained that, like all requests for information (RFI), it is a public document that will be widely circulated. The question is how we can bring it to the attention of people who we think might be interested.

Dr. MacKay pointed out the RFI is very open-ended and it seeks information about what current NLM services are most or least valuable to the biomedical research community, and why. Dr. MacKay suggested that the Board prepare a response to this request. Dr. Buchanan agreed that a board response would be great, but thought the Board should discuss how to get broad input to the RFI. She then observed that, looking at the makeup of the working group, it would be good to identify some ways to get input on outreach and community service involvement. She felt the group is weighted heavily toward private institutions versus public institutions. Dr. Lindberg said that we may need to explain why NLM should be doing outreach at all. He said that it wasn't until 1987 or later that NLM had a budget for outreach. He noted that we received money from Rep. Natcher for outreach and every year NLM had to explain what we did with the money.

Ms. Humphreys said that prior to learning of Dr. Collins decision to create a working group on NLM's future, the Board had discussed setting up a strategic planning committee. But, we don't think it would be helpful to have two dueling planning processes.

A discussion followed by Board members about the value of consumer information and outreach. Dr. Ball agreed with Dr. Buchanan about the need for public sector involvement on the planning committee and said the Board should prepare its view on the future direction of the NLM. SIS Director Steve Phillips, a former Board Member himself, echoed Dr. Ball's view that the Board's authoritative voice on the NLM would be a great source of input to the planning committee. Dr. Greenes said that he was concerned about the scientific core of the field, as informatics is now applied in most of the ICs, in one form or another. So NLM needs to strengthen that role. We've now have insufficient funding for the underlying science of informatics, yet the NIH informatics budget overall is growing. There is the opportunity to integrate the science in this field. That voice needs to be heard.

Dr. Smith said it would be very important to compile a thorough response from our individual constituencies. We need to see that those responses are carefully prepared and brought to the attention of the advisory group.

Dr. MacKay noted that the working group and Dr. Collins would be thinking very broadly, trans-NIH. Dr. Roskies agreed and asked Dr. Lindberg about his recruitment process that took place back in the 1980s. Dr. Lindberg said that he felt, at the time, that it would be better to be enthusiastically a part of the NIH in every way we could. He also felt that the research arm of the NLM should work closely with the library arm even though a tunnel separated the two entities physically. He noted that there was not a long-range plan when he became the director. Dr. Lindberg reminded the Board that all of NLM milestones were decisions made by this Board including the Visible Human, developing a comprehensive source of consumer information, and increasing public access to the biomedical literature.

Ms. Humphreys believes that Dr. Collins and the working group understand the Board's special role in advising on NLM policies and programs and that they will value input from the Board.

Responding to a question from Dr. MacKay about the best way to organize the input and to a suggestion from Dr. Smith that those interested Board members meet separately to discuss further after the official Board meeting, Ms. Humphreys said that the entire Board should have

an opportunity to edit the statement. Then, she asked that the Board consider participating on a subcommittee to develop input for the working group. Dr. MacKay asked those who could do so to stay for an hour after the meeting tomorrow to discuss next steps.

VI. REPORT FROM THE DEPUTY DIRECTOR FOR SCIENCE, OUTREACH, AND POLICY, NIH

Dr. MacKay introduced Dr. Kathy Hudson, the Deputy Director for Science, Outreach, and Policy at the NIH. Dr. MacKay said Dr. Hudson, who joined the NIH in 2009, oversees NIH science policy, legislation, and communications.

Dr. Hudson thanked the Board for inviting her to talk about policy priorities in clinical research, clinical trials results reporting and data sharing. She said she also wanted to discuss a proposed policy encouraging the use of a single institutional review board for clinical trials that are conducted at multiple sites.

Dr. Hudson reported that clinical trials research represents about 12% of NIH's total budget and noted that clinical trial data sharing is of a particular importance in order to inform what research we support and should not support, to prevent the duplication of unsafe trials and to meet the ethical obligation that we have to participants in clinical trials. We tell participants in clinical trials that while they are unlikely to benefit from the study, others will benefit from the knowledge gained. If the results are not made public, then we are really not making good on that promise.

Dr. Hudson said that there has been poor publication of results of NIH funded trials. A study found that many months after trials are completed a substantial number still have not published their results. It varies somewhat by phase of trial and sponsor of the trial. Nonetheless, what we need to do is get this number up to 100%.

Just before Thanksgiving, a Notice of Proposed Rulemaking (NPRM) on data reporting from clinical trials into ClinicalTrials.gov was published. This proposed rule would implement the clinical trials reporting provisions of the FDA Amendments Act of 2007 (FDAAA). It applies to both publicly and privately funded trials of any FDA regulated product, whether it be a drug, device, or biologic. It requires trial registration within 21 days of enrollment and submission of aggregate results.

There are enforcement provisions. If you fail to comply as a grantee, and of course, grantees are institutions, not investigators, funding from federal sponsors should cease. So that is actually a very large stick. There are also FDA civil monetary penalties of up to $10,000 per day, per offense. So as we move forward and as these rules become final we'll need to verify with the NLM that submission of information is up to speed and to communicate that with the appropriate NIH or other government funders. We will notify both Institutions and Investigators suspected of noncompliance and then help them achieve compliance.

Dr. Hudson said that there are trials that are not covered by FDAAA, including Phase I trials, Small Feasibility Device studies which are essentially Phase I, and trials interventions that are not FDA regulated products. Dr. Collins opted to extend the requirements to submit to

ClinicalTrials.gov to all NIH funded clinical trials irrespective of phase or intervention.

The law requires the submission from trials of approved products but it also permitted the Secretary to expand that to unapproved products. NIH did opt to exercise that option, subjecting 7,400 additional trials annually to such regulation. Access to clinical trials data for those products that didn't make it on the market is important as there may be safety or efficacy concerns that would that should be known to the scientific community.

The NPRM was published in November and the draft NIH policy was published at the same time. The comment period ends on March 23.   The expectations would be identical for NIH supported trials irrespective of phase and irrespective of intervention. The data elements submitted would be identical. We will be able to respond to the comments for both the NPRM and for this draft NIH policy at the same time in an identical and consistent way.

Dr. Hudson mentioned that NIH Associate Director for Data Science, Phil Borne, is thinking about how to encourage and provide opportunities for data sharing across the board, not just in clinical trials. Last month, the IOM released a report on *Strategies for Responsible Sharing of Clinical Trials Data* discussing patient level data. There have been a number of companies that have adopted this as a policy and other countries may adopt such a policy. The IOM recommended that participant level data be available. NIH is starting to think this complicated matter through, both in order to make sure people don't use such data in inappropriate and inaccurate ways and also to make sure we protect the privacy of individual research participants. NIH has recently completed a plan for data sharing, in addition to public access to journal articles that reflect NIH support work. We are asking investigators to detail their plans for data sharing of the results of their studies, including clinical and pre-clinical studies. Recognizing how difficult it was to specify requirements for summary clinical trial results, we need to think carefully about how to provide guidance on this.

Dr. Hudson then discussed another proposed policy in clinical research – the use of a single IRB for multi-site studies. It has become clear that the inconsistencies among IRB reviews of the same study actually have very little to do with protecting the research participants involved. There are some models for using a single IRB, including the NCI central IRB for the Cancer Cooperative groups (which must be used unless you can beat their turnaround time), and the NINDS NeuroNext and Stroke Research Networks. The Clinical and Translational Science Awards, managed and operated by the National Center for Advancing Translational Sciences are in the process of trying to develop a mandatory single IRB across the board. There are many reasons why moving to a single IRB makes sense. It is also consistent with NIH recommendations for the proposed modernization of the Common Rule, which governs the inclusion of human beings in research. There has also been strong interest in this single IRB by the Congress.

We know that investigators strongly support the idea of doing anything to shorten the time from when they have a great idea to the time when they are actually able to ask their scientific question. The draft policy would apply to NIH funded multi-site studies in the U.S. The IRB would be identified by the applicant and approved by the funding IC. Some costs for IRB review are included in the award, and there are important exceptions as well.   Dr. Hudson concluded by

noting that this proposal was published in December with a sixty-day comment period. NIH has received about 165 comments.

Dr. Hudson's presentation engendered questions and discussion about the many significant issues associated with broader data sharing requirements. Asked by Dr. Greenes what mechanism would ensure that grants comply with data sharing requirements, Dr. Hudson said that grantees would have to attest to their compliance, and it would count in the scoring of a future application. Dr. Greenes asked if there would be oversight of compliance at the end of the grant as well. Dr. Hudson said that had yet to be determined, but suggested that future funding could be withheld.

Dr. Esther Sternberg said, regarding a study that is measuring environmental attributes and linking them to physiological and behaviorable variables, she is grappling with such questions as: When is data sharable? When does it risk the whole design of the study? When is it going to risk people making subjects anxious over something that may not need to be anxious about? Does NIH have guidance on such matters? Dr. Hudson said she did not have guidance on that. She noted that it's not dissimilar from a more common occurrence in health systems. What is the difference between quality improvement activities versus research? This is an active area of discussion and debate.

Dr. Ralph Roskies said that even when there is nothing secret or confidential to worry about, agencies have not come to terms with the fact that it costs money to maintain data. And how are you going to do that past the term of the grant? Dr. Hudson agreed that it's an important issue, stating that Phil Bourne, NIH Associate Director for Data Science, is spending a lot of his time thinking about support for the sharing of data well beyond the data accrual period.

Dr. Roskies asked Dr. Hudson if she expects to have this understood before she mandates that the proposers have to have address data sharing? Dr. Hudson said no, not beyond what is already mandated for clinical trials data sharing and for genetic data sharing, and asked Jerry Sheehan to confirm this.

Jerry Sheehan said that, as a first step, the new NIH policy will require the submission of a data management plan that can be reviewed with a research application. So, what you're proposing to do with your data can be evaluated to see if it is consistent with the community's expectations for that type of data. Betsy Humphreys commented that some people will have an obvious place to store their data. In these cases, submission of the data management plan will verify that applicants know where their data can be most usefully deposited.

Dr. Hudson commented that in addition to having a place to put it, and support for somebody to maintain it, there is also the issue of motivations and rewards for sharing. Presently, you get academic credit if you publish your clinical trials in the New England Journal, but you don't get academic credit if you've submitted your data and it's not citable. So starting to work on the cultural change regarding credit and what is citable in the biomedical research community is going to be important as well.

VII. NOTICE OF PROPOSED RULEMAKING: CLINICAL TRIALS REGISTRATION AND RESULTS SUBMISSION

Dr. MacKay introduced Jerry Sheehan, NLM Assistant Director for Policy Development, to discuss the Notice of Proposed Rulemaking (NPRM), issued by the DHHS on November 19, 2014. It describes proposed regulations for registering and submitting summary results of certain clinical research studies submitted to ClinicalTrials.gov.

The NPRM implements provisions of the FDAAA of 2007, which requires rulemaking around particular issues that Congress didn't resolve before enacting FDAAA.

Moving from a law to a regulation is a lengthy process. Since he last updated the Board in September, Mr. Sheehan said, the NPRM has been issued for public comment. As Dr. Hudson indicated earlier, NIH also announced a proposed policy that would extend similar registration and results reporting requirements to all clinical trials funded by NIH.

The NPRM is a detailed regulatory proposal. Of its 116 pages, only about 18 are the proposed regulatory text that would go into the U.S. Code of Federal Regulations (CFR). The balance describes and justifies the proposals. The NPRM is directed at the people who would submit trial information, establishing the rules against for compliance. The NPRM clarifies who is a "responsible party" for registration and results submission. It is either the sponsor of a clinical trial or a designated principal investigator.

The NPRM clarifies that "Applicable clinical trials" are controlled interventional studies of drugs, biological products, and devices that are regulated by the FDA, excluding phase 1 trials of drugs and biological products and small feasibility studies of devices. It proposes an algorithm that uses registration data elements to determine if a trial is an applicable clinical trial.

The NPRM would require registration of applicable clinical trials no later than 21 days after enrollment of the first participant. Required data elements include those specified in FDAAA, but FDAAA also allows modification to registration data elements as long as the changes do not reduce but, rather, enhance the available information.

The NPRM proposes major changes for results reporting. Most notably, it proposes to expand the set of trials subject to results reporting to include trials of products that have not been approved, licensed, or cleared by the FDA. The NPRM also proposes additional data elements for results submission and more rapid updating of certain data elements.

For adverse events, the NPRM proposes summaries of all serious adverse events and all other adverse events that occurred more than 5% of the time in any trial arm. It solicits public comment on other information that might help people interpret the adverse events and on the value of an all-cause mortality table listing how many study participants died.

Both the NPRM and draft NIH policy are open for public comment until March 23.

Dr. Roskies asked whether negative comments were ever received. Mr. Sheehan said comments received to date have been overwhelmingly positive. Comments on the burden of registration and results submission will come in closer to the closing date.

Mr. Sheehan attributes some of the complexity of the NPRM to FDA's desire for considerable clarity for enforcement purposes. Betsy Humphreys said that the new law combines the worst features of ambiguity, inconsistency, and specificity. Without interpretation through rulemaking it would be very tough to determine whether a certain study was is in or out, and who's responsible for carrying out the new requirements.

Asked by Dr. Kenneth Walker to explain the significance of the NPRM, Mr. Sheehan replied that it is to increase the transparency of clinical research results for the benefit of patients, the public and research communities. Dr. Walker asked why it is restricted to drugs and medical devices and Ms. Humphreys replied that the scope was specified in the law.

Asked how enforcement of the NIH policy would work, Mr. Sheehan replied that NIH and other Federal agencies would enforce the policy for trials they support by withholding grant funds. The direct fines for non-compliance would be enforced by FDA. Finally, Dr. Walker asked whether NIH has honestly made this process as simple as it can be. Yes, Mr. Sheehan replied, given all of the constraints, inconsistencies, ambiguities, etc.

VIII. NLM'S ROLE IN PRESERVING THE COUNTRY'S CULTURAL HERITAGE

Ms. Joyce Backus, NLM Associate Director for Library Operations, said she would be discussing NLM's historic and current role in identifying, collecting, preserving, training the professionals, and providing permanent access to the country's cultural heritage, because these are all part of the preservation picture.

It began in the nineteenth century with a pathologist who led NLM's predecessor library for 30 years. John Shaw Billings was appointed library director in 1865, at age 27, and created the foundation of today's collection and its indexing and cataloging operations. At that time, the library was a room of books loaned to Army surgeons. When he sought congressional funding for publication of the Library's complete catalogue in the 1870s, Billings had already envisioned a national medical library.

Fast forward to 1944, the Rockefeller Foundation commissioned a report that criticized the then Army Medical Library strongly and made recommendations for improving our facilities, products, services, and our staff. This report had such an impact on Colonel Joseph McNinch, library director from 1946 to 1949, that he said that it was his bible.

In 1951, under director Dr. Frank Rogers, the Army Medical Library produced a report that was in essence the first scope and coverage policy for the collection. In 1976, the Library's Board of Regents adopted a high level "Collection Development Policy of the NLM." Like the 1951 report, the 1976 policy accented the freedom to collect materials in any appropriate format, opening the door for new technologies and data storage methods.

Ms. Backus showed the Board the online version of today's Collection Development Policy. The policy requires that we maintain a dialogue with the Library of Congress and National Agricultural Library to keep duplication to a minimum and issue joint collecting statements to define areas of mutual interests. Over the years we have developed cooperative statements on veterinary science, human nutrition and food, biotechnology, and the AIDS literature.

Ms. Backus then gave an overview of how the NLM physical space has been modified to accommodate growing collections. Space-saving compact shelving was installed on the lowest basement level beginning in the 1970s. More recently compact shelving was added to the second basement level, after the installation of special fiber-reinforced polymer to strengthen the flooring, adding over 70,000 linear feet of space. At the current rate of growth, we are good until 2030.

Ms. Backus then mentioned and showed examples from several specific products to collect, preserve, and ensure permanent access for the public, including *Profiles In Science*, Images from the History of Medicine Database, PubMed Central (PMC) which includes digitized back files as well as currently published journal articles, and Digital Collections, which complements the PMC by providing access to historical monographs and other non-journal materials.

In 2010, NLM became a partner in a grant from the Alfred P. Sloane Foundation that helped establish the Medical Heritage Library -- a digital curation collaborative among America's leading history of medicine collections to promote free acts and open access to quality materials. So far, NLM has contributed over 10,000 items from our collections electronically to the Medical Heritage Library dating from 1610 to 1923.

What about Web collecting and archiving? We want to preserve the cultural heritage of biomedicine whether on physical media such as paper, or electronic media at risk of loss. We have a General Health & Medical Blogs collection that includes both patients and the providers, and also subjects, such as H7N9, Avian flu, and an Ebola collection, which includes information from NCBI, CDC, news outlets, and other government sources.

An important aspect of preservation and providing permanent availability is dissemination. One of our more interesting recent experiments involves getting information out involves Linked Data, which facilitates discovery and linking. Last November, we released our Medical Subject Headings (MeSH) terms as Linked Data.

To close, Ms. Backus referenced the beautiful book, *Hidden Treasure*, which presents images and essays about works from the NLM collection. In the foreword, Dr. Lindberg tells us that there are times when we need to see and hold original intellectual works.

Board member Ms. Sandra Martin asked Ms. Backus about storage after 2030. Ms. Backus replied that NLM is collecting less of the print literature. We've found that the print and online versions of publications are not equivalent. So we preserve the electronic versions sent from publishers when they choose not to participate in PMC.

Consultant Dr. Kenneth Walker asked how many books and journals does the Library own and what percentage of those are digitized. About 18 million items, Ms. Backus replied, but that figure includes extensive holdings from the archives and manuscripts. We have the 10,000 or so items in the Digital Collections and all of the materials from the PubMed Book Shelf, which is another way we archive materials.

Basically we have electronic copies of far less than 50% of our collection, added Betsy Humphreys. Of course, as we begin to acquire more things electronically and add them to the collection, the percentage is going to go up simply because less will arrive in physical formats. But it is absolutely true that at this moment that there are many things in the NLM collection that are not readily accessible in electronic form.

Dr. Walker asked how NLM compares to the Library of Congress. Ex-officio member Kathryn Mendenhall replied that they have the same issues that the NLM has. The early material in their vast collection had to be microfilmed but they are also looking at how best to preserve the born digital information that is so prevalent.

In fact, Ms. Humphreys continued, for a very high percentage of the electronic articles that are published today, publishers are using a standard format developed by NCBI. Therefore, people can design to that format and we all can worry together about how to migrate large volumes of articles in that single format forward – an easier task than migrating articles in many different formats.

Board member Ms. Yokote asked how NLM could set priorities about what to digitize.

Board member Dr. Roskies asked whether there have been instances where people have digitized things and put them on a medium which, ten or 15 years later, you can't find readers for. Yes, said Ms. Backus. In those cases, we have had to re-preserve.

Board member Dr. Fleming asked whether PubMed Central is the main hedge against an online publisher going out of business and their archives disappearing. Yes, Ms. Humphreys replied, for journals that are deposited there it absolutely is.

Ms. Mendenhall mentioned another important part of the answer to Dr. Walker's question, why not digitize everything? Rights information and copyright is a huge part of any digitization effort.

As Ms. Backus well illustrated, said Ms. Humphreys, NLM and its predecessors have long been the backbone of preservation of the country's medical heritage. However, as in many similar institutions that have a piece of this responsibility, for many of the items that we have collected, there is no backup.

IX. DISCOVERING AND APPLYING KNOWLEDGE IN CLINICAL DATABASES

Dr. George Hripcsak said the long-term goal of his ongoing project is to learn from data in the EHR and to apply that knowledge to relevant problems. His research is supported by an NLM

grant now entering its 16th year. According to NIH Reporter, there are 84 publications that cite this grant, including more than 20 in the past two years.

The advent of the EHR has greatly amplified the ability to carry out observational research, opening the possibility of covering emerging problems, diverse populations, rare diseases and chronic diseases in long-term longitudinal studies.

In the US, there are a billion patient visits per year. It has cost $2.5 trillion to produce the resulting data and we need to use it as best we can. However, there are challenges. People often point to lack of penetration of electronic health records as an issue in using them for research, but we've made a huge leap forward in recent years, getting to 30% usage. Standards are an important problem, but NLM is working on that. Privacy is a hard problem, but he can envision a solution.

Dr. Hripcsak said the biggest challenge comes from the inaccuracy, incompleteness, complexity and resulting bias inherent in the recording of the health care process—in other words, the quality of the data and the bias that it produces.

Unfortunately, health care data are complex. A lot is in narrative form and people make up abbreviations as they go along and that makes it harder to interpret. The good news is that natural language processing has become fairly mature and what you see here is a success. The data are highly biased because medicine is a complex, feed forward network. The patient is sick, you sample and intervene, and that changes his or her state. So what you're measuring is directly affecting how you measure it.

Dr. Hripcsak presented a chart showing severity of illness and mortality. Interestingly, the healthiest people are dying more often than the second healthiest people, suggesting you should be a little bit sick to save your life. If a patient comes to the ER severely ill and dies soon after, there is no incentive for the doctor to spend time documenting the patient's symptoms in the health record, so the death will be recorded without the symptoms. It will therefore appear that a healthy person died. The question is, how do we get from a naive use of health care data to a more complex and correct use of the data? Can we deconvolve the truth?

There is something called "the physics of the medical record," and the idea is to study the medical record and not the patient. The medical record is in effect the recording of the patient; we need to understand that recording and undo the damage that we've done in that recording in order to know more about the patient.

Dr. Hripcsak then described an early experiment of his, which looked at 3 million patients, 21 lab tests and 60 concepts derived from notes, using natural language processing. The idea was to put the data into a relatively simple equation, searching for linear correlations among patients. Some interesting problems emerged; for example, in some cases, pancreatitis causes hyperglycemia, so cause and effect were reversed. Why would that be? You have to know what you're doing —you might accidently flip cause and effect because you forget this is the time of diagnosis not the time the patient got the disease.

We can use health records to study physiology over a population and geographically over a larger sample. We can look at where there's more fast food, more healthy food and various income levels, and see how physiology changes across the city.

Dr. Hripcsak said he was giving an informatics talk, not a clinical talk, yet the whole purpose of his research is to advance clinical medicine. This project studies electronic medical records to better understand how health care processes cause data problems. By correcting those problems, we hope to improve reuse of the data for clinical research and quality improvement.

The Observational Health Data Sciences and Informatics (OHDSI) initiative is an international collaboration of about 92 members who do observational research around the world. Its goal is to collect a billion patient records over the next 10 years. What it tells you is that a sample with one tenth of the size of the world population is feasible. That is quality information that we use for discovering drug side effects, etc. What's important about this initiative is that all the participants are tightly tied to clinical studies. What we're doing, in effect, is a first test case and then saying, "Is there any study you'd like to do on 2 million patients from around the world?" We're pushing toward the point that patients would be able to go in for a medical appointment, say, "Here is my disease, my gender, my age," and we could then see how often that side effect actually occurs. Health record data has value for clinical research. There needs to be a more formal study of health records, a tighter integration of clinical goals and the methodological research.
Dr. Robert Greenes asked whether Dr. Hripcsak and his collaborators would like to get to a point where you have a patient that you're seeing and you take patients who are very similar, and find out how they did on a particular drug.

That's exactly what we want to do, Dr. Hripcsak replied. To have a large enough pool, 2 million patients aren't enough, but maybe with a billion you could start to figure it out. We did an experiment to see how the world treats diabetes, depression and hypertension. The pool of patients was treated for three years. The interesting thing was that 20% of 20 million patients are on a unique sequence of drugs. It was a huge discovery.

X. EXTRAMURAL PROGRAMS REPORT

Dr. Valerie Florance began by requesting the Board's approval for EP's operating procedures—an action that is taken every year. She summarized them and noted the section in the BOR book that described them in detail. The operating procedures cover the types of adjustments that can be made to award amounts with and without BOR approval. Special Council Review is another facet of operating procedures, which calls for increased scrutiny of new applications from well-funded investigators (i.e., those with over $1 million per year in direct costs from active NIH research project grants). The existing procedure was covered at tab 7A in the book. The operating procedures were amended to include the Special Council Review back in 2012 and then re-affirmed them every February. Dr. Florance asked for a vote of approval to continue using the procedures that were described. The Board approved this action.

The second item, which is presented to the Board every other year, is a report on the inclusion of women and minorities in clinical research, a report that is required by NIH. NLM makes sure that the grants it awards are complying with NIH requirements in this area. The draft inclusion

report for the 2013-2014 biannual report was provided at tab 7B. With BOR approval, the NLM Director signs it and sends it to the NIH Director. The NLM doesn't support clinical trials in the traditional sense, but does support extramural research that involves human subjects. In 2013, NLM had four extramural research projects that had enrollment of about 16,000 subjects. The Board, in a voice vote, gave unanimous approval to the draft report.

Then Dr. Florance made a presentation covering options NLM could consider for a new kind of grant, the 'person-oriented grant'. At the September BOR meeting, Board chair Dr. Trudy MacKay reported back on EP subcommittee discussion of person-oriented grants as opposed to project-oriented grants, which is what are given now. The idea for person-oriented awards, also called sustained excellence awards, came up in response to a question among the IC Directors — how can we do a better job of fostering innovation? Research grants focused on projects are said to support incremental advances, and but more breakthroughs are desired. The general concept was to fund the researcher for more than five years, with a lot more money, and have review focus on his or her past accomplishments, not on specific aims or hypotheses. She noted that there are other ways to foster innovation that NIH uses right now. One of them is the NIH Director's Pioneer Award and, in fact, NLM has supported several of these. This is a high risk, high award grant for people who haven't worked in this kind of area before. Another consideration is a MERIT award, which extends the funding and length of an existing research project grant that received an excellent priority score on a continuation request. In this approach, the PI is asked to provide insight into new directions that might be pursued if more years/funds were available. A number of NIH Institutes use this mechanism now. Dr. Florance asked BOR members whether, considering the nature of informatics as a science, the field need a person-oriented research grant? She stated that NLM ought to keep the focus on ideas. That's the core of what we want to fund in extramural grants: good science and good ideas. Dr. MacKay opened the floor for discussion of Research Excellence Awards or person-oriented grants. There was lively debate about the need for this type of grant, and whether it represented a step backwards in terms of collaborative research. These grants specifically are not given to teams and yet many of the advances in informatics come from interdisciplinary teams. Others concurred that the issue of the multi-disciplinary teams is very important. Dr. Florance mentioned that there is also a way to phrase a request for grant proposals so that it incentivizes collaboration.

Dr. MacKay supported the notion of the MERIT award approach, as discussed in the EP Subcommittee. If somebody comes in and gets a good score on their new R01, it should be possible for NLM to say at that point that we really like your research; what if we were to give you an extra year or two on that R01, what would you do with it? In that way, the person would get a little extra money and time but it wouldn't eat up much of the small extramural grants budget. Dr. Florance agreed that this was possible and could be implemented easily. Just deciding on a mechanism that achieves stability without taking away from the breadth of the portfolio is challenging. The discussion ended with a sense that the "Sustained Excellence" person-oriented grant did not seem well suited to NLM's research interests or extramural budget at this time.

XI. NLM AND THE CHANGING LANDSCAPE OF IT SECURITY

Ivor D'Souza, Director of NLM's Office of Computer and Communications Systems (OCCS), described how IT security has evolved since the 1960s and how NLM protects data from today's security threats.

In the early years, Mr. D'Souza noted, most security threats were operating system based. Then, the Internet brought a new concern—network security. The first threat to come from the Internet was from emails containing viruses and other malicious content. At that time, in the 1990s, most of NLM's Web sites consisted of static pages with hard-coded links that could be protected by a firewall or other security appliance. Protection was easier in those days than it is now.

Web 2.0 in the mid-2000s changed everything. NLM moved from static pages to more interactive content. Security now has to protect Web servers, application servers and database servers. The multi-tier system increases the probability of vulnerability. There's more to protect, and there are more tools hackers can easily and freely obtain.

Mr. D'Souza said NLM counters today's threats with a balanced combination of technology, processes, and people. Single points of failure are eliminated by building redundancy into the system. There are multiple services, databases and data centers. Firewalls and other techniques limit access to NLM's computer system. Multiple levels of defense are built into the system. And, no one has excessive privileges. People have access only to what they need to access for their job. The bottom line, he continued, is that NLM is reluctant to trust. He said if there's one reason NLM's IT security stands out; it's because of the staff. All IT staffers play a significant role in IT security. As an example of NLM's security success, Mr. D'Souza noted that NLM has been a leader in what's known as continuous diagnostics and mitigation (CDM). NLM started doing it in 2005. NIH adopted the NLM platform in 2011 and HHS followed suit in 2012.

Following the presentation, Dr. Ralph Roskies asked about balancing people's desire for access with security. Mr. D'Souza said NLM historically has a strong culture of appreciating security. Gail Yokote asked how NLM works with third-party vendors. Mr. D'Souza replied that NLM does input validation and works with partners to make sure what's being brought in does not have malicious content. Dr. Robert Greenes asked about denial of service protection. Mr. D'Souza replied that NLM had a service, tested it by creating our own attacks, and eliminated it because it wasn't worth the money.

XII. PUBMED COMMONS

Ms. Hilda Bastian of NCBI told the Board about PubMed Commons, which provides a forum for discussing published articles indexed in PubMed.

PubMed Commons was created because of scientific community interest. A working group representing multiple areas of expertise provides advice for the project. Only authors of publications in PubMed are allowed to comment. Comments cannot be made anonymously or under a pseudonym. People can rate the helpfulness of a comment, but cannot rate the

publication. Comments go online and are moderated afterward. Comments are made under a Creative Commons license.

PubMed Commons began as a pilot in 2013 and is in the final stages of evaluation. Bastian said the quality of the comments has been high, but usage has been low. There currently are 8,445 members and 2,706 comments, which tend to focus on the most current material in PubMed. Comments include discussion of future research; interpretation of results; generalizability and application of research; and enriching and updating the scientific record by author and community curation. Ms. Bastian noted that sharing information in real time speeds scientist awareness about a topic because they don't have to wait for the next paper or the next scientific conference to learn more.

Managing poor comments is an important part of the team's work. Membership in the Commons may be suspended if someone persistently breaches the guidelines. The team encourages positive engagement. Ms. Bastian observed that scientists are accustomed to peer review before publication so it's a culture change to get them to put effort into review after publication. To encourage discussion, the team launched PubMed Commons Journal Clubs to set up accounts, established identities, and online discussions.

In questions following the talk, Dr. Esther Sternberg asked about screening for conflict of interest. Bastian said one of the guidelines requires members to declare conflict of interest, but acknowledged there's no great solution at the moment. Dr. Ralph Roskies asked about comment moderation. Bastian said it's both human and computational. Dr. Robert Greenes asked about competition. Bastian said she doesn't consider discussions in other venues to be competition and hopes people recognize the value of adding those discussions to the Commons so they can become part of the record. NCBI Director Dr. David Lipman commented that usage is low because there's no incentive for commenting and comments can't be done anonymously. He called PubMed Commons a worthwhile experiment and said the benefits far outweigh the costs.

XIII. APPOINTMENT OF NOMINATING COMMITTEE FOR THE NEXT BOR CHAIR

NLM Board of Regents Chair Dr. Trudy MacKay announced the appointment of the nominating committee for the next chair. The committee consists of Kathryn Mendenhall of the Library of Congress, Dr. Charles Rice of the Uniformed Services University of the Health Sciences, and Dr. Cathy Nace of the Defense Health Headquarters.

XIV. ENVIRONMENTAL HEALTH ANIMATIONS

Dr. Alla Keselman, a senior social science analyst in NLM's Division of Specialized Information, demonstrated environmental health animations for the science classroom. They are geared toward a middle school audience. Dr. Keselman noted that while students may learn about the science of pollution, they aren't always taught about the health effects. That's where the SIS resources fit in. SIS developed an Environmental Health Student Portal that covers four main areas: air pollution, water pollution, chemicals in everyday environments and climate change. The portal was developed with input from teachers and other collaborators who

requested more videos on the website. SIS decided that with a proliferation of free or relatively low-cost animation and editing tools, it could produce engaging videos in-house. The assignment went to the division's tech-savvy interns. They created a variety of videos on topics including the dangers of lead; health implications of ground level and stratospheric ozone; particulate matter; and mercury and health. Dr. Keselman played a sampling of the videos and then introduced Queen Alike, an SIS intern and recent graduate with a bachelor of science in community health and an interest in nutritional eating behaviors in children and adolescents.

Ms. Alike currently is producing an animation on arsenic. She used NLM and other federal information resources to create a storyboard, blending the scientific content with an engaging plot. She created inquisitive adolescents characters. Once the storyboard was complete, Alike used a low-cost tool to animate the content.

Dr. Henry Lewis praised the presenters for focusing on the learning style of today's students. He asked if the videos have been tested and promoted to schools. Dr. Keselman said all the videos are now in the public domain and SIS is brainstorming how to promote and test them nationally. Dr. Lindberg encouraged her to work with local teachers first. Dr. Holly Buchanan asked what SIS envisions for the future. Associate Director, Dr. Steven Phillips emphasized the importance of data visualization. Dr. Lewis and Dr. Sternberg also noted the importance of outreach and engaging the public and youth. NLM Deputy Director Betsy Humphreys added projects like the environmental health animations can give others an idea of how to use the library's information. Dr. Keselman said the videos are on the Environmental Health Student Portal and the NLM YouTube Channel.

XV. ADJOURNMENT

Dr. MacKay adjourned the Board of Regents meeting at 11:45 a.m. on February 11, 2015.

ACTIONS TAKEN BY THE BOARD OF REGENTS:
- ➢ Approval of the September 9-10, 2014 Board Minutes
- ➢ Approval of the February 9-10, 2016 Future Meeting Dates
- ➢ Issued a Board Resolution in Honor of Dr. Donald A.B. Lindberg
- ➢ Approval of Grant Operating Procedures
- ➢ Approval of Inclusion Report for Women and Minorities
- ➢ Created Nomination Committee for Next Board Chair

Appendix A - Roster - Board of Regents
Appendix B – Resolution for Dr. Donald Lindberg

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

Donald A.B. Lindberg, M.D.   Trudy MacKay, Ph.D.
Director, National Library of Medicine   Chair, NLM Board of Regents