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

MINUTES OF THE BOARD OF REGENTS
February 9-10, 2016

The 171st meeting of the Board of Regents was convened on February 9, 2016, at 9:00 a.m. in the Donald A.B. Lindberg 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 4:10 p.m., followed by a closed session for consideration of grant applications until 4:30 p.m. On February 10th, the meeting reopened from 9:00 a.m. until adjourning at 11:45 a.m.

MEMBERS PRESENT [Appendix A]:
Dr. Alessandro Acquisti, Heinz College, Carnegie Mellon University
Dr. Robert Greenes, Arizona State University
Ms. Sandra Martin, Wayne State University
Dr. Daniel Masys, University of Washington
Dr. Esther Sternberg, University of Arizona
Dr. Jill Taylor, Wadsworth Center, New York State Department of Health
Ms. Gail Yokote [Chair], University of California, Davis

EX OFFICIO AND ALTERNATE MEMBERS PRESENT:
Mr. Christopher Cole, National Agricultural Library
Dr. Joseph Francis, Veterans Health Administration
Capt. David Goldman, Office of the Surgeon General, PHS
Col. Helen Hootsmans, United States Air Force
Dr. Jane McAuliffe, Library of Congress
Col. Michael Nelson, United States Army
Dr. David Neri, United States Navy
Dr. James Olds, National Science Foundation
Ms. Linda Spitzer, Uniformed Services University of the Health Sciences

CONSULTANTS TO NLM PRESENT:
Dr. H. Kenneth Walker, Emory University School of Medicine

SPEAKERS AND INVITED GUESTS PRESENT:
Dr. Isaac Kohane, Harvard Medical School [via videoconference]
Dr. Michael Lauer, Office of Extramural Research, National Institutes of Health
Dr. Neil Thakur, Office of Extramural Research, National Institutes of Health

MEMBERS OF THE PUBLIC PRESENT:
Ms. Andrea Baruchin, Friends of the National Library of Medicine
Mr. Glen Campbell, Friends of the National Library of Medicine
Mr. Jason Chong, Booz Allen
Ms. Madeline Halpern, ICF International

Ms. Lesley Macherelli, 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:
Ms. Betsy Humphreys, Acting Director, NLM
Ms. Anne Altemus, Lister Hill Center, 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
Dr. Olivier Bodenreider, Lister Hill Center, NLM
Ms. Kathy Cravedi, Office of the Director, NLM
Mr. Todd Danielson, Office of the Director, NLM
Ms. Darlene Dodson, Office of the Director, NLM
Ms. Victoria Douglas, 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
Ms. Martha Fishel, Division of Library Operations, NLM
Dr. Valerie Florance, Division of Extramural Programs, NLM
Dr. Kin Wah Fung, Lister Hill Center, NLM
Ms. Katie Funk, National Center for Biotechnology Information, NLM
Dr. Dan Gerendasy, Office of Health Information Program Development, NLM
Mr. David Gillikin, Division of Library Operations, NLM
Mr. John Harrington, Lister Hill Center, NLM
Dr. Michael Huerta, Office of Health Information Program Development, NLM
Dr. Vojtech Huser, Lister Hill Center, NLM
Ms. Christine Ireland, Division of Extramural Programs, NLM
Dr. Stefan Jaeger, Lister Hill Center, NLM
Ms. Janice Kelly, Division of Specialized Information Services, NLM
Dr. John Kilbourne, Division of Library Operations, NLM
Mr. Kenneth Koyle, Division of Library Operations, NLM
Dr. David Landsman, National Center for Biotechnology Information, NLM
Ms. Jennifer Marill, Division of Library Operations, NLM
Dr. Clement McDonald, Lister Hill Center, NLM
Ms. Kathy McKay, Office of the Director, NLM
Mr. Dwight Mowery, Division of Extramural Programs, NLM
Dr. Jeffrey Reznick, Division of Library Operations, NLM
Mr. Jerry Sheehan, Office of the Director, NLM, on detail to the Office of Science and
Technology Policy
Dr. George Thoma, Lister Hill Center, NLM
Ms. Patricia Tuohy, Division of Library Operations, NLM
Dr. Rebecca Williams, National Center for Biotechnology Information, NLM
Dr. Fred Wood, Office of Health Information Program Development, NLM

I. OPENING REMARKS

Ms. Gail Yokote, NLM Board of Regents Chair, welcomed new members Dr. Alessandro Acquisti, Professor of Information Technology and Public Policy at Carnegie Mellon University, Dr. Daniel Masys, Affiliate Professor of Biomedical and Health Informatics at the University of Washington, and Dr. Jill Taylor, Director of the Wadsworth Center at the New York State Department of Health, alternates, and guests to the 171st Board meeting. She then introduced Capt. David Goldman, MD, MPH, to present from the Office of the Surgeon General.

II. REPORT FROM THE OFFICE OF THE SURGEON GENERAL (OSG), PHS

Capt. David Goldman, MD, MPH, Chief Medical Officer and Chief Professional Officer for Physicians in the US Public Health Service, reported on recent initiatives and activities of the Office of the Surgeon General (OSG).

The Surgeon General spoke to over 70,000 people at 134 events in 20 states in four countries last year. OSG themes include community-based prevention and health equity. Physical activity, healthy eating, emotional well-being and suicide and violence prevention, and tobacco-free living, are emphasized. Surgeon General Murthy continues to encourage walking in the workplace and is very engaged in working with community leaders to make environments walkable. In October, 2015, the Surgeon General attended a walking summit and filmed a PSA with actress Allison Janney.

The OSG's addiction campaign, said Capt. Goldman, will culminate in a report that will focus on providers and state that addiction should be treated as a chronic disease. The Surgeon General will write every prescription provider in the country asking them to pledge to examine their own opioid prescribing. To launch this campaign, the Surgeon General joined the National Association of State Alcohol and Drug Abuse Directors at their November conference, participated in the Institute for Healthcare Improvement's roundtable on prescription opioids, met with the White House director of drug control policy, and joined Congressman Joe Donnelly to speak to the press about the explosion of opioid use in the US. He also appeared with Dr. Oz to discuss substance addiction and filmed a public service message on addiction with CBS, which is scheduled to run later this month.

The OSG will continue to focus on tobacco-free living. In his role as chair of the National Prevention Council (NPC), he is asking all participants on the Council to develop campus-wide tobacco-free policies. He will be developing reports on tobacco control and the benefits of quitting targeted for 2018 and on addressing tobacco control and health disparities targeted for 2019. The other major NPC initiative relates to healthy eating. He is asking all Council members to implement healthy food guidelines in new and existing food service contracts.
As a result of the 2015 White House Conference on Aging, the OSG and the NPC are working with the CDC to produce a healthy aging action plan later this year, and there will be a SG report on nicotine delivery systems and young adults.

Dr. Goldman then discussed some of the emergency response activities with respect to Ebola. Over 600 officers set up clinical trials in West Africa. A few weeks ago, the World Health Organization declared that West Africa is now Ebola free.

Since the last BOR meeting, there was a mass shooting in Oregon. The Commissioned Corps did deploy a multi-disciplinary strike team to that area, and to Flint, Michigan to help the county health department in its outreach to the community there.

Dr. Sternberg asked Capt. Goldman about the Zika virus. He said that as action plans are developed, the Commissioned Corps would be involved. NLM Acting Director Betsy Humphreys noted that NLM is working with government agencies to make information about Zika virus, the Flint, Michigan water situation, and the unfortunate gas leak in California, available. NLM is making sure that the medical subject headings and standards are up to date on Zika. NCBI has produced a special Zika Virus resource to facilitate retrieval, viewing and downloading related sequence data.

Dr. Francis said one of the challenges in creating livable and walkable environments is the need for certain quantitative tools to model what the economic impact would be from creating more green space. Dr. Sternberg said that she is working with GSA and noted that she could share some information about that topic with Dr. Francis. She is measuring 11 attributes and linking them to behavioral variables in real time. The findings will be released to the American Institute of Architects in May.

III. SEPTEMBER 2015 MINUTES AND FUTURE MEETINGS

The Regents approved without change the minutes from September 16-17, 2015 meeting. The May 2016 meeting will take place on May 3-4, 2016, the 2016 fall meeting will take place September 13-14, 2016, and the Board approved holding the winter meeting February 7-8, 2017.

IV. REPORT FROM THE NLM ACTING DIRECTOR

Acting Director Betsy Humphreys said that as part of the FY 2016 Omnibus, NIH received an additional $2 billion over the 2015 level. NLM received $394.7 million, an increase of $57.7 million over the 2015 level. $44.5 million was earmarked for NCBI plus a general increase of $13.2 million.

Ms. Humphreys announced that the DeBakey Medical Foundation gave the NLM a very generous gift to support digitizing and enhancing access to the Michael E. DeBakey archives and related collections. Given the breadth of his career, his papers connect to many others in the NLM collection. This gift will also support other exciting programs in the History of Medicine Division (HMD), including fellowships and lectures The Foundation for Advanced Education on the Sciences (FAES) is going to assist NLM in the administration of the fellowships. A public announcement of the gift was released that day.

Ms. Humphreys updated the Board on NLM personnel. Dr. Collins had informed her that he was finishing up interviews for the new NLM director this week. We may know more by the end of March. Tomorrow afternoon the portrait of Don and Mary Lindberg will be unveiled. It will then be hung temporarily outside of the Lindberg Room. All are invited, compliments of the Friends of the NLM, host of the unveiling event.

Ms. Humphreys then informed the Board that Dr. David Lipman had decided to step down as the Director of NCBI. [NOTE: Subsequently, on March 9, 2016 the Director, NIH issued a statement that Dr. Lipman had agreed to continue his leadership role as Director, NCBI and would also serve as Associate NIH Director for Biomedical Information Resources.]

She also highlighted the retirement of two distinguished members of the NLM senior staff:
- Dr. Steven Phillips retired at the end of November, 2015. His most recent position at NLM was Associate Director of Specialized Information Services (SIS), but he also served as a member of the Board from 1993 to 1997, and as its Chair in 1997.
- Dr. Michael Ackerman retired in January 2016 after 44 years in the government. As NLM's Assistant Director for High Performance Computing and Communications, he. Was instrumental in managing NLM's Visible Human Project and development of the ITK Segmentation and Registration Toolkit.

Ms. Humphreys then introduced two new arrivals to the NLM. Vojtech Huser, MD, PhD, joined the Lister Hill National Center for Biomedical Communications in September 2015. He had previously worked in the NIH Clinical Center. Kevin Fain, JD, DrPH, joined NCBI in September 2015 as a staff scientist. He previously worked as an FDA attorney specializing in pharmaceutical and clinical trial regulation. Ms. Humphreys also called the Board's attention to the several new fellows in the Lister Hill Center and NCBI, described in the Board book.

With respect to legislation, under the Consolidated Appropriations Act of FY 2016, every public communication issued by an agency now has to be accompanied by the statement that it was paid for by the public. NLM is awaiting guidance on how to implement this requirement.

Recently, Humphreys noted, the Senate abandoned the effort to consider the House-passed 21st Century Cures Act. They have instead announced that they are going to develop several bills addressing different topics. There is concern that this strategy will make it difficult to include increases for NIH. The first bill that emerged from this had to do with health IT. Its goals are laudable, although some of the specifics may be problematic.

The Cybersecurity Act of 2015 requires HHS to report to Congress at the end of 2016 on the preparedness of HHS and health care industry stakeholders in responding to cybersecurity threats. It also requires HHS, with NIST and DHHS, to convene a one-year task force of health care industry stakeholders.

Dr. Greenes asked Ms. Humphreys about the interoperability provisions of the Cures Act. He said much of the bill is about HIE. More needs to be discussed rather than rushing into the passage of this legislation. The NLM Acting Director said that there was certainly a great deal of room for improvement in the draft. She said there should be stronger encouragement for those generating the data to standardize it when they generate it. She pointed out that the bill's provisions don't really address labs and standardization adequately.

With respect to the Precision Medicine Initiative (PMI), Tab D includes a list of five funding opportunity announcements. Two of the five funding opportunities make use of special "Other Transaction Authority" which enables very rapid competitions and awards which are anticipated

to be made soon. It is hoped that the PMI and the enrollment of a large cohort of people will be another impetus for the improvement of interoperability and improved transfer of health data. Standardizing clinical research data could help drive greater standardization of healthcare data.

On BD2K, Ms. Humphreys said that the NIH Director expects oversight of the BD2K program to be moved to NLM after a new NLM Director is named. She then called upon Dr. George Komatsoulis, senior bioinformatics specialist the NCBI, to discuss one of the BD2K initiatives, pilot testing of a Commons credit model, which would allow NIH grantees to choose among Commons compliant Cloud services providers to obtain the high-performance computing and data storage option best suited to their research.

Ms. Humphreys noted that NLM's Pill Image Recognition Challenge was announced in the *Federal Register* on January 19, 2016. There is great interest in this across the Administration. Through this Challenge, the NLM seeks high-quality image matching algorithms that rank images in the NLM RxIMAGE database of prescription pill images by similarity to consumer images of unlabeled prescription pills. NLM intends to use this work to develop publicly accessible software and an API that can identify an unknown prescription pill from a user photo.

Ms. Humphreys mentioned several other items described in the Board Book. NLM's *People Locator* system helped to locate a Pakistani man who made a call for help electronically to *People Locator* after he was trapped in a building following a devastating magnitude 7.5 earthquake that had hit South Asia. The first Donald A.B. Lindberg and Donald West King Lecture in Medical Informatics and/or Pathobiology was presented by Russ Altman, MD, PhD at the NIH Masur Auditorium in the Clinical Center on October 7, 2015. It can be accessed at http://videocast.nih.gov/summary.asp?Live=16888&bhcp=1. NLM is participating in National History Day (http://nhd.org), a year-long history competition amongst middle and high school students from around the USA and its territories, for the first time, joining other federal partners including the Library of Congress and the Department of Agriculture.

She then called the Board's attention to a recent announcement that NLM has launched MedPix, a free online medical image database originally developed by the Departments of Radiology and Biomedical Informatics at the Uniformed Services University. The URL for this new database, which includes over 53,000 images from over 13,000 cases, is https://medpix.nlm.nih.gov/.

Dr. Walker said that Ms. Humphreys mentioned last year that about 27 percent of the information from the NLM was freely available. Joyce Backus confirmed that 35 percent of PubMed now links to free full text. In response to a question from Dr. Walker, Ms. Humphreys said that she expects the percentage will continue to increase, due to open access publishing.

Ms. Humphreys concluded by showing an ABC News video clip of Benjamin King, an actor on the Disney Channel show "Liv and Maddie," featured on the recent cover of the *NIHMedlinePlus* magazine talking about his successful struggle with Crohn's disease. King is working to raise awareness about Crohn's and thanked the *NIH MedlinePlus* magazine for sharing his story with the public.

V. STANDARDIZATION OF PATIENT MEDICATION DATA

Ms. Humphreys introduced the topic by summarizing the series of steps that led NLM to be designated the HHS Coordinating Body for Clinical Terminology Standards in 2004 and to play an important role in the standardization of electronic health records, including patient medication data. NLM's work on the Unified Medical Language System (UMLS), which Dr. Lindberg initiated shortly after he arrived at the Library in 1984, gave NLM a unique perspective on the universe of existing health terminologies, classifications, and code sets, and an understanding of why there weren't, as yet, agreed upon terminology standards for clinical information. Since 1990, the Library worked with many others to define a strategy that would move the U.S. toward standards for electronic health data:

- Establish a mechanism for designating U.S. *National* Standards
- Pick best available as starting point
- Broaden participation in standards development
- Support development (last resort! for critical gaps), ongoing maintenance, and low/no cost distribution
- Promote use and improvement through: Early Federal adoption, conformance and production testing, demonstration projects, cost/benefit research, incentives
- Coordinate development to achieve interlocking set of standards – *responsive to feedback from real use*

Ms. Humphreys commented that she was generally quite opposed to the development of new terminology standards, as opposed to the maintenance and expansion of existing standards to meet additional needs. However, the development of RxNorm, which would be described by Dr. Kilbourne, was an exception to this rule, since it filled a glaring hole in the standards covering medication information.

The establishment of National Information Center on Health Services Research and Health Care Technology (NICHSR) in 1993 gave NLM some authority and budget to pursue this strategy for clinical terminology and coding standards. In 1996, HHS drafted NLM to co-chair the working group responsible for developing the HIPAA regulations governing the use of code sets in administrative transactions. The doubling of the NIH budget gave NLM ability to support ongoing maintenance and free dissemination of standard clinical terminologies for the country.

With respect to the strategy for achieving US health data standards, is the passage of the ARRA/HITECH Act in 2009 and its incentives for "meaningful use" of electronic health records (EHRs), NLM and other government agencies are currently focused on last two steps of the strategy: promoting use and improvement through early federal adoption, conformance and production testing and demonstration projects; and coordinating development to achieve interlocking set of standards responsive to feedback from real use.

Ms. Humphreys displayed some of NLM's standards milestones to show how they fit into NLM long range planning. The NLM Board issued a special 2009 report on interoperable information, *Enhancing NLM Contributions to the Nation's Heath IT Agenda*. The report had four major recommendations: to reorient the NLM standards agenda to focus on interoperable health

information to address key deficiencies in EHRs; to implement an active feedback loop and enhanced support for UMLS and standards users; to promote clinical and translational research use of standards adopted for routine healthcare; and to effect the convergence of genetic and clinical standards needed for personalized healthcare.

Ms. Humphreys asked Drs. John Kilbourne and Olivier Bodenreider to discuss how NLM did what the Board recommended with respect to patient medication data.

Dr. Kilbourne explained that RxNorm is standard terminology for "clinical drugs" required in the U.S. for certification and "meaningful use" of EHRs. RxNorm was developed to solve two problems that had become evident by 1998. The HL7 standards development organization was attempting to define what information about a drug needed to be included in clinical data exchange in order to facilitate clinical decision support. NLM was trying to develop a better mechanism for determining which drug names meant the same thing so they could be accurately represented in the UMLS Metathesaurus, which is organized by concept. Lexical matching methods that assisted with determining synonymy among names of other types of concepts, e.g., diseases, did not work well for drug names.

National Drug Codes (NDCs) were not a solution for clinical data exchange because they are not clinically-oriented codes. They represent a drug at the package level and are issued by each labeler/manufacturer (not the FDA). He showed a list of NDCs for one drug, Ranitidine 150 Mg oral tablet with hundreds of codes associated with it, as each different package size (e.g., 25 count container, 50 count container) produced by each different manufacturer has a different NDC. There is no central published list of all NDCs and NDC data are inconsistent across sources.

HL7 needed a drug model based on clinically relevant criteria (e.g. ingredient) not on packaging criteria, and the NLM needed a standard clinical drug name to which all variant names could be linked. The answer to both problems was RxNorm, which is oriented around ingredient, strength, and dose form, e.g., "Ranitidine 15 Mg/Ml Oral Solution". The initial RxNorm model NLM developed was not perfect, and it has required elaborations, or additions but we have kept it as simple as possible.

Dr. Kilbourne reviewed milestones in the development of RxNorm, including its first independent release (outside the UMLS Metathesaurus) in 2004, the initiation of monthly releases and the issuance of RxTerms, an entry vocabulary useful in e-prescribing in 2008, and solidified NDC data in 2011.

People find RxNorm useful, and it is heavily used. The Centers for Medicare and Medicaid (CMS) and the Office of the National Coordinator (ONC) require it as the standard for medications and medication allergies and electronic health record certification. The National Council for Prescription Drug Programs (NCPDP), Veterans Affairs and Department of Defense all use RxNorm.

Dr. Kilbourne said RxNorm's philosophy and approach involves active engagement with stakeholders, limited scope (names and codes for drugs), actual use in clinical systems, and simplicity of the model.

Dr. Olivier Bodenreider described the development of tools (RxNav, RxMix, and RxClass) that facilitate use of RxNorm. These tools allow people to navigate and search RxNorm without having to write code or establish a local database. They also integrate RxNorm data with other sources of drug information (drug classes, drug-drug interactions, and pill images).

The usage of RxNorm has grown over time. There are about 900 downloads monthly and the application program interfaces (APIs) are very heavily used. There were more than 1 billion queries in 2015 and 30,000 unique users monthly. The users of RxNorm are NLM applications (MedlinePlus Connect), EHR product developers, pharmacy benefit managers, healthcare insurance companies, clinical institutions, and academic researchers.

Dr. Bodenreider said that RxNorm is used for many purposes: NCPDP SCRIPT's standard for e-prescribing requires RxNorm; DoD and VA rely on RxNorm to mediate drug information across their electronic medical record systems; CMS uses RxNorm in their Formulary Reference File, as part of the guidelines for Medicare drug benefits; drug value sets used in clinical quality measures for Meaningful Use are defined in reference to RxNorm; and OHDSI, the Observational Health Data Sciences and Informatics research group, uses RxNorm to analyze prescription data.

Dr. Bodenreider said there are some remaining challenges for RxNorm. The limited scope of RxNorm has worked well, but having only the drug names and codes has its limitations. For example, having drug classes and interactions as an integral part of RxNorm might be desirable as well. There is also limited coverage of over-the-counter and international drugs in RxNorm.

Dr. Greenes said that RxNorm is a very useful resource. He asked to what extent the SPL is more computable in terms of the fields for linking to. Is there any app or API development in this area? Dr. Kilbourne said that FDA was working on such a product. NLM is working on this issue at the research level but not as an app.

Dr. Masys asked whether there was an NLM overall strategy for recognizing, receiving and deciding to implement mobile-optimized APIs for specific resources. Ms. Humphreys said this issue surfaced several years ago, and NLM publicized the fact that it was making the majority of its data available via APIs. Many developers knew about our APIs, but those new to health applications did not, so we worked on making them more visible to a broader audience. In general, NLM APIs are heavily used.

Dr. Greenes said this question was important in terms of long-term planning. Ms. Humphreys agreed and said that this presentation was designed to raise issues that might be addressed in the next long-term plan.

VI. WATCH IT, PARASITE!

Lister Hill Center researcher Dr. Stefan Jaeger discussed a program that aims to diagnose malaria with image analysis and machine learning. The team in Lister Hill's Communications Engineering Branch (CEB) includes Dr. Sameer Antani and several postdoctoral fellows and the project is being conducted in collaboration with the National Institute of Allergy and Infectious Disease (NIAID)

Dr. Jaeger began his presentation with information about how mosquitoes infect humans with malaria, the scope of the problem, and how the disease is treated. The standard method for malaria diagnosis in the field is microscopy of blood film, which is slow and often error-prone. The problems include patients dying from a false negative, unnecessary use of antibiotics, and false positives which involve the unnecessary use of anti-malaria drugs which can cause complications.

The idea is to use image processing and machine learning to do the counts automatically. This is one of a number of imaging projects in the CEB. Using image processing and machine learning for population screening is already successful for automated screening of chest x-rays to distinguish normal x-rays from those with lung diseases, in particular, TB. (Information on how the system is being used in Kenya to run field trials and analyze the chest x-ray with image analysis to try to detect abnormality automatically was presented to the Board at its May 2015 meeting.) Another project features photo matching functionality to retrieve similar cervical cancer cases, and also, detect abnormalities in digitized histology slides.

Dr. Jaeger noted that they are implementing the malaria screening as a mobile application, so it runs on a smartphone. They are using an adapter to connect the smartphone to a standard microscope and have developed an app that uses the camera of the phone to take a picture of a blood slide through the eyepiece of the microscope. The image analysis software, which is a part of the app, then counts the cells automatically and reports the proportion of infected red blood cells, so that a human operator does not need to count. He said that if they can do this quickly and reliably, it would have a huge impact.

They plan to use their first prototype in Bangladesh and have acquired 200,000 annotated cells from 200 patients that they can use for training. The simple prototype app is currently running basic versions of the algorithm on the smartphone. He said that more sophisticated versions of these basic steps: cell detection and segmentation, and cell classification, will follow soon.

Dr. Masys commented that it was important to engage actual intended users in the development of systems and cautioned that, in his experience, international users might be embarrassed to report usability problems to developers. Drs. Jaeger and Antani agreed with both points and said that they had been working closely with intended users in Bangladesh.

Dr. Greenes asked whether the system can differentiate amongst the different types of malaria. Dr. Jaeger answered that this was not possible at this point, but they are working on it. He noted that it was necessary to have sufficiently annotated image data of the other types of malaria to train the classifier. Since Bangladesh primarily had *P. falciparum* type of malaria, the team chose to focus on that.

Col. Nelson asked about the impact of image quality on the system performance. Dr. Jaeger responded that they could let their software ask the operator whether the image quality is adequate. Or, they can train the software to detect bad image quality automatically. Col. Nelson followed up with a question about the affordability of microscopes in the field, and if anybody is looking at lower cost platforms. Dr. Jaeger responded that they are looking into this, but the field isn't quite there yet. He said that startup companies are working on small microscope attachments to smartphones or all-in-one solutions that combine a microscope with a camera and processor.

Dr. Taylor talked about another possible application—being able to check the quality of water and enumerate legionella colonies on bacterial plates. She also inquired whether 1,000 cells was an accurate number to count for each patient. Dr. Jaeger replied that, to confirm that a patient has been cured of malaria, a much higher number is counted.

VII. CLINICALTRIALS.GOV AND ITS ROLE IN CLINICAL RESEARCH TRANSPARENCY

Dr. Rebecca Williams described ClinicalTrials.gov in the context of the overall trial reporting system (TRS). Much of her presentation was based on recent research, including a paper published by her colleagues Drs. Deborah Zarin and Tony Tse in 2016. (Zarin DA, Tse T. <u>Sharing individual participant data (IPD) within the context of the trial reporting system (TRS)</u>. *PLoS Med*. 2016 Jan 19;13(1):e1001946)

The TRS is based on three components: prospective registration, summary results reporting, and individual participant data sharing. At ClinicalTrials.gov, there are currently over 208,000 studies, and about 500 new studies are registered each week. The registry is more comprehensive for those studies that are subject to legal requirements or other policies that require registration. Dr. Williams explained how NLM and NIH are focused on implementing the Food and Drug Administration Amendments Act (FDAAA), in particular finalizing the rules that will fully implement the Act. Studies have estimated that compliance with the law is improving, but is not yet where it needs to be. In 2014, NIH proposed a policy to require registration and results reporting in ClinicalTrials.gov for all NIH funded trials, whether subject to FDAAA or not. To help ensure that ClinicalTrials.gov is meeting its scientific and ethical objectives, NLM is interested not just in the number of studies registered but also the quality of information. One marker of this is the completeness with which outcome measures are described. Dr. Williams presented data showing that this, too, has been improving over time.

Dr. Williams described the current interest in disclosure of de-identified individual participant data (IPD). The Institute of Medicine issued a report in 2015 summarizing benefits and risks associated with IPD sharing and, at the beginning of 2016, the International Committee of Medical Journal Editors announced a proposed policy that would require IPD sharing for published research. Dr. Williams described the paper written by her colleagues that puts IPD sharing in the context of the overall TRS, describes the different types of IPD, and uses a case study to illustrate the roles of registration, summary results reporting, and IPD. Dr. Williams described the importance of prospective registration as the foundation of the TRS, supporting the activities of summary results reporting and IPD sharing that follow.

Dr. Masys predicted that there will be substantial difficulty in getting general agreement among contributors to provide individual participant data, due to concerns regarding re-identification of de-identified data via data mining techniques.

Dr. Francis said that he appreciated the fact that this is open access. He said in addition to individual patient data about outcomes, understanding baseline characteristics is key, and that a hot topic among his VA colleagues is heterogeneity of treatment effects. He sees this as a step in that direction. He asked about RxNorm, and capturing and standardizing codable structured language.

Dr. Williams agreed that this is of interest and that there are a couple of relevant points. One is that summary results information includes baseline characteristic information, but investigators may not provide all relevant data (the system currently only requires age and gender, but they encourage reporting all relevant baseline characteristics important to a particular study). Second, she spoke about the challenge they have as a repository and how a basic guiding principle is that what is reported to ClinicalTrials.gov needs to be consistent with what was planned. As such, ClinicalTrials.gov can't require that additional analyses be done to help understand some of the issues Dr. Masys identified, however we can accommodate such reporting when the analyses were done.

Dr. Masys said that this requirement could be viewed as another administrative roadblock to getting clinical trials launched. He asked about ClinicalTrials.gov having an API for automated systems that allow people to not have another redundant Web application.

NLM Acting Director Ms. Humphreys answered that it does have an API and that this might be built into commercially available and open source products. However, she believes that developers are waiting for the final rule to avoid writing software that has to be re-written when the final requirements are known.

Dr. Williams added that ClinicalTrials.gov has multi-modal ways of accepting data. One is interactive data entry forms, but they've always accepted XML uploads so if a system understands the requirements. She said the challenge has been the lack of standard ways of collecting and rolling up the data to get up to the required summary level. The NCI has its own portal for monitoring clinical trials that they fund, and we've created a way to interact with their system so CTSAs can provide data directly to NCI and someone can log into our system, grab the data from the NCI system, and pull it into ours.

Ms. Humphreys said ClinicalTrials.gov has revealed that there are many studies for which it is unclear if any useful evidence can result, e.g., due to trial design or inadequate recruitment, which raise ethical issues about why people were put at risk to participate in such studies.

Dr. Williams then mentioned a paper by a researcher in the field of acute kidney injury, who used ClinicalTrials.gov to assess ongoing studies in the field. She evaluated whether the studies were adequately powered to assess that outcome and found that most had insufficient numbers of participants to answer the research question.

VIII. PUTTING THE PATIENT AT THE CENTER OF PRECISION MEDICINE

Dr. Isaac Kohane from Harvard Medical School conducted his presentation via videoconference, due to inclement weather in Boston that led to flight cancellations. He began by talking about the history of precision medicine from the perspective of having served on the National Academy of Sciences committee that delivered a 2011 report on the subject and having just had his article, "Time for Patient Driven Health Informational Economy?," published in the January issue of *The New England Journal of Medicine*.

Dr. Kohane's talk centered on efforts to "instrument" the healthcare enterprise for discovery, including Informatics to Integrate Biology and Bedside (i2b2), a national center for biomedical computing funded by NLM and the precursor to the NIH Common Fund, and SMART HealthIT, funded by the Office of the National Coordinator for Health Information Technology.

Dr. Kohane said that despite some notable false starts, he thinks it is now time for a patient-driven health information economy. As an example, he talked about an intelligent software apps portal and progress made with EHR data liberation and patient control and the use of i2b2 throughout the Harvard medical system. To demonstrate its importance, Dr. Kohane presented information about detection of victims of domestic abuse from data about encounters with different diagnoses through a health system. The technology predicted domestic abuse two years before the health care system detected it. He said, the system should be asking every single patient "Do you feel safe at home?"

Dr. Kohane commented that the easy part was getting the system to work technically and mapping categories of data from the Harvard hospitals for over 6 million patients in real time. The hard part was getting the hospitals to agree to data sharing and making it easy to do.

He believes that the way to make data available to others is by publishing explicit and public programs or interfaces to access different data sets from the genomic to the complex phenotypic. They have embraced open source notebooks such as Jupyter.

He said that there are still many things that need to be overcome to complete the vision of precision medicine, but he feels that NLM can play a leadership role.

Dr. Acquisti asked about privacy concerns and risks that the data might be used for other purposes. Dr. Kohane replied that although he's a fan of being open with data, he thinks technology alone is not going to be the solution and that there needs to be expectations and guidelines around behavior.

Dr. Masys asked where he saw NLM in terms of putting the patient at the center of precision medicine and what would be the next actionable step to accelerate discovery and improvements in the quality and consistency of care.

Dr. Kohane replied that the data liberation movement has to go forward to get the data out of institutions and more into patients' hands. He also pointed to the open note effort, where patients share clinical notes with their providers and correct factual errors and that we should not give up

on the blue button mission. He said it would make a huge difference to have formatted output of data that could be downloaded and shareable.

IX. EXTRAMURAL PROGRAMS REPORT

EP Director Dr. Valerie Florance spoke about NLM's historical role in providing informatics training to MDs, so they have a background to undertake biomedical informatics research.

She began by summarizing recent recommendations of Working Group on Biomedical Workforce of the Advisory Committee to the NIH Director, giving a brief overview of the physician-clinician workforce report. The Working Group found there were 9,000 physician scientists in the NIH-funded workforce, that about 90 percent of them were MDs, that this group lacked racial, ethnic, and gender diversity, and that they were receiving their first NIH grants relatively late in their careers. The Working Group recommended a number of actions NIH should take, including offering more MD/PhD programs, supporting more post-doctoral physicians through fellowships, and developing new career award mechanisms that target clinicians. The Working Group also recommended increasing the amounts in the NIH Loan Repayment Program that helps clinicians pay educational debts after medical school training.

Shifting her focus to NLM programs that have supported the training of clinician-informaticians, Dr. Florance described two programs. One of them, the senior fellowship in bioinformatics was available between 1993 and 2004. It was an individual fellowship the recipient could use at any chosen academic location to take appropriate coursework and undertake research in an area of biomedical informatics. The other program is the still-extant post-doctoral training offered at NLM's university-based training programs. Dr. Florance reviewed data from these two programs, highlighting some similarities and differences in the support model and outcomes. Between 1993 and 2004, NLM awarded 37 two-year fellowships, 20 of them going to clinicians. About 45 percent of fellowship recipients later obtained additional NIH grants; about half of the 20 fellows acknowledged their fellowship in articles they wrote about their research. During the same period there were 139 post-doctoral fellows in NLM university-based training, of whom 71 were MDs or MD/PhDs. In that group about 40 percent obtained additional funding from NIH, but they were significantly less likely to produce articles that referenced their grants compared to the fellowship recipients.

She showed some examples of graduates of each program, including typical current job titles of awardees in both programs. In the university-based training program cohort, a larger number of trainees went into industry, appeared to be working in hospitals or providing health care, while more of the fellowship recipients appeared to hold academic appointments. She noted that NLM does not expect all of its trainees to become academicians, so these outcomes were seen as appropriate.

She said that the question she hoped the Board members would consider is whether NLM should strengthen its offerings for clinicians, through some sort of fellowship or other approach that would allow them to get informatics training mid-career, and welcomed hearing from the members about their views on this.

Following her presentation on training for clinician-scientists, Dr. Florance asked the Board to reaffirm NLM's operating procedures for grant adjustments. She explained each type of adjustment that could be made before awards are processed, and noted that the Board's Extramural Programs Subcommittee takes responsibility for the Special Council Review that NIH requires where additional consideration is given to applications from investigators that have active NIH grants amounting to one million dollars or more in direct costs. She also noted that new applications being considered for funding obtain early concurrence through the EP Subcommittee and are discussed there as needed. She asked for a vote to approve and reaffirm the operating procedures for the coming year. It was moved, seconded, and approved.

X. PUBLIC ACCESS TO GOVERNMENT FUNDED RESEARCH PUBLICATIONS

Dr. Neil Thakur from the Office of Extramural Research, Office of the Director, NIH, opened the session. The NIH Public Access Policy went into effect in 2008, requiring that all papers arising from NIH funds be made public on PubMed Central (PMC) within 12 months of publication.

In an effort to get full compliance, in 2013 NIH took the step of delaying grantees' funding until all the papers mentioned in their progress reports were deposited in PMC. That step yielded positive effects. Around 87 percent of the qualifying papers published between 2008 and 2015 have been submitted to PMC, and the policy applies to over 100,000 published articles annually.

About 650,000 papers have been deposited in PMC under the NIH Public Access Policy. This has helped to make NIH-supported research free to read, but much information remains pretty costly for scientists, and there are more papers out there than scientists or clinicians can read. The amount of literature is growing at an enormous rate—8 or 9 percent annually since World War II. This can lead to increasing inefficiency in our scientific workspace.

Rather than asking people to just read or collaborate more, Dr. Thakur mentioned opportunities on the horizon to use text mining and other computational tools to analyze the literature and help people absorb more information in their particular field of science. In addition to the obvious technical challenges, there is a policy challenge: to pull all of the papers together in a field, you have to negotiate individually with a large group of property holders. As a step in the right direction, NIH has made all author manuscripts submitted under the Public Access Policy available for bulk download in XML format. NIH plans to make text mining easier, by developing text mining tools, and encouraging private sector development, too.

Dr. Greenes asked whether NIH might partner with some of the social media sites like ResearchGate, where researchers share papers, ask and answer questions, and find collaborators. It might raise the profile of NIH's public access efforts.

Dr. Masys asked about the 13 percent of NIH grantees who aren't in compliance with the Public Access Policy. Do we know why? It's not willful disregard, replied Dr. Thakur, as much as the challenge to get people focused on complying. Lister Hill Center Director Dr. Clem McDonald noted from personal experience that the process can be complex, with responsibilities of grantees and journals not clearly spelled out.

Dr. Thakur noted that Katie Funk and her team at NCBI revamped the NIH Manuscript Submission System in 2015, reducing the processing time of a submitted paper from six-eight weeks to about two weeks.

Jerry Sheehan, NLM Assistant Director for Policy, described efforts of the White House, where he is currently on detail at the Office of Science and Technology (OSTP), to extend a modified version of the NIH Public Access Policy to the rest of the federal science community. This is great endorsement for what NLM and NIH have done.

In a February 2013 memorandum, OSTP directed federal agencies that spend more than a $100 million a year on R&D to develop plans for increasing access to the results of their funded research. Those results fell into two categories: scholarly publications, as in the case of the NIH Public Access Policy; and digital data. This project aligns with the White House's emphasis on open government and open data initiatives, to make the results of federally funded science increasingly accessible to students, teachers, business and entrepreneurs as well as the research community, to speed discovery.

Mr. Sheehan then described the policies on scholarly publications and digital data. The first mirrors a number of the elements on NIH Public Access Policy. NLM agreed to assist other federal agencies by supporting the deposit of peer-reviewed manuscripts or published articles in PubMed Central within 12 months of publication. In addition to serving as a public access repository, NLM will provide use of the NIH Manuscript Submission system, searchable citation and funding metadata in PubMed, agency-branded PMC storefronts, and PMC usage statistics for all funded papers to other federal agencies, among other features.

Digital data requirements are also loosely modeled on the NIH experience with data sharing. The objective is to maximize access to the data collected through federally funded R&D while recognizing limitations on that access, too. Privacy and confidentiality must be taken into account, as well as proprietary issues.

Almost three years after the White House memo, public access plans have been approved, cleared, and posted publicly by 16 federal agencies and departments. These include the Departments of Agriculture, Defense, and Energy, four HHS agencies (beyond NIH), NASA, the Department of Veterans Affairs, and others. Some offices that don't spend $100 million on research and development, like the HHS Office of the Assistant Secretary for Preparedness and Response, weren't required to join this program, but did so anyway, seeing this as something that supported their mission and their interest in making information accessible to those who need it.

We are now moving from the planning phase into the implementation phase, Mr. Sheehan noted. In their new solicitations for extramural research applications, agencies are starting to include requirements that applications include a data management plan which can be reviewed as part of the grants review process. As for publications, 11 or 12 of participating agencies have a requirement for publications to be made accessible within one year. So these standards are becoming the norm across the federal science landscape. In the remainder of the fiscal year, we expect to achieve compliance with these standards.

Dr. Masys commented that this new policy will be a boon to the informatics community, especially those who have been involved in Clinical and Translational Science Awards (CTSA) program for research data management. Much more training and experience is needed, as most investigators haven't a clue about how to compose a data management plan.

Dr. Florance pointed out that the Library just funded five grants for electronic instructional resources related to research data management. Three of them are headed by librarians, with the idea that those resources can be used at the ground level that to help the community and the organization to understand that research data management is essential.

Dr. Masys observed that the government's interest has always been at the end of the processing pipeline. But, as seen by the investigator, a data management plan has a lot of front end decisions to be made. How do you get quality data that's timely? How do you prove that it's accurate? How do you adhere to Good Clinical Practice standards? How do you maintain security, particularly with personally identifiable data? Mr. Sheehan responded that these questions are becoming increasingly important as expectations and requirements for data management plans are established.

Mr. Sheehan then gave a quick overview of the various participating agencies' status regarding public access to publications. The good news for NLM and NIH is that PMC has become the selected repository for the all HHS agencies, the VA, NIST and NASA.

Next, Katie Funk of the PMC team addressed the group. She outlined the site's three fundamental principles: It's full-text. It's free access. It's in an XML archive, as opposed to a PDF archive. We see this as a great way of preserving the published results of research in a software- and hardware-independent format.

Ms. Funk listed several reasons why PMC was a good fit for agencies responding to the OSTP memo. That document called for agencies to leverage existing archives. PMC had at that point been an archive for 13 years, had a number of relationships with journals and publishers, and included many articles that were co-funded by various agencies. PMC is well known and well used. It has 3.7 million articles being accessed by 1.2 million users each workday.

Dr. Masys expressed concern that articles from partner agencies like NASA would be out of scope for PMC, which centers on life sciences research. Ms. Funk pointed out that there are astrophysical journal publications in PMC, and NLM used to support SPACELINE, an NLM-NASA literature partnership that lapsed in 2005, so there's always been a bit of overlap.

Dr. Masys asked whether new Medical Subject Heading (MeSH) terms would be needed for the indexing of these new holdings. No, replied Ms. Funk. PMC doesn't MEDLINE-index public access papers unless they appear in a MEDLINE journal.

Continuing, Ms. Funk said there is value in having these cross-discipline scientific articles in one place. Science isn't done in a silo; there are things coming out of NASA research that will impact NIH research and vice versa.

Finally, Ms. Funk said, PMC staff is working to make sure that the public can find, access, and analyze this research. For about a decade, PMC has had an Open Access Subset. It currently has 1.2 million articles. As Dr. Thakur mentioned, Author Manuscript Collection is now also available under open access conditions. There are about 300,000 additional papers that can be downloaded for text mining as well and other uses that are Fair Use. This means that about 80 percent of NIH research findings in PMC are now available for text mining between these two collections.

There is also a global aspect to this work. PMC supports sister sites through the PMC International Program. PMC will also be supporting the Gates Foundation's open access policy.

Dr. Masys expressed delight that NLM is becoming the National Library of Science and Engineering in addition to the National Library of Medicine. He suggested PubMed Central consider creating a "PubScience Central" subset, to distinguish life sciences content from that of other disciplines.

XI. NLM EXHIBITION PROGRAM: HISTORY AND OVERVIEW

History of Medicine Chief Dr. Jeffrey Reznick observed that libraries large and small embrace and celebrate their historical collections. They do this to encourage patrons to explore them and to learn from them. So NLM has embraced and celebrated its own historical collections through exhibitions, at least since the 1870s, when our predecessor institution, the Library of the Army Surgeon's Generals Office, lent photographs to the famous 1876 International Exhibition.

The NLM 2000-2005 Long Range Plan identified exhibitions as an important component of the Library's outreach strategy to the public, with an explicit recommendation to produce historical exhibits and programs that promote understanding of science, medicine, and health and highlight NLM's collections and services. The Long Range Plan of 2006-2016 sustained this focus by enjoining NLM to promote knowledge of its services through exhibitions and public programs.

Today, NLM lends items from our historical collections for exhibitions curated by other organizations, including Smithsonian museums and the New York Metropolitan Museum of Art. These collaborations earn goodwill for the Library and publicize its collection and services.

HMD Exhibition Team head Patricia Tuohy then discussed the exhibitions that NLM has developed over the last 20 years, acknowledging the work of the exhibition curators, which has resulted in thought-provoking exhibitions that raise awareness of our collections. 1996 was a pivotal year in the Library's exhibitions. "Emotions and Disease" opened, a groundbreaking show exploring the history of the relationship between patients' emotions and their illnesses, conceived by current Board member Dr. Esther Sternberg. The scientific community, the history of medicine community, and the public all warmly received this exhibition, which generated a great deal of interest and excitement.

Building on this early success, NLM formed the Exhibition Program, a small staff of experts trained in history, education, and museum studies. Contract designers and fabricators round out our team. In 2001, following the success of an onsite installation, "Frankenstein; Penetrating the Secrets of Nature," NLM partnered with the American Library Association to obtain National

Endowment for the Humanities funding to create a traveling version. "Frankenstein" traveled to 82 libraries over a five-year period, then the Exhibition Program extended its run for another five years. In that decade, it had had more than 1.2 million visitors. "Changing the Face of Medicine," an exhibition that celebrated the history of American women in medicine, suggested by Dr. Tenley Albright, a former chair of the Board of Regents, developed a novel database of the information about 339 pioneering American women physicians.

An important step in the evolution of the Exhibition Program was developing resources for educators and students. These resources include onsite programing associated with exhibition narratives, plus coordinating activities for community groups, students, and paraprofessional visitors, plus K-12 lesson plans, and higher education modules available on the Web.

In 2007, NLM partnered with the Reginald F. Lewis Museum of African American History and Culture in Baltimore to co-curate a traveling exhibition. "Opening Doors," about African American Surgeons, using a simplified banner format to represent the content of the exhibition. Because the content of the exhibition was novel and highly interesting and the banner format was so adaptable, seemingly everyone wanted to host "Opening Doors." This unexpected surge of grassroots interest gave birth to the NLM traveling banner exhibition program. We now count over 600 academic and medical libraries, public libraries, and cultural centers around the world as our customers. We have 34 copies of 16 different exhibitions being hosted by 31 libraries in 31 cities and two countries February alone.

In 2011, following an introduction by Mr. Bruce James, another former Board of Regents chair, the Exhibition Program began a successful collaboration with the National Museum of American History. NLM has also partnered with Mount Vernon to develop a traveling exhibition about George Washington and medicine. They are currently supporting our efforts to open a special display about food, enslavement, and the Mount Vernon plantation in November 2016.

In 2015, NLM renewed its partnership with the American Library Association to manage the tour of the banner and iPad adaptation of "Native Voices: Native People's Concepts of Health and Illness." "Native Voices" will be experienced at 104 sites over the next four years.

Ms. Martin mentioned that her home institution, Wayne State University, has been a beneficiary of several NLM traveling exhibitions. She asked whether the popularity of the traveling exhibition program might also mean that it's a challenge to book the shows. Yes, said Ms. Tuohy, the exhibitions schedules fill up quickly. The most recent traveling show, "Confronting Violence," is already booked through 2019 and has a waiting list. Ms. Humphreys commented that the Library tries to provide additional copies of traveling exhibitions that are especially popular, like this one, on the topic of domestic violence.

Dr. Sternberg added her thanks for the NLM exhibition program in all its forms. She mentioned her perspective, coming to medical history and exhibitions as a scientist, thinking science is the ultimate field. She has since learned that science is essentially meaningless without a context. These exhibitions provide historical context, showing how it shapes the way we do our science and raising important questions for researchers. Ms. Martin added that exhibitions not only connect the community to science, but point to NLM as a trusted source of information.

Dr. Walker asked whether NIH as a whole supports the exhibition program. Ms. Humphreys replied that there are people in high places at NIH who are very interested in the history of NIH and the history of scientific discovery, and NLM can take advantage of that.

Dr. Francis asked whether NLM's new collaborations with NASA, regarding public access, might also help the Library tap into what they have learned in terms of public outreach. They have a group of amateur outreach specialists (often retired rocket scientists) that bring programs to schools, universities and public groups. Dr. Reznick said that there are good models at NASA, the Smithsonian, and other institutions, and that NLM and the NIH History Office are considering future collaborations.

Dr. Greenes asked about funding responsibilities for the traveling shows. It varies, replied Ms. Humphreys. NLM pays to create the exhibition and sometimes for additional copies. Usually, the host institution pays for shipment. Sometimes, shipment is underwritten by grants and other funding from outside groups, which lessens the burden on host institutions and broadens reach.

XII. SELECTION OF NOMINATING COMMITTEE FOR NEXT BOR CHAIR

Ms. Yokote announced the three members of the Nominating Committee: Dr. Francis will chair it, and be joined by Mr. Cole and Dr. Rice.

XIII. FUTURE DIRECTIONS OF NIH EXTRAMURAL PROGRAMS

Dr. Michael Lauer, NIH Deputy Director for Extramural Research began by referring to an opinion piece by two scholars from Penn State, which appeared in *PNAS*. They argued that celebrating the amount of R&D expenditures badly misses the point. They went to various universities' Web sites to see how they describe their research programs and found statements like, "We do $700 million in research." They argued that saying that kind of thing is like an airline saying, "We spend more money transporting passengers than anybody else." It's a meaningless measurement.

Reading the Southwest Airlines inflight magazine recently, he saw a column from its CEO. One statement captured his attention: "The mission of this airline is no different than it was back in 1971. We want to deliver people to where they want to go, safely, on time, with their bag, and with a smile, and with low-fares and no hidden fees." This sentence is actually remarkably profound because all of it, really, is quantifiable. Even "with a smile," because you can look at passenger complaint rates; it turns out Southwest is near the bottom. Southwest has a set of quantifiable outcomes. The authors of this particular paper made the case that we need to refine the conversation about how we think of about extramural research.

He admitted that many times, when he was a division director at the National Heart, Lung, and Blood Institute, he would be asked a question like, "What are you doing about mitochondrial disease?," and the answer would be invariably be something like, "We're funding 35 grants" or "We're putting X amount of money on it." So that's where the conversation ended, with the grant award instead of going further, like, "Were the studies actually done?" and, "If the studies were actually done, were they published?" "And if they were published, did they generate any

interest?" And the latter could be measured in terms of citations. And actually the authors say here, "This is an optimal finish line." But you can go beyond that. You can start talking about new molecular entities and devices, and better health care delivery.

Dr. Lauer showed a slide from Dr. Jon Lorsch, Director of the National Institute of General Medical Sciences, summarizing all the many woes we hear about with regard to research. It's not reproducible. Peer review doesn't work. The workforce is too big, or too small. There's not enough creativity; there's too much creativity. Post-docs are in the system for way too long. The scientific reward system is all wrong. We can't make discoveries. Education is no longer education. There is no stability and sustainability. The academic business model is being questioned. The system is inefficient. Funds are being distributed in an unequal way. And early-career investigators are in danger.

Dr. Lorsch has said, we are focused on the wrong metric because it's all based on projects. He has argued that we ought to have another metric: scientists. After all, they actually do the work. To illustrate that point, Dr. Lauer showed a graph plotting the number of NIH grant applicants and grantees, 2011-2015. The number of unique individuals who have at least one grant is 27,500, a figure that has remained remarkably constant. However, the number in the pool of researchers who *want* to be funded has gone up, from about 82,000 to 89,000. What does this mean and what implications does this have for policy?

Now, the scientist has received his or her award. How do we measure the impact of research? I often hear comments like, "It can't be done, and therefore don't bother." This idea of measuring impact makes even some very eminent scientists nervous.

Dr. Lauer next mentioned a *JAMA* article from about a year ago. The authors came up with the acronym "PQRST" acronym, for Productivity, Quality—that might be, for example, in systematic reviews that might look at the experimental design of clinical studies and you come up with an assessment there, Replication, Sharing— of data or resources, and Translation. This manifesto on research metrics has received a lot of attention.

We might ask, "How well does our system of peer review predict the productivity of grants where we measure the productivity of grants in terms of highly cited papers?" He then presented data from about 7,000 NHLBI grants that were funded over a period of about 25 years. Each dot represented a grant or a group of grants. The X axis showed the percentile ranking of the grant. The Y axis showed the number of highly cited papers, which we define as being in the top 10 percent of its field for the topic for the year. There was a lot of scatter. There were also a very large number of projects that are producing very little, down near zero, and also see a few projects that are exceedingly productive.

Dr. Lauer showed a graph seeking to convey how well peer review predicts high productivity grants, then adds the component of "productivity per million dollars spent." The association is completely flat. In other words, you have these extremely productive projects which account for a very large portion of all the output, but they are spread out across the peer review spectrum.

Does this mean that peer review is worthless? An article in *The Wall Street Journal* that said that grant awarding is a crap shoot. Some have proposed that peer-review panels identify the top 25-30 percent, and after that you initiate a lottery system. So how do we do an overall analysis? Dr. Richard Nakamura, Director of the NIH Center for Scientific Review and Dr. Lauer posted a piece in *The New England Journal of Medicine* a couple of months ago and these are some of the points we made. First, if you look at the portfolio of NIH- funded papers, we've got a corpus of now millions of them that have come out over the last 30 years or so. Their citation metrics, overall, are actually quite good. In fact, they are cited more than twice as often as what would be expected based on their field, the year of the publication, and the article type. But we still have to ask, could the grants system be working better?

One issue is that what the initial peer reviewer see may not be necessarily the same as the grant that is actually awarded. Budgets often get renegotiated down because we want to be able to fund more grants. And then the final, perhaps more profound issue is, what is it that we expect from experts? Dr. Philip Tetlock at the University of Pennsylvania has done interesting work on expert opinion. Among his findings: experts who were more confident in their predictions were more likely to be wrong. And experts who framed their predictions in terms of questions were more likely to be right.

There are many other questions that we can ask. What about the outcome of basic vs. applied science? What about different types of grant mechanisms? What about big science vs. small science? How can we ensure more diversity in the workforce? What about time vs. money? Does it make more sense to fund people for longer periods of time, even with less money each individual year?

Dr. Lauer concluded by referencing the NIH Strategic Plan. He gave credit to Dr. Larry Tabak, Principal Deputy Director of NIH, who did a lot of the work on this report, which was well received on Capitol Hill in December. A key objective was "enhancing stewardship." Our goal is to excel as a federal science agency that manages for scientific results.

Speaking as a former NIH intramural scientist, Dr. Sternberg said she was struck when she left NIH, where her whole vision of productivity was papers, citations, and getting her research to the outside real world, to find that there were other measures of success, for example, at the Defense Department, where intellectual property, patents and products formed the metrics.

Dr. Greenes asked whether the Strategic Plan is moving away from basic research towards the applied. That's always a question, said Ms. Humphreys, mentioning NCBI scientist Dr. Eugene Koonin, who did years of basic research and was able to see some of his work fed back into recent genetic engineering discoveries. What NIH was trying to do in the Strategic Plan is make clear that you can't draw a straight line from basic to applied research, just as you can't draw such a line from the study of a certain disease and resulting therapy for it. You need to support both types of research.

Dr. Michael Lauer next spoke about clinical trials, which many view as too expensive and too complicated. If we're spending $80 or $100 million on a clinical trial, that's X number of R01 grants that are otherwise being sacrificed. There's been a great deal of interest among many of us

to figure out ways in which we can do trials more efficiently, given that the overall funding pool has been steadily declining over the last 10 years.

Dr. Olds noted that the NSF has a bimodal grants model, for large and small projects. The same is done at NIH to a degree, Dr. Lauer said. "Little projects" can be done and these will probably add up into a big corpus of science that otherwise wouldn't exist. The hard question is, how do you know whether spending billions of dollars on the Human Genome Project (HGP) is a better use of money then funding multiple smaller grants? It's impossible to say. HGP was a big science project, but it makes possible a new body of small science that otherwise wouldn't exist.

Dr. Masys pointed out that, in one of his early slides, Dr. Lauer mentioned an optimal "finish line" that was citation to publication. To him, that embodies this community consciousness that NIH's job ends at the publication of a paper and the citation of it by another scientist in another paper. But isn't almost all literature not going to get read and, therefore, won't make a difference? If you want to improve health, there should be another type of finish line: the NIH investment in mechanisms for translation that are more effective than publishing papers and citing them. At the very least, responded Dr. Lauer, we should be funding research that produces something that can be measured. The disconnect, said Dr. Masys, is that the average congressman, who is going to be your investor, is imagining that this line goes all the way out to less diabetes, less morbidity—all these numbers that show the world's actually getting better as a result of things we've done. As we've noted, the line is not always a straight one.

Dr. Francis observed that science works not in a linear arrangement of arrows but in many complicated relationships. Some person's career didn't lead to a lot of papers and citations, or a breakthrough that improves public health, but something else happened with that failed researcher so that he becomes a member of the NLM Board of Regents or stimulates students to go into STEM. As a measurement guy in health care, he continued, I see two concerns: (1) We have too many measures; and (2) the measures are rewarding the wrong behavior. We are teaching to the test and we are losing something of our humanity in the process. Dr. Lauer concurred; one of the key points is to choose a few headline metrics, like Southwest Airlines did. The only way that those metrics turn out well is if people do a good job.

Sharing her experience at DARPA and DOD, Dr. Sternberg mentioned that those institutions typically give you a small grant initially. It's like a trial period. If it works, then they give you a much larger grant dollars and if it doesn't, good bye. There's interest, said Dr. Lauer, in funding NIH clinical trials with a similar mechanism. The U2 grant is for the first year and awards a relatively small sum; it's essentially a way of asking, can you get your act together? If everything is looking great, we'll give you a larger sum of money to get the project done.

XIV. ADJOURNMENT

Ms. Yokote adjourned the Board of Regents meeting at 11:45 a.m. on February 10, 2016.

ACTIONS TAKEN BY THE BOARD OF REGENTS:

➢ Approval of the September 16-17, 2015 Board Minutes
➢ Approval of the February 7-8, 2017 Future Meeting Dates
➢ Approval of the Grant Operating Procedures

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

Betsy L. Humpheys, M.L.S.   Gail A. Yokote, M.S.
Acting Director, National Library of Medicine   Chair, NLM Board of Regents