NIH SCIENTIFIC MANAGEMENT REVIEW BOARD

February 23, 2011

TELECONFERENCE SUMMARY

Board Members Present:

Norman R. Augustine, Chairman
Josie Briggs, M.D.
William R. Brody, M.D., Ph.D.
Gail H. Cassell, Ph.D.
Richard J. Hodes, M.D.
Stephen I. Katz, M.D., Ph.D.
Thomas J. Kelly, M.D., Ph.D.
Griffin P. Rodgers, M.D., M.A.C.P.
Arthur H. Rubenstein, M.B.B.Ch.
Susan B. Shurin, M.D.
Solomon H. Snyder, M.D.
Harold E. Varmus, M.D.

Ex-Officio Members Present:

Francis S. Collins, M.D., Ph.D.

Designated Federal Official:

Amy P. Patterson, M.D., Executive Secretary

Opening Remarks

Mr. Augustine welcomed the Scientific Management Review Board (SMRB) members, invited speakers, and guests. Drs. Jeremy Berg and Eugene Washington have resigned from the Board; their contributions were acknowledged, and they were wished well in their future endeavors. Mr. Augustine reviewed the purpose of the meeting; the SMRB would receive an update from two NIH groups tasked with evaluating the SMRB's recommendations on translational medicine and therapeutics (TMAT). The TMAT report was transmitted to the NIH Director and the HHS Secretary shortly after the SMRB's December 2010 meeting and is now posted on the SMRB Web site.

Dr. Collins reviewed NIH activities since the last SMRB meeting, noting that NIH has accepted all of the 2010 SMRB recommendations and that the Board's report on TMAT has been transmitted to the Department of Health and Human Services (HHS) Secretary Kathleen Sebelius and to Congress. Dr. Collins submitted a proposal to create a new center, the National Center for Advancing Translational Sciences (NCATS) to the HHS Secretary, with the intent of establishing NCATS by October 2011. Dr. Collins acknowledged that NIH has a strong history of supporting, discovering, and developing new therapeutics, diagnostics, and prevention strategies. NIH intends to continue to support these kinds of vigorous efforts in translational science in each of the 27 institutes and centers (ICs). He stated that NCATS is intended to catalyze new approaches to increase understanding of the translational process, which ultimately will improve the overall discipline of translational science.

Dr. Collins explained that formal advice on how to proceed with the development of NCATS was sought from two distinct groups. The first, composed of NIH senior leadership across the agency, is charged with issuing recommendations on the mission and functions of NCATS. The second, an expanded working group of the NIH Advisory Committee to the Director chaired by

Maria Freire, is charged with identifying strategies for NCATS to collaborate with the private sector. He also mentioned the creation of a third group charged with analyzing activities within the National Center for Research Resources (NCRR) that should be included in the new NCATS. He stated that Principal Deputy Director Lawrence Tabak would discuss the findings of this Task Force.

Mr. Augustine thanked Dr. Collins for his comments and careful consideration of the Board's recommendations. He briefly reviewed the meeting agenda, and the Board approved the minutes from the September 14–15, 2010, meeting. Dr. Patterson reviewed the NIH Conflict of Interest Policy.

Update from the NIH NCRR Task Force

Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, NIH
Co-Chair, NCRR Task Force

Dr. Tabak explained that the NCRR Task Force met with subject-matter experts selected by NCRR leadership and consulted multiple stakeholders throughout its process. The Task Force concluded that many NCRR programs would benefit from the scientific synergies that would result from their transfer into other ICs. Following are the Task Force recommendations for the relocation of specific NCRR programs:

(1) The Task Force concurred with the SMRB's original recommendation to transfer the Clinical and Translational Science Awards (CTSAs) into NCATS.

(2) The Task Force recommended placing the Research Centers in Minority Institutions program in the National Institute on Minority Health and Health Disparities.

(3) The Task Force recommended placing the Science Education Partnership Awards program in the Office of the Director (OD) of NIH. The program would be combined with the Office of Science Education, which is currently located within the Office of Science Policy in the NIH OD.

(4) The Task Force recommended placing the Institutional Development Award program in the National Institute of General Medical Sciences (NIGMS).

(5) The Task Force recommended that the Biomedical Technology Research Centers (BTRCs) be transferred either to NIGMS or to the National Institute of Biomedical Imaging and Bioengineering (NIBIB). Specifically, grants related to biomedical imaging and point-of-care diagnostics would be transferred to NIBIB, and all other BTRCs would be assigned to NIGMS. Similarly, the Task Force proposed assignment of the majority of the research grants for technology research and development, the small business funding opportunities (SBIR and STTR), and Biomedical Informatics Research Network grants to NIGMS; a subset of these related to biomedical imaging and point-of-care diagnostics would move to NIBIB.

(6) The Task Force recommended placement of the following NCRR programs in a permanent new infrastructure entity to be located within the Division of Program Coordination, Planning, and Strategic Initiatives within the OD: the extramural construction program, the Research Facilities Improvement Program, the Animal Facilities Improvement Program, the Shared Instrumentation Grant program, the High-End Instrumentation grant program, and the

Division of Comparative Medicine.

A great deal of feedback focused on the value of keeping the Division of Comparative Medicine intact, despite the rather large breadth of the program that spans infrastructure, capacity building, and programmatic work.

Discussion

Dr. Kelly noted the concerns of the scientific community regarding the decision to eliminate NCRR and redistribute its programs. He questioned the depth of consideration for this important change and expressed concern that the SMRB had not discussed this major structural change in any significant manner up to this point. He asked whether it would be appropriate for the SMRB to undertake an in-depth study of whether NCRR should be eliminated. He also inquired whether the NCRR Task Force considered leaving NCRR intact and only transferring the CTSA program to NCATS.

Dr. Tabak replied that the Task Force did consider maintaining NCRR, but concluded after significant deliberation that it would be better to take advantage of new scientific opportunities by juxtaposing the remaining NCRR programs with other relevant institutes and centers. Dr. Tabak noted that the NCRR Task Force undertook a deliberate and thorough process when considering the SMRB recommendations and the potential impact of NCATS on NIH institutes and centers. The Task Force held six formal meetings and consulted with stakeholders to conduct extensive analyses of and determine the best placement for each NCRR program. There has been no intention of eliminating any NCRR programs.

Mr. Augustine emphasized that the SMRB, in considering its TMAT recommendations, met on five separate occasions over a period of several months. He acknowledged that the SMRB's timing was driven by an awareness of the budget cycle and the desire to issue its recommendations on translational medicine in time for NIH to propose change in the next cycle.

Dr. Cassell voiced a desire to see the Division of Comparative Medicine remain intact since it already underwent a substantial reorganization in the 1970s and 80s. She asked Dr. Tabak to comment on the Task Force discussions about the Division of Comparative Medicine. Dr. Tabak acknowledged that the Task Force had received many comments on this topic and had initially recommended separating the Division of Comparative Medicine; however, leaders and stakeholders provided compelling reasons for keeping the program intact, leading the Task Force to deviate from its initial proposal.

NIH Update on the Recommendations of the Institute and Center Directors' Working Group on the Proposed National Center for Advancing Translational Sciences

Thomas R. Insel, M.D., Director, National Institute of Mental Health
Co-Chair, ICD Working Group on NCATS

Dr. Insel, co-chair of the Institute and Center Directors' Working Group on the Proposed NCATS (ICD-NCATS), reported on the progress of the Working Group, which was tasked with providing advice and recommendations regarding the mission, functions, and organization of NCATS. The Working Group is composed of leadership from across NIH, including several

SMRB members and senior staff from the Office of the NIH Director. The group has met seven times since receiving its charge in early January 2011.

Throughout its discussions, the Working Group was mindful that the NIH ICs have a long-standing history of conducting and supporting translational research. Discussion focused upon enabling and enhancing efforts to advance translational science throughout NIH. Most of the Working Group meetings were briefings on current programs, including both those listed in the SMRB Translational Medicine and Therapeutics (TMAT) report and other potential programs for inclusion in the new center.

The ICD-NCATS Working Group also held a joint meeting with the Advisory Committee to the Director (ACD)-Proposed NCATS Working Group, which provided a helpful perspective from industry, academia, venture capital firms, and non-profit organizations about the risks and benefits arising from the creation of NCATS. Overall, reception of the proposal to create NCATS was positive. ACD-NCATS members encouraged NIH to frame NCATS as a catalyst for translation and believed that the creation of NCATS is an opportunity to take interesting NIH science and make it compelling science for the development of therapeutics. The ACD-NCATS Working Group viewed NCATS as an opportunity to study the process of treatment development, which industry doesn't do well. ACD-NCATS members stressed the need for a new generation of clinical pharmacologists and suggested that NCATS could provide the necessary training.

The Working Group concluded that the recommendations in the TMAT report were appropriate, emphasizing the Molecular Libraries Program, Rapid Access to Interventional Development program, Therapeutics for Rare and Neglected Diseases program, and the CTSAs. It was believed that translation should focus on diagnostics, devices, biologics, and vaccines, but that the time for that kind of focus would come later. For now, NCATS should start small, focus on the programs selected for inclusion, and find ways to optimize and integrate them.

NCATS could be a home for the developing FDA-NIH partnership and promoting regulatory science. NCATS also could house the Cures Acceleration Network, as suggested in the TMAT report.

ICD-NCATS Working Group members agreed that the mission for NCATS should be to advance the discipline of translational science and catalyze the development of novel diagnostics and therapeutics across a wide range of human disease conditions. Dr. Insel ended his presentation by noting that NCATS could provide an open-access environment to experiment with innovative approaches to develop therapeutics, to consider ways to reengineer the drug pipeline, and to collaborate with other NIH ICs to create a network, and to promote and facilitate interactions with the FDA and other regulatory agencies to advance the field of regulatory science.

Discussion

Dr. Snyder commented on the challenges of interfacing with the pharmaceutical industry in bridging the gap between basic science and clinical medicine. Dr. Insel acknowledged this point and noted that the Working Group consulted with the ACD-NCATS Working Group, which included many industry representatives, to obtain industry input and perspective.

Public Comment

Dr. Bobbie Ann Austin of the Association for Research in Vision and Ophthalmology (ARVO) stated that NCRR has benefited vision researchers by placing critical programs within a single Center, which unifies diverse research areas. In a recent survey, 55 percent of U.S. ARVO members indicated they received direct or indirect support from such programs. Dr. Austin worked with five different working groups composed of NCRR stakeholders to prepare recommendations for the NCRR Task Force. Overall, the groups recommended that the SMRB carefully analyze the proposed changes and their consequences to prevent conflicts of interest during grant reviews, which could result from moving programs from an IC with a diverse mission to those with more defined missions. One concern expressed by ARVO members was that discontinued funding of high-use core instruments and facilities, which are currently by NCRR, could hamper scientists' ability to follow up on existing studies and collect preliminary data for grant applications. They recommended that existing NCRR programs be moved to the OD and that respective funds, resources, and staff be transferred with the programs. A second concern was that moving NCRR IDeA programs to an IC with a defined constituency could result in loss of funding in states where other facilities may not exist. They recommended that IDeA programs be funded at the current level in a permanent division. The full version of this group's recommendations is posted at www.arvo.org/advocacy. The Animals-in-Research Committee also prepared a statement about NCRR animal programs, which can be found at www.arvo.org/animals.

Dr. Stuart Zola of the Yerkes National Primate Research Center (NPRC) stated that the NPRCs believe that placement in the NIH OD maintains the centers' commitment to both fundamental and translational sciences. The NPRCs feel that within the NIH OD they'll be able to take greater advantage of their broad breadth of research than if the program was placed in an IC. He believes this will allow NPRCs to contribute more completely to other NIH priorities like training and outreach.

Dr. Judith Van Houten, principal investigator of the University of Vermont IDeA Network of Biomedical Research Excellence award and President of the IDeA Principal Investigator Association, expressed interest in finding mechanisms by which the RCMI and IDeA programs could retain their synergies after being placed in separate ICs under the NCRR Task Force straw model. She asked Dr. Tabak to follow up on their recent conversation on that point. Dr. Tabak replied that NIH will explore mechanisms to ensure continuing collaboration between the RCMI and IDeA programs. Dr. Van Houten also asked for more information about membership within various NIH committees and councils that lack IDeA-state representation. Dr. Tabak responded that NIH strives to maintain appropriate membership on NIH councils.

Ms. Amy Comstock Rick of the Parkinson's Action Network (PAN) strongly supported the creation of NCATS. PAN expressed its support for NCATS in writing to the House and Senate. She argued that NCATS would need partnerships with the private sector to meet the challenges involved in moving promising discoveries through the "valley of death." Concerned about reactions to the new center, she noted that requests to slow the creation of NCATS did not represent the views of all stakeholders. The existence of the valley of death, the problems it causes for therapy development in the U.S., and the lack of private-sector money for some classes of therapy development were undisputed by those who objected to the creation of

NCATS and resulting closure of NCRR. For some diseases and patients, she said, nothing is moving through the pipeline. Ms. Rick observed that while stakeholders debated the SMRB's recommendation to create NCATS, no one was addressing the impact inaction was having on the biomedical community's ability to address the problems of research hurdles and a dried-up therapy pipeline, and that stakeholders should instead focus on the needs for basic, translational, and clinical biomedical research. She believed that adequate analysis related to NCATS has already been completed. Ms. Rick stressed that the plan for NCATS should move forward and that, instead of arguing, NIH and its stakeholders should present a united front to make the NIH budget and biomedical research a funding priority.

Mr. James O'Leary, representing Genetic Alliance, said that his organization supports the creation of NCATS. Genetic Alliance is a network of more than 10,000 health organizations that is committed to improving human health outcomes, including accelerating the development of new therapeutic options for patients and consumers. Mr. O'Leary said that in 2010, although more than $100 billion was spent on research, only 20 drugs came to market, and fewer than 200 of the 7,000 rare diseases have available therapy options. The current system of therapeutic development has been failing patients and consumers and translational medicine must be transformed. Genetic Alliance believes that NIH can and must leverage its existing and emerging programs and resources to accelerate translational medicine. It viewed the passage of the Cures Acceleration Network as evidence that the American public and Congress share an expectation that NIH will play a leading role in improving human health outcomes through translational research. Genetic Alliance considers the creation of NCATS to be an unparalleled opportunity to advance translational medicine and improve human health. Mr. O'Leary stressed that NIH should remember the broad needs of translation, including the meaningful involvement of individual families and communities in the process and the effective engagement of the public. He said the CTSAs' work in community engagement should not be lost and that NIH should continue to increase focus on translation across the ICs. Mr. O'Leary urged stakeholders and NIH to work together to realize the promise of NCATS to accelerate translation and provide solutions for those who suffer.

Dr. R. Balfour Sartor, distinguished professor of medicine, microbiology, and immunology; Director, University of North Carolina at Chapel Hill Multidisciplinary Center for IBD Research and Treatment; and co-director, Center for Gastrointestinal Biology and Disease, endorsed the decision to keep the NCRR Division of Comparative Medicine intact. He said that there are approximately 50 animal research centers that are critical for a number of R01-funded investigators, and the Division has effectively facilitated that research. Dr. Sartor noted that the Division of Comparative Medicine has done an excellent job in expanding and optimizing both veterinary and basic science expertise in a cost-effective manner that would not have been possible for individual investigators. The dual expertise has also allowed the Division to communicate with both the producers and users of the animals.

Dr. Adam Clark of FasterCures applauded the SMRB's recommendation to create NCATS, which he believed will expand NIH's investments and efforts to speed the translation of basic discoveries to clinical application. FasterCures views NCATS as a significant development for the future of translating basic discoveries into needed treatments and cures. FasterCures believes NCATS has the potential to cut across boundaries and address fundamental scientific and biomedical challenges in the transition of basic research to clinical application through

interdisciplinary expertise. The integration of efforts will produce synergy that will benefit Americans through improved health and a more efficient and effective investment of their tax dollars. As outlined recently in the FasterCures white paper "Crossing Over the Valley of Death," many new drugs drop out of the development pipeline for a variety of reasons, including lack of funding for critical translational studies and insufficient investment in the technical expertise needed for technology development and transfer. Dr. Clark said that it is necessary to invest in the steps between discovery and application—target validation, assay qualification, product refinement, and preclinical development— that are often the bottlenecks to moving drugs forward and exist across the drug development enterprise. He expressed hope that NCATS would provide a significant stimulus to move ideas out of the lab and into the clinic.

Dr. Richard Bucciarelli, Director of the University Of Florida Department Of Pediatrics and representing the American Pediatric Society, Society for Pediatric Research, Association of Medical School Pediatric Department Chairs, American Academy of Pediatrics, and Academic Pediatric Association, applauded NIH for its dedication to the translation of basic scientific advances into therapeutics and urged the Board to seriously consider the needs of children and their families as it provides guidance to NIH on its reorganization. He said that translational research is especially important for children, who are frequently left without the scope or quality of therapies that are available to adults. Effective translational research for children requires infrastructure that recognizes the unique nature of children and supports pediatric efforts from basic science through phase 4 translational research. Dr. Bucciarelli outlined the contributions that the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the CTSA Consortium have made to the effort to expand knowledge about diseases that affect children and their development. The CTSA Consortium Child Health Oversight Committee's support of pediatric researchers and trainees has been particularly valuable in ensuring that the CTSA program works for the benefit of children. The pediatric community, Dr. Bucciarelli said, supports NIH's effort to promote translational research and urges the Board to affirm its commitment to child and family health by recommending that NCATS:

- establish child health research as a key priority;
- support the promotion of the roles of NICHD and the CTSA Consortium Child Health Oversight Committee in advancing child health research;
- remain cognizant of ongoing child health research conducted at NICHD and other ICs and work to facilitate translational research relevant to children across the ICs; and
- maintain its commitment to research, training, and career development programs in recognition of the need for training the next generation of clinical and translational research professionals with expertise in children.

Mr. Augustine thanked all the public speakers for their comments and said he was confident that the NIH leadership will consider carefully the comments, as will the SMRB when it has future deliberations on these and other subjects of a related nature.

SMRB Comments

Dr. Rubenstein asked if there is a way to gauge whether the official representatives of all of the programs in NCRR, particularly grantees, find the current reorganization plans acceptable. He

wondered if NIH had been able to gauge this yet. Dr. Tabak said that it is too early to gauge their response since the final NCRR recommendations had just been posted the previous day, but the public comment period shows that a number of groups are in agreement and supportive of the final recommendations. It is not yet clear if the responses heard during the public comment time are widespread and applicable to all programs. Dr. Rubenstein also asked if NIH has a timetable and method for assessing the response to the NCRR recommendations and the SMRB discussion. Dr. Tabak said that additional input and comments were welcome on Feedback NIH and that on March 14, there will be a stakeholder town hall meeting in which participants will be able to share their views.

Next Steps and Closing Remarks

Mr. Augustine acknowledged the breadth of the work accomplished by the SMRB in 2010, as well as the NIH efforts to effect the Board's recommendations. The Agency is in the process of considering what it might ask of the SMRB next. A meeting will take place in autumn 2011. Mr. Augustine anticipates that NIH will provide the SMRB with updates on the implementation of the Substance Use, Abuse, and Addiction recommendations, in addition to updates regarding the TMAT report.

Dr. Collins acknowledged the hard work of the SMRB on a range of complex topics and the skillful leadership of its Chair. He said the comments from both the Board and the public were helpful. He believes NIH is on the right trajectory to ensure that grantees feel well served. NIH will continue to engage the public regarding its reorganization and increased focus on translational science . At the Fall meeting, in addition to updates Mr. Augustine mentioned, Dr. Collins anticipates sharing information on NIH's progress in implementing the SMRB's Clinical Center recommendations. He acknowledged that NIH is very busy implementing the SMRB's recommendations, but the Agency remains grateful for the SMRB's efforts. Despite current budget-related anxieties, NIH will continue to pursue its mission to make a difference in biomedical research and human health.

Adjournment

Mr. Augustine thanked all the speakers who participated in the call and expressed his appreciation for the hard work of his colleagues on the Board. The teleconference was adjourned at 1:01 p.m.

We certify that, to the best of our knowledge, the foregoing meeting summary of the NIH Scientific Management Review Board is accurate and correct.

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Norman Augustine
SMRB Chair

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Amy P. Patterson
SMRB Executive Secretary