



NIH SCIENTIFIC MANAGEMENT REVIEW BOARD



TELECONFERENCE

May 29, 2012

MEETING SUMMARY

Board Members Present:

Norman R. Augustine, Chairman
Josephine P. Briggs, M.D.
William R. Brody, M.D., Ph.D.
Gail H. Cassell, Ph.D.
Anthony S. Fauci, M.D.
The Honorable Daniel S. Goldin
Eric D. Green, M.D., Ph.D.
Richard J. Hodes, M.D.

Stephen I. Katz, M.D., Ph.D.
Roderic Pettigrew, M.D., Ph.D.
Deborah E. Powell, M.D.
Griffin P. Rodgers, M.D., M.A.C.P.
William L. Roper, M.D., M.P.H.
Arthur H. Rubenstein, M.B.B.Ch.
Susan B. Shurin, M.D.
Solomon H. Snyder, M.D.

Ex-Officio Members Present:

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

Designated Federal Official:

Amy Patterson, M.D., Executive Secretary

Opening Remarks

Mr. Augustine welcomed Board members and guests to the teleconference. Dr. Patterson called the roll. Mr. Augustine reminded the attendees that previous reports produced by the Scientific Management Review Board (SMRB) are available on the SMRB Web site and reviewed the agenda for the teleconference.

Dr. Collins thanked the SMRB members for their diligence and dedication to the National Institutes of Health (NIH).

Mr. Augustine informed the attendees that this meeting was announced in the Federal Register and that public comment would be allowed at designated times throughout the teleconference. He reminded all participants that written statements may be submitted to the SMRB at any time.

The minutes from the October 26, 2011, SMRB meeting were approved as written.

Dr. Patterson reviewed the NIH conflict of interest policy, and members reported no conflicts.

SMRB Recommendations: NIH Update

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

Director, National Institutes of Health

Dr. Collins reminded the SMRB that it has issued four reports since its first meeting in April 2009: Report on Deliberating Organizational Change and Effectiveness (DOCE; December 2010); Report on Substance Use, Abuse, and Addiction (SUAA) Research at NIH (November 2010); Report on the NIH Clinical Center (December 2010); and Report on Translational Medicine and Therapeutics (TMAT; December 2010). Dr. Collins acknowledged the challenge of implementing the SMRB's recommendations but noted that a significant amount of progress has been made to date. He also noted that the NIH is considering each recommendation with great seriousness.

Dr. Collins began by reviewing the SMRB recommendations regarding the NIH Clinical Center. He reminded the group that the SMRB was charged with analyzing and providing recommendations for the fiscal sustainability and utilization of the NIH Clinical Center. In its recommendations to NIH, the SMRB stated that the Clinical Center should "have an expanded vision and role; a streamlined governance structure; and a stable, adequate budget for fiscal viability and sustainability."

Since these recommendations were issued, NIH has undertaken a series of steps towards their implementation. Firstly, NIH has established a Clinical Center Governing Board to provide strategic and operational oversight with the objective of facilitating high-quality, cost-effective clinical research. This group has also been asked to provide budget recommendations that promote stable funding for the NIH Clinical Center. Dr. Collins also referred to the institution of a Clinical Center Extramural Collaborations Committee, which has been charged with developing a funding opportunity announcement (FOA) that promotes clinical research collaborations between intramural and extramural investigators. At this time, a schedule for the implementation of the FOA has been drafted and the notice of intent to publish will be issued in June 2012. The FOA will be published in August 2012 and applications should be received by November 2012. Ultimately, awards are expected to be issued in July and August of 2013.

Dr. Collins acknowledged that the SMRB also recommended that the Clinical Center budget be funded through a line item in the budget. He reported that NIH leadership is weighing the pros and cons of this recommendation, ultimately examining the associated complexities and any untoward consequences. In addition, mechanisms for using financial resources for collaborating with the extramural community are still being analyzed to determine the most appropriate path forward. To date, the NIH Clinical Center continues to be funded through the NIH intramural program.

Dr. Collins next discussed NIH's implementation of the recommendations regarding SUAA-related research. He stated that the SMRB was charged with considering whether changes within NIH could further optimize research into substance use, abuse, and addiction and, after consulting with stakeholders and deliberating the topic, the SMRB recommended that NIH

establish a new Institute that encompasses all substance use-, abuse-, and addiction-related research. This recommendation also entailed the dissolution of the National Institute of Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA). The Board also recommended that NIH identify other related research portfolios for inclusion in the new Institute.

On November 18, 2010, Dr. Collins accepted the SMRB recommendation to create an addiction-related Institute. Dr. Collins acknowledged that the implementation of this recommendation has not been as straightforward as it appeared at the outset, but that NIH leaders, including Principal Deputy Director Dr. Lawrence Tabak, continue to make progress in identifying precisely how to make this transition with the best scientific outcome. He noted that in early 2011, the SUAA Task Force was convened to gather data and consult with scientific staff from NIH Institutes and Centers (ICs) on this issue. In April 2011, the Task Force developed draft principles to guide reorganization, and by fall of 2012, the NIH Task Force and Strategic Planning Committee intend to:

- Complete the SUAA portfolio analysis and develop an integration plan for public comment.
- Develop a scientific strategic plan that includes input from stakeholders. To accomplish this, the Task Force has:
 - Issued Requests for Information (RFIs), which were open from February 8 to May 11, 2012, and generated 494 responses.
 - Held a web meeting about the RFI outcome on April 2, 2012.
 - Planned a meeting with a targeted set of stakeholders for June/July 2012.
- Release the Portfolio Integration Plan with an accompanying public comment period.
- Release the Scientific Strategic Plan with an accompanying public comment period.

Dr. Collins stated the final recommendations from this Task Force are expected in December 2012. Dr. Collins informed the SMRB that this schedule should allow the new Institute, the National Institute of Substance Use and Addiction Disorders (NISUAD), to become part of the Fiscal Year 2014 NIH budget. He noted the name NISUAD has not been formalized; suggestions from the Board for the new Institute's name are welcomed. He added that NIH has already received some negative feedback on the proposed SUAA reorganization, particularly from the beverage industry, but continues to seek out the new organization that best serves the science.

Dr. Collins next provided an update on progress related to the SMRB recommendations for TMAP, which led to the creation of the new National Center for Advancing Translational Sciences (NCATS). He reminded the group that the SMRB was charged with designing an NIH network and describing its attributes, activities, and functional capabilities for advancing therapeutic development.

In response to its charge, the SMRB recommended that a new Center be created with a mission to support and strengthen translational medicine. The SMRB also recommended that NIH relocate some existing components into the new Center, including the Clinical and Translational Science Awards (CTSAs), and evaluated the impact of these changes on entities such as the National Center for Research Resources (NCRR), which housed the CTSAs. As a result, Dr.

Collins noted, the NIH NCRR Task Force was created, and it reviewed and concurred with the SMRB recommendation. The Task Force concluded that many programs remaining in NCRR following the transfer of the CTSA's to the new Center would benefit from relocation to and enhanced scientific adjacency within other ICs. In January 2011, following input from NCRR leadership and NCRR subject matter experts, a straw model was released for public comment. In February 2011, the Task Force reported its results to the SMRB, and final recommendations were issued to the NIH Director in March 2011. Finally, on December 23, 2011, NCRR was officially dissolved and NCATS was created when the President signed the Consolidated Appropriations Act of 2012 (P.L. 112-74).

Dr. Collins stated that the timeframe for creating NCATS, from the release of the SMRB recommendation to the presidential enactment, was one year and sixteen days—a remarkable achievement. With a few exceptions, Dr. Collins believed that the new Center has been accepted by the research community; once the objective of NCATS became clear, most people's anxiety related to the change was resolved. Dr. Collins briefly reviewed the transition of specific programs as a result of the NIH NCRR Task Force; these transitions have been summarized in previous SMRB documents. Dr. Collins credited Dr. Tabak for managing this redistribution. Dr. Collins informed the SMRB that Dr. Thomas Insel is the Acting Director of NCATS; Dr. Kathy Hudson is the Acting Deputy Director; Dr. Josephine Briggs serves as the Acting Director of the Division of Clinical Innovation, where the CTSA's reside; and Dr. Christopher Austin is the Director of Preclinical Innovation.

Dr. Collins reviewed the mission of NCATS, which is “To catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.” He stressed that the new Center will focus on systematic approaches to widen the bottleneck that exists between basic research and clinical application. He also reviewed programs and initiatives that have been imported into NCATS. These include clinical and translational science activities, such as the CTSA's; rare diseases research and therapeutics, including Therapeutics for Rare and Neglected Diseases and the Office of Rare Diseases Research; and re-engineering translational sciences, including the NIH Chemical Genomics Center, the Bridging Interventional Development Gaps program, and Toxicology in the 21st Century program.

Dr. Collins informed the SMRB of new initiatives currently under way at NCATS. One ambitious program is the development of tissue chips for drug screening, which NCATS is undertaking in conjunction with the Defense Advanced Research Project Agency (DARPA). These “chips” will mimic human physiology to identify signals of toxicity of compounds before they are given to human patients. Because of the low concordance between toxicity results in animal models and humans, this approach could produce better predictors of toxicity in humans compared to traditional models.

A second program that was recently announced involves rescuing and repurposing compounds that were abandoned late in the drug-testing process. Dr. Collins explained that compounds to be included in this program have passed safety testing in humans but lacked efficacy for a given disease; this innovative approach matches pharmaceutical compounds with NIH scientists' ideas for new uses for these compounds. Secretary of Health and Human Services Kathleen Sebelius

announced that Pfizer, AstraZeneca, and Eli Lilly and Company have agreed to join the program with their abandoned compounds, and Dr. Collins expressed belief that other companies are likely to join as well.

Dr. Collins briefly mentioned another NCATS program focused on using target validation to develop new tools and methods to efficiently and systematically identify efficacious drugs. There are great opportunities to use human cells or human genomics, and conversations about how to collaborate with pharmaceutical companies on this process are ongoing. Dr. Collins noted that a joint workshop on target validation between NIH leadership and members of industry will take place soon. He added that the NCATS programs are being facilitated through the Cures Acceleration Network (CAN), originally authorized through the Affordable Care Act and was appropriated \$10M in the FY 12 NIH budget.

Dr. Collins briefly reviewed next steps for NCATS. A search committee is actively seeking to hire leadership for the new Center. An advisory council for CAN is being established; the roster has been decided, and the regulatory approval process is ongoing. Dr. Collins reported that new requests for applications (RFAs) have been issued for June 2012 for CTSA's and the Therapeutic Discovery Program. Lastly, he informed the SMRB that the Drug Development Forum plans to conduct studies through the Institute of Medicine to review the goals of CAN; this meeting is scheduled to take place June 4–5, 2012. A CTSA review is planned for late 2012.

Discussion

SMRB Members

Dr. Cassell lauded the rapid progress on all fronts, noting that there were numerous challenges. Dr. Collins thanked her for her comments and concurred that the ongoing work with the private sector is exciting.

Dr. Rubenstein offered his congratulations on the progress, noting that NIH handled the initial opposition to some of the SMRB recommendations well. Dr. Rubenstein added that the changes at the Clinical Center will encourage collaborative research at NIH, which is very positive.

Mr. Augustine agreed with the sentiments expressed by members of the SMRB, noting that change is not always easy, and the courage and effort of NIH leadership should be commended.

Lastly, Dr. Snyder asked Dr. Collins why the beverage industry would oppose a new NIH institute merging NIAAA and NIDA. Dr. Collins explained that alcohol is a legal beverage that is socially acceptable, and the industry is concerned about its products being considered synonymous with illegal drugs. Health benefits have been argued for some alcoholic beverages. Mr. Augustine stated that NIH's role is to address research issues and hoped that these types of concerns can be minimized.

Presentation from SMRB Working Group on NIH SBIR/STTR Programs

Solomon H. Snyder, M.D.

Chair, SMRB SBIR/STTR Working Group

Dr. Snyder, the chair of the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Working Group, presented an update on the group's progress. The Working Group was tasked with considering how the SBIR and STTR programs might best be utilized. Dr. Snyder acknowledged that the programs are currently quite effective, and he chose to approach this task by ensuring that there is a solid rationale for making any changes. He reported that as he learned more about the program, he came to believe that there is a rationale for improvement.

The Working Group roster was provided to the SMRB, as follows:

Non-Federal

Solomon Snyder, M.D. (*Chair*)
 William Brody, M.D., Ph.D.
 Gail Cassell, Ph.D.
 The Honorable Daniel Goldin
 Arthur Rubenstein, M.B.B.Ch.
 Norman Augustine (*ad hoc*)

Federal

Josephine Briggs, M.D.
 Richard Hodes, M.D.
 Roderic Pettigrew, M.D., Ph.D.
 Susan B. Shurin, M.D.
 Harold Varmus, M.D.

Dr. Snyder provided a brief legislative history of the SBIR/STTR programs. SBIR was formed through the Small Business Innovation Development Act of 1982 (PL 97-219), which calls for federal agencies with extramural research and development budgets greater than \$100 million to allocate 2.5 percent of their overall budget to the SBIR program. STTR was formed through the Small Business Technology Transfer Act of 1992 (PL 102-564), which requires federal agencies with extramural research and development budgets greater than \$1 billion to allocate 0.3 percent of their overall budget to the STTR program.

As defined by the U.S. government, the mission of the SBIR/STTR programs is to “support scientific excellence and technological innovation through the investment of Federal research funds in critical American priorities to build a strong national economy.” Dr. Snyder commented that understanding how these programs fit with the NIH mission is important.

The goals of the SBIR/STTR programs are to stimulate technological innovation; meet federal research and development needs (note: the STTR program requires small businesses to formally collaborate with research institutions); foster and encourage participation in innovation and entrepreneurship by socially and economically disadvantaged persons; and increase private-sector commercialization of innovations derived from federal research and development funding. Dr. Snyder noted that these goals can and should vary depending on the agency.

Dr. Snyder asked the SMRB to consider why these programs should be changed at NIH. He believed that the way these programs are run is worth exploring, because NIH funds one of the largest SBIR/STTR programs (second only to the Department of Defense (DoD)). Unlike DoD's mission, NIH's mission focuses on increasing the fundamental knowledge base about the nature and behavior of living systems and on the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. This makes the NIH SBIR/STTR programs a unique challenge, because the NIH mission is not focused on developing products and technologies for use by NIH, and identifying what has potential “commercial value” that

aligns with the NIH mission can be both challenging and complex. As a result, ICs tend to approach the task differently.

Dr. Snyder stated that it is important to consider how these programs might be improved within NIH, in part because reauthorization of the SBIR/STTR programs requires increasing the percentage of the budget over the course of the next six years, despite the projection of flat overall budgets during this time frame. For example, the funding set aside for SBIR will increase from 2.5 percent to 3.6 percent over the next six years

Dr. Snyder stated that the charge to the SMRB was to recommend strategies NIH can implement to optimize its utilization of the SBIR/STTR programs in keeping with its mission. He informed the SMRB that the working group considered this charge with respect to fostering innovation within small businesses that aligns with the priorities of the NIH ICs, funding quality proposals that have the greatest potential for successful commercialization, and leveraging existing resources and expertise to enable grantees' success. Dr. Snyder stated that many small biotechnology companies are focused on innovative approaches that larger companies will not consider, but NIH must be mindful of its own priorities.

With respect to funding, Dr. Snyder believes the SMRB should consider whether targeted requests for proposals or more open funding mechanisms, similar to an investigator-initiated R01, are preferable, and the amount of money allocated to each type of funding program. He noted that the funding should be prioritized to studies that in addition to having high scientific quality also appear to show promise for successful commercialization. Dr. Snyder also observed that applicants and grantees may require a higher level of support to navigate the NIH review, funding, and management processes; small companies may be less familiar with government processes and might require additional guidance.

Dr. Snyder informed the SMRB that the working group is applying a framework and process for considering change, as outlined by the DOCE Working Group. Currently, the SBIR/STTR Working Group is assessing the need for change; it will then evaluate the options for change and, lastly, implement and evaluate the change. The guiding principles are to strengthen the ability of NIH to carry out its mission; provide an environment for collaboration, coordination, and interaction; bring together synergistic efforts; enhance public understanding, confidence, and support; and increase operational efficiency.

The SBIR/STTR programs have undergone review five times in the last six years by different agencies, including the National Research Council, the NIH Office of Extramural Research, and, most recently, the Government Accountability Office in 2011. Dr. Snyder found these previous reports to be thorough, and because the NIH SBIR/STTR programs have acted in response to these reports, he initially had reservations about issuing another set of recommendations from the SMRB. After further consideration, however, he acknowledged that it is important to consider how to improve current processes.

Dr. Snyder reviewed the data collection lifecycle for the SBIR/STTR programs, which comprises seven steps:

Step 1: Program outreach to prospective applicants

- Step 2: Concept development and proposal submission
- Step 3: Scientific peer review
- Step 4: IC funding decision
- Step 5: Discovery and development
- Step 6: Commercialization
- Step 7: Outcome evaluation

He stated that currently, members of the SBIR/STTR Working Group are reviewing data and research related to these various steps and will report back to the Working Group with their findings. The Working Group is also conducting interviews with the Directors and SBIR/STTR staff of different ICs. Thus far, the group has reviewed the National Institute of Mental Health (NIMH), the National Institute on Deafness and Other Communication Disorders, and the National Institute of Environmental Health Sciences. The group plans to continue discussions with ICs through June 2012. At the SMRB stakeholder meeting on July 11, 2012, the Board will hear from SBIR/STTR staff at other federal agencies and representatives of the Small Business Administration. Lastly, at another stakeholder meeting in October 2012, the SMRB will hear from representatives of the small business community, SBIR/STTR grantees, representatives from angel/venture capital investors, and academic inventors.

Dr. Snyder summarized the Working Group's preliminary findings, noting that all of the NIH SBIR/STTR programs are meeting their statutory objectives. He believed the flexibility allowed for each IC was appropriate and a considerable strength within the program. He also stated that the ICs vary considerably in terms of degree of program management, budget, implementation of pilot initiatives, assessment of success, etc., creating a unique opportunity to leverage lessons learned. Dr. Snyder provided the example of the way ICs obtain applications; small ICs tend to allow investigators to present their ideas for funding because they do not have a large support staff, whereas larger ICs tend to have program staff that can develop outreach, hold meetings throughout the country, devise key priorities, make targeted announcements, and work with grantees. NIMH, for example, devotes considerable energy to targeted funding opportunities with flexibility in how money is allocated for phase I and phase II research. Dr. Snyder explained that drug development, even for an initial phase with limited activity, can be costly, and NIMH works closely with its grantees to adjust funding accordingly.

This being said, Dr. Snyder acknowledged that there were areas for improvement and noted that any recommendations would be made in an effort to strengthen the program's operations. These include establishing reliable metrics and outcomes that can be used to assess the program's impact on supporting small businesses and advancing human health; strengthening the application process to save small businesses time and effort; enhancing scientific peer review and the criteria by which applications are judged; and defining and tracking success, considering the public's investment in these programs.

Dr. Snyder stated that establishing reliable metrics can be challenging, as they are largely based on the way metrics are defined. In earlier reviews of SBIR/STTR, commercialization was used as a metric. In the context of research and development, commercialization was defined as the ability to induce investment in the company. By that definition, 30 to 40 percent of NIH SBIR/STTR applications have been successful; however, the NIH Task Force did not believe

that the metric was adequate. Dr. Snyder quoted fellow Working Group member Goldin, who suggested that a goal of the SBIR/STTR programs might be “to mature the technology of the company in order to secure investment by the company.” This will be a topic for additional discussion.

Dr. Snyder also stated that the application process could be strengthened and some activities could be broadened to be NIH-wide rather than confined to a specific IC. He noted that the issue of open outreach versus targeted funding requires additional thought, but he believed that the flexibility in the current system works well and avoids rigid bureaucracy. Dr. Snyder stressed that the scientific peer review process should be adapted to consider the goals of product development; unlike basic research, innovation cannot always be the primary funding motivator in this context. Lastly, the turnaround time for funding is particularly problematic for small companies that require the capital to sustain their business; further deliberation is needed to determine ways to expedite the review process.

Dr. Snyder briefly reviewed the next steps of the SBIR/STTR Working Group. The group will continue consultations and data analyses that are currently ongoing. It hopes to present an update at the first stakeholder meeting on July 11, 2012. The group will then draft its preliminary findings and recommendations for discussion at the October 2012 SMRB meeting.

Discussion

SMRB Members

Mr. Augustine expressed approval of the current approach and interest in future presentations.

Public Comments

There were no questions or comments from the public.

Next Steps

Norman R. Augustine

Chairman, Scientific Management Review Board

Mr. Augustine reminded the SMRB that the next meeting is scheduled for July 11, 2012, on the NIH campus. He informed the SMRB members that they will be polled for availability for a face-to-face meeting in October 2012 and a teleconference in November or early December 2012.

In a letter sent to the SMRB in April, the NIH Director notified the members that the SMRB will be charged with deliberating the value of investment in biomedical research. Mr. Augustine observed that the SMRB could consider how to assess the value of investments in research and identify appropriate metrics, noting that one of the statutes for the SMRB is “to review the research portfolios of the NIH in order to determine the progress and effectiveness and value of the portfolio and the allocation among the portfolio activities and the resources of NIH.” Thus, this new charge falls under the purview of the SMRB and will be a topic of future discussion.

Any SMRB members interested in serving on a working group for this topic should contact Mr. Augustine and Dr. Patterson.

Dr. Augustine announced that changes in SMRB membership will take place at the July 11, 2012, meeting. Replacement members are currently in the approval and clearance process. Dr. Patterson will inform all members of their standing. It was noted that past members of the SMRB may be consulted on an ad hoc basis.

Dr. Collins thanked Dr. Snyder and the SBIR/STTR Working Group for their work thus far. He said he appreciated the concern about whether change to these programs was warranted but believed the working group offered a great opportunity to perform a thorough review and determine any improvements. He noted that, in addition to an upcoming increase in funding for the programs, there will soon be new opportunities for companies with venture capital support, and this will require a broader view of potential applicants. Dr. Collins also urged the Working Group to consider creative ways to shorten the review process, including non-traditional methods.

Dr. Collins acknowledged the importance of understanding return on investment and emphasized that NIH should seriously consider the return on investment for every taxpayer dollar. A recent report from the Information Technology and Innovation Foundation, produced jointly with United for Medical Research, considers this point from the perspective of American competitiveness. This report will be distributed to all SMRB members. The new charge to the SMRB to place a value on research investment will be formally announced at the July 11, 2012, SMRB meeting. Dr. Collins thanked the SMRB members for their continued efforts.

Mr. Augustine echoed Dr. Collins' thanks and adjourned the teleconference.