NIH SCIENTIFIC MANAGEMENT REVIEW BOARD

October 26, 2011

Board Members Present:

Norman R. Augustine, Chairman
William R. Brody, M.D., Ph.D.
Gail H. Cassell, Ph.D.
Anthony S. Fauci, M.D.
Eric D. Green, M.D., Ph.D.
Richard J. Hodes, M.D.
Stephen I. Katz, 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, speakers, and guests and reviewed the meeting agenda. He noted that the reports produced by the Scientific Management Review Board (SMRB) are available on the SMRB website. The minutes from the meetings held on November 10, 2010, December 7, 2010, and February 23, 2011, were approved as written. Mr. Augustine also announced that Dr. Roderic Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), would replace Dr. Jeremy Berg on the SMRB. Brief member introductions were made.

Dr. Patterson reviewed the NIH conflict of interest policy.

Status of NIH Today and Looking to the Future
Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

Dr. Collins thanked the SMRB for its productivity during the past year and said that NIH has been working diligently to follow up on the Board's recommendations. He acknowledged the superb leadership of the NIH Institutes and Centers (ICs), including the newly appointed Director of the National Institute of Dental and Craniofacial Research (NIDCR), Dr. Martha Somerman.

Dr. Collins stated that scientific research is at a paradoxical point: The opportunities in biomedical science have never been more exhilarating, but the discipline is facing a historic resource challenge due to current economic conditions. Priorities will need to be set, and some projects may need to be scaled back so that advances can be made in other areas. He stated that it will be critical for the biomedical community to clearly articulate the value of medical advances and their positive impact on our nation's economy. Dr. Collins emphasized that NIH is committed to investing in basic research and currently spends 52 percent of the total NIH budget on this type of research. He noted that President Obama also recognizes the importance of these endeavors and reviewed several recent examples that demonstrate how discovery is advanced through technology.

Dr. Collins also discussed the importance of the biomedical workforce and stated that encouraging new investigators and new ideas, though challenging, is critical for our future. NIH has several initiatives to nurture young scientists and encourage them to attain independent research status, including the Lasker Clinical Research Scholars Program and several programs funded through the Common Fund: The Transformative Research Award, the NIH Director's Pioneer Award, the New Innovator Award, and the NIH Director's Early Independence Awards. He also acknowledged that greater racial and ethnic diversity is needed in the biological sciences, noting a recent publication by Dr. Raynard Kington, former deputy director and acting director of NIH, which found a substantially lower success rate for African Americans in the NIH grant process. He noted that issues like this must be addressed through enhanced recruitment and other avenues. For example, the process of reviewing grants often provides valuable insight that can increase one's chance of success. He noted that NIH must consider the possibility of inherent bias within the system. The Advisory Committee to the Director's (ACD's) Working Group on Diversity in the Biomedical Research Workforce is currently considering this topic; its recommendations are due by December 2011 and will be finalized by June 2012.

Dr. Collins raised the issue of the optimal size of the biomedical workforce, i.e., is it too large or too small? He noted that scientists tend to assume that the only acceptable pathway is that of a tenure-track investigator at a top-tier university, which he considers a disservice to biomedical research given the broad needs for research advancement. He stated that a better understanding of the dynamics of the workforce is needed considering Americans' interest in science, the demand for people with scientific training, and whether post-doctoral training in other areas could be useful. With more information, we may be able to create a new model for training the biomedical research workforce. Dr. Collins stated that a NIH working group has been created to examine this topic.

Dr. Collins also stated that funding is an obvious and serious challenge to the future of biomedical research. He presented a graph demonstrating that funding for NIH between 2003 and 2009 was essentially flat until Fiscal Years 2009 and 2010, when American Recovery and Reinvestment Act (ARRA) funds supplemented the NIH budget. As a result, success rates for applicants for NIH grants continue to decline; the 2011 estimate of 17.4 percent of applicants obtaining funding is the first time in NIH's recorded history that the success rate has been below 20 percent (25 percent to 35 percent is considered a healthier figure). He noted that funding restrictions are not likely to be resolved quickly, and NIH must prioritize its efforts with great care. Strategies for adjusting to restricted budgets include trimming funding amounts consistently across grants, evaluating and rearranging the research portfolios of each grant and IC (which is currently underway), and making alterations in the management of NIH resources (for example, instituting a cap on the number of R01s held by each investigator). The NIH website has data on how much money would be involved in different scenarios

(report.nih.gov/budget_and_spending/index.aspx). No final decisions have been made.

Dr. Collins concluded his presentation by stating that the United States needs to innovate, and NIH should lead biomedical research innovation.

Discussion

Dr. Rubenstein inquired about the current support for establishing the National Center for Advancing Translational Sciences (NCATS); namely, whether concerns about creating the new center have changed over the last several months. Dr. Collins stated that people have come to embrace the plan as they better understand the goals of the center, which he reiterated is not to be a drug development company. He also noted that NIH has garnered support from the biotechnology and pharmaceutical sectors, the White House, and the Senate. The House of Representatives has not yet voted on a bill that includes funding for NIH and NCATS. Given the current federal funding environment, it is not clear whether the center will be officially established in Fiscal Year 2012, but progress on its creation is being made. Dr. Green, co-chair of the search committee for the NCATS director, added that the search committee has received a lot of positive feedback regarding the need for NCATS.

Dr. Snyder asked about the expected level of funding for NCATS. Dr. Collins reported that the Senate appropriations bill creates NCATS by bringing existing programs (and their funding) from other parts of NIH and also adds $20 million for the Cures Acceleration Network (CAN), which was authorized in 2010 but had not received appropriated funds. Dr. Collins added that House support is less clear; the relevant appropriations subcommittee chair has questions about NCATS, but hopefully his concerns can be addressed.

Dr. Cassell requested that NIH share with the SMRB some of the recent economic analyses reported in Dr. Collins' presentation. She also requested information comparing the United States investment in biomedical research to that of other countries; Dr. Collins responded that NIH can provide the SMRB with reports and slides that show the requested economic analyses, including a report from United for Medical Research released in May 2011, as well as data comparing the U.S. with China, India, and Europe.

Mr. Augustine asked how many grants would be funded if they were evaluated on their merits alone. Dr. Collins estimated that approximately one-third of grants are very promising, worthy of funding, and could pass a rigorous review process. Currently, only one-sixth of applications are funded. As a result of the low percentage of applications being funded, investigators spend more time writing and re-writing grant proposals in order to procure funding.

Dr. Cassell asked whether NIH can make a compelling case that the quality of applications being submitted is as high or higher now than in the past. Dr. Collins responded that it is difficult to apply a metric of worth to grant applications across a 20- or 30-year time span but thought that current proposals were scientifically rigorous in the way that problems are being approached and in the arguments in favor of that approach. Dr. Katz concurred, noting that today some applications that peer reviewers find to be scientifically exceptional and outstanding are left unfunded—something that did not happen 20 years ago. Dr. Shurin added that, in the experience of the National Heart, Lung, and Blood Institute (NHLBI), grants that were not initially funded but later were granted ARRA funding

have so far performed at least as well (using publication rate as a metric) as proposals that scored slightly higher in peer review and received funding in the first round. This information indicates that some very good proposals are not being awarded due to lack of funding. Dr. Shurin stressed that as resources become more limited, study sections tend to become more conservative, so study sections must be guided to consider innovation as a metric. Dr. Cassell noted that private foundations that struggle with funding sometimes consider partnerships; Dr. Collins agreed that this is an opportune time to consider new collaborations with foundations and private partnerships.

Dr. Cassell expressed concern that when one focuses too heavily on innovation, areas that are considered to be more mundane – but are important public health issues – tend to become underfunded (e.g., sepsis). Dr. Collins acknowledged potentially neglected fields of research, noting that it is his job and that of the IC directors to consider public health and identify research needs.

Dr. Snyder inquired about whether the funding rate of applications is artificially low due to a surge in applications. Dr. Collins responded that the total number of applications has increased somewhat but not dramatically since the stimulus funding; the main reason for falling success rates is the falling purchasing power of NIH funds (down 20 percent since 2003) brought about by flattening budgets and rising inflation in the cost of conducting research. He said that indirect costs could be re-managed, but that could have serious consequences at a time when universities are already facing serious fiscal difficulties. Dr. Cassell recommended reevaluation of how indirect costs are apportioned, such as improved management to avoid overbuilding. Administrative costs, such as reporting and Institutional Review Board (IRB) oversight mechanisms (e.g., single IRB for multi-site trials), also might be considered. Dr. Collins stated that NIH should consider certain processes, such as lessening the administrative burden of low-risk research, eliminating duplicative IRBs, and reorganizing funding formulas.

Mr. Augustine recounted his experience dealing with major change in the defense industry and observed that most people can stand change, but not uncertainty.

Dr. Brody expressed concern that many extramural institutions are in denial about the harsh economic realities facing biomedical research and still adhere to the belief that "if you build it, they will come" (i.e., if they develop capacity, NIH funding will follow). He stated that the current funding crisis feels fundamentally different and more serious than years past. Dr. Brody advised NIH to make adjustments slowly and deliberately to avoid harming its long-term investments, but he warned that Congress could still make drastic changes. Dr. Collins agreed, noting that he has had similar discussions about the serious budget situation with members of the American Association of Universities and Institute of Medicine, and he will soon speak to the Association of American Medical Colleges. He observed that the Darwinian approach may not be sufficient to select the most deserving extramural grant proposals.

Advancing Translational Sciences
Kathy Hudson, Ph.D.
Deputy Director for Science, Outreach, and Policy, National Institutes of Health

Dr. Hudson reminded the Board of the enormous challenges that they sought to address in their Report on Translational Medicine and Therapeutics (TMAT) – namely that the current process is "error prone, failure prone, slow, and extraordinarily expensive." The report, which was finalized in December 2010, recommended the creation of a new NIH Center focused on translation, and in January 2011, Department of Health and Human Services (DHHS) Secretary Kathleen Sebelius notified Congress of DHHS's intent to create such a Center, which would be named the National Center for Advancing Translational Sciences (NCATS).

Dr. Hudson reported that Dr. Collins had formed several working groups to formulate an appropriate mission for the new Center and ensure the smooth transition of affected programs:

- *IC Directors-NCATS (ICD-NCATS) Working Group*. The ICD-NCATS Working Group, co-chaired by Drs. Eric Green and Tom Insel, was tasked with making recommendations regarding the new center's mission and its role within NIH. The working group decided that the mission of NCATS should be "*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*." Dr. Hudson stated that the working group determined that the primary goal of NCATS should be enabling—not performing—the development of therapeutics. The group also emphasized that NCATS should not compete with but should complement ongoing efforts in other ICs and in the private sector, and NCATS activities should also reinforce NIH's commitment to basic research. The working group concurred with the SMRB's recommendation that the new Center be composed of 1) components of the Molecular Libraries Program, 2) the Therapeutics for Rare and Neglected Diseases (TRND) Program, 3) the Rapid Access to Interventional Development (RAID) Program, 4) the Clinical and Translational Science Awards (CTSA) Program, 5) the FDA-NIH Regulatory Science Initiative, and 6) the new Cures Acceleration Network (CAN); ultimately, 7) the Office of Rare Disease Research was also added.
- The *CTSA/NCATS Integration Working Group*. This working group, chaired by Dr. Katz, was created in order to ensure a smooth integration of the CTSA program into NCATS. Dr. Hudson noted that the goal is to have a mutually beneficial relationship in which NIH and NCATS continue to support the important work done by the 60 CTSA programs, and the CTSAs help to support the NCATS mission. She said that the working group had recently presented their recommendations to Dr. Collins.
- *Advisory Committee to the Director Working Group on NCATS (ACD-NCATS)*. Dr. Hudson displayed the membership of the ACD-NCATS Working Group, which was chaired by Dr. Maria Freire. They were charged with providing high-level advice on the creation of NCATS and how the new center could interact with the private sector. The group recently delivered their report to Dr. Collins, and the report is available on a Web site that can be accessed via a blue button titled "Promoting Translational Sciences" on the NIH home page. The ACD-NCATS Working Group report found that NCATS can 1) catalyze translation by promoting innovative research, 2) galvanize and support new partnerships, 3) support and augment the discipline of regulatory science and its application, 4) expand the precompetitive space, 5) harness the power of the Clinical and Translational Sciences Awards (CTSA) Program, 6) transform the field through training, and 7) streamline administrative processes.

Dr. Hudson discussed plans for CAN, which was authorized in the Patient Protection and Affordable Care Act of 2010 but has not yet been appropriated funding. Dr. Hudson reported that the Senate appropriations bill for Fiscal Year 2012 includes $20 million for CAN, and 20 percent (or $4 million) of that money can be used for flexible research authorities, which would give NIH the option of using Flexible Research Awards similar to those used by the Defense Advanced Research Projects Agency (DARPA). Other funding options include Large Grant Awards (up to $15 million) and Partnership Awards, which encourage partnerships with the private sector and which will be especially important given the tight budget climate.

Dr. Hudson reported that Dr. Collins' July 2011 article in *Science* laid out his vision for NCATS and helped to correct early wrong impressions about NCATS. He has also met with pharmaceutical and biotechnology companies, venture capitalists, academic health professionals, and others to try to identify bottlenecks in the drug development pipeline that NCATS could help to overcome.

Dr. Hudson reviewed the proposed organizational chart for NCATS. She stated that, unlike most NIH ICs, it will not have divided extramural and intramural programs because NIH hopes to have a more porous interface between these two groups. NCATS will also have two fundamental research components: the Division of Preclinical Innovation and the Division of Clinical Innovation. The legislation establishing CAN mandated an advisory Board, and it must be composed of at least four venture capitalists, eight disease advocates, and representatives from a variety of fields of expertise. NIH intends to have the CAN Board also serve as the NCATS Council and Board of Scientific Counselors. She also noted that NIH is currently soliciting applications for the new director of NCATS and highlighted attributes of the ideal candidate (including broad expertise and both academic and private sector experience). The search committee for the NCATS director is co-chaired by Drs. Eric Green and Tom Insel and includes members from NIH, academia, biotech, pharma, FDA, and patient advocacy groups.

Dr. Hudson presented the proposed NCATS budget for Fiscal Year 2012. She stated that while the Senate has included language regarding NCATS in its Fiscal Year 2012 appropriations bill for agencies including NIH, the House of Representatives has yet to produce or vote on its version of the 2012 appropriations bill. The Senate bill provides $582.4 million for NCATS, which is the sum of the imported programs plus an additional $20 million for the new CAN program.

In the interim, NIH is launching a program to predict drug safety through collaboration with DARPA and the Food and Drug Administration (FDA). The scientific goal of this project is to develop a chip that will mimic the physiological processes of various organ systems; a secondary benefit of the collaboration is to learn from DARPA's style of project management. Another pilot project is to consider NIH's potential matchmaking role in the rescue and repurposing of compounds abandoned by pharmaceutical companies.

Dr. Hudson concluded by mentioning that the President is strongly supportive of NCATS and that she had invited the President to the NCATS ribbon-cutting ceremony.

Discussion

Dr. Cassell expressed enthusiasm for the pilot projects presented by Dr. Hudson. She asked about

funding for regulatory science projects, noting that the FDA can only provide limited financial support. Dr. Hudson explained that while the FDA is unable to contribute funding, it currently serves as an instrumental advisor to the toxicity-on-a-chip program. Dr. Patterson added that the NIH-FDA Regulatory Science Initiative involves resources from FDA as well as the insights and expertise of FDA personnel; FDA is part of the Initiative's peer review process and helps to evaluate proposals and make decisions.

Dr. Rubenstein suggested engaging smaller biotechnology companies in addition to large pharmaceutical companies, as these companies tend to be highly innovative. Drs. Hudson and Collins, agreed, adding that they have recently met with entrepreneurs in the fields of therapeutics, diagnostics, and devices.

Dr. Cassell asked about the role of the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs; participants noted that these topics were scheduled for discussion later in the meeting.

Optimizing Substance Use, Abuse, and Addiction Research at NIH
Lawrence A. Tabak, D.D.S., Ph.D.
Co-Chair, Substance Use, Abuse, and Addiction Task Force, and Deputy Director, National Institutes of Health

Dr. Tabak provided an update on the SMRB's recommendation to reorganize substance use, abuse, and addiction (SUAA) research at NIH. He stated that in response to the recommendation, Dr. Collins convened a SUAA Task Force to guide the reorganization. He noted that NIH scientific staff from the potentially affected ICs were convened to identify principles that should guide the proposed reorganization, and members of the Task Force are currently conducting a detailed portfolio analysis of grants, contracts, and intramural research in order to create and launch a scientific strategic plan. New opportunities that emerge from this effort will be explored by experts at NIH and relevant stakeholders across the country. Plans are being developed for stakeholder outreach and should be available soon.

Dr. Tabak stated that the SUAA Task Force intends to release a portfolio integration plan in the fall of 2012 and a scientific strategic plan by the end of 2012. This time frame will allow for the integration of the recommended changes into the Fiscal Year 2014 NIH budget proposal. He noted that the National Institute for Drug Abuse (NIDA) and National Institute on Alcohol Abuse and Alcoholism (NIAAA) have made outstanding progress since the reorganization was proposed, and the integration of these Institutes may be nearly complete by the time the plans and budget have been formalized. Full implementation of this reorganization, however, has been shifted by one year as a reflection of the complexity of the portfolios and to ensure time for public input into the process. The name of the combined research entity has not been decided yet.

Discussion

Dr. Powell lauded NIH's decision to delay final reorganization plans until a thorough outreach effort and strategic scientific plan had been completed. Dr. Tabak gave credit to NIAAA Acting Director Ken Warren and NIDA Director Nora Volkow for their strong leadership and collaborative spirit.

Public Comment

Mark Goldman, Ph.D., a representative of the Research Society on Alcoholism, expressed concern that the SUAA Task Force report did not define the scope of the problem that the reorganization is attempting to address. He stated that the absence of a clear scope is not a failing of the group, but rather indicates the complexity of this field of research. He noted that compulsive behaviors are difficult to identify and enumerate, given that they can encompass issues related to tobacco, alcohol, drugs, gambling, and even obesity. Dr. Goldman recommended that NIH convene a consensus conference with all relevant stakeholders to discuss the core of this problem.

Bankole Johnson, D.Sc., M.D., Ph.D., M.Phil., F.R.C.Psych., from the University of Virginia School of Medicine requested consideration of a focused cost analysis and asked that researchers be engaged in the discussion to better understand how potential changes might affect their grants or their futures. Substance abuse as a topic can become overly broad. There should be a focus on definitions of the relevant aspects of the disease, which could influence the research support structure. For example, NIDA has a support structure for providing HIV resources; similar resources should be considered for tobacco and alcohol so that the focus of the institute fits the national need. He also stressed the need to seek ways to collaborate with industry.

Martin Woodle, Ph.D., from the Institute for Translational Biomedical Science said that he began the company in order to help address some of the same problems identified by the SMRB. There is a key role for small biotechnology companies in scientific innovation, and NIH should consider ways to augment and utilize small biotechnology companies that may not be fully drawn into translational research. He observed that translational activities can be mundane and cautioned that even bringing various activities to work together for the first time will not seem innovative or exciting.

NIH Clinical Center: Organizational and Budgetary Challenges
Stephen I. Katz, M.D., Ph.D.
Chair, Clinical Center Governing Board, National Institutes of Health

Dr. Katz provided an update on the activities of the Clinical Center Governing Board (CCGB), which was established in response to the SMRB's report on the NIH Clinical Center (CC). The latter recommended simplifying the governance of the CC. He reviewed the CCGB's membership and its purpose, which includes providing the following:

- Strategic and operational policy direction and oversight of the Clinical Center.
- Strategic and operational oversight over changes to the mission of the Clinical Center, and to implementation of the recommendations of the SMRB.
- Recommendations on the optimal size and scope of the Clinical Center, and how best to maximize the quality of research conducted.
- Policy and operational recommendations on cross-cutting scientific and administrative issues that affect both the NIH's Institutes and Centers and the Clinical Center.

- Recommendations on the Clinical Center's annual budget request after considering the recommendations of the ABCR and the overall NIH budgetary environment.

Dr. Katz reminded the group that members of the SMRB unanimously agreed that funding for the CC should be established by a line item within the budget of the Office of the Director. He stated that while this idea was embraced by the CCGB, its actual implementation was more legally complex than anticipated. Because this complexity could not be resolved before consideration of the 2013 budget, implementation of the funding mechanism for the CC will be delayed. The CCGB has, however, developed recommendations to review CC funding requests based on the current patient census and has initiated collaborative efforts with the NIH Office of Intramural Research to seek additional budgetary efficiencies.

Dr. Katz stated that the CCGB has addressed other SMRB recommendations and priorities regarding the CC, including the opportunity for external investigators to access the CC's resources. For example, a new bench-to-bedside program, titled the NIH/Clinical Center Cooperative Program of Bench to Bedside Research Projects, has been developed through a cooperative agreement between intramural and extramural participants with funding from the relevant ICs. Dr. Katz provided a program outline with a list of project requirements for these activities and told the SMRB that a request for information has been issued. The request for applications is anticipated to be published in late 2012 or early 2013. The program will have unique requirements: 1) extramural investigator must have an intramural collaborator; 2) applications must be submitted by extramural PI; 3) the project must use the resources of the CC; 4) the project must be signed off by the CC and IC scientific and clinical directors; 5) awards will be for three years at more dollars than the current bench-to-bedside program (up to $500,000 per year in direct costs); and 6) the IC director will determine the exact funding source (intramural vs. extramural).

Discussion

NIH Legal Advisor Barbara McGarey, Office of the General Counsel, discussed the legal challenges associated with the implementation of the SMRB's funding recommendations for the CC. She explained that funds for CC activities not included in the CC budget currently are provided by participating ICs. For this reason, it is extremely challenging to assess the exact cost of running the CC. It would be critical to identify the exact cost of running the CC because once the CC budget becomes a line item in NIH's appropriated budget, it cannot be supplemented (e.g., with IC funds). Ms. McGarey said NIH does not want to move forward with the CC line item proposal—and thereby remove IC funding flexibility for activities in the CC—before the total CC budget figure is calculated and before the implications of this proposed change are understood fully. Dr. Hodes asked whether there was a way the ICs could get around the prohibition against supplementing an appropriation by co-funding certain CC activities. Ms. McGarey answered that it would depend on how the appropriation language is written and what activities are to be funded by the line item.

Dr. Katz noted that the CCGB is exploring alternative options for funding the CC with Dr. Collins. For example, it might be possible to put a small percentage of the total NIH budget into a management account for the CC—in keeping with the idea that the CC will be opened up to the extramural community. This would still require knowledge of the total amount used to run the CC. Dr. Cassell asked whether the lack of flexibility described by Ms. McGarey would be a problem in the event of an

emergency, such as a disease outbreak. Dr. Katz responded that there still may be some flexibility in future budgets and that the NIH Director has access to discretionary funds in the event of a serious biomedical emergency. Dr. Fauci said that a discretionary fund may not be needed, but that in this case, this complexity is a question of whether the CC funding is or is not a line item. Dr. Collins said he appreciated the questions and comments, and any decisions on this point must be clearly documented. He added that he had learned from his experience with NCATS that there will be a long lead time and a lot of unpredictability.

Overview of the Small Business Innovation Research and Small Business Technology Transfer Programs at NIH

Sally J. Rockey, Ph.D.
Deputy Director for Extramural Research, National Institutes of Health

Dr. Rockey reviewed the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs' roles and responsibilities at NIH. She explained that the purpose of the SBIR program is to stimulate technological innovation, use small business to meet federal research and development needs, foster and encourage participation by minority groups, and increase private sector commercialization. Dr. Rockey noted that the STTR program is very similar, but it requires participating small businesses to partner with nonprofit research institutions (primarily universities). SBIR was first authorized in the Small Business Innovation Development Act of 1982, and STTR was authorized 10 years later in the Small Business Research and Development Enhancement Act of 1992. Dr. Rockey provided the funding requirements of SBIR and STTR and a list of participating agencies. According to the legislation establishing the SBIR program, all agencies with an extramural research budget exceeding $100 million must allocate 2.5 percent to an SBIR program. STTR is a smaller program that requires 0.3 percent funding from agencies with extramural research budgets greater than 1 billion dollars. With a 2011 contribution of $682 million, NIH is the second largest funder of the SBIR and STTR program; only the Department of Defense (DOD) has a larger program with $1.4 billion. All NIH ICs have SBIR and STTR programs except the Fogarty International Center (because it has an international focus) and the three centers without funding authority: NIH Clinical Center, Center for Information Technology, and Center for Scientific Review. Dr. Rockey explained the reauthorization history of SBIR and STTR. SBIR was last reauthorized by Congress on September 30, 2008, and STTR was last reauthorized on September 30, 2009; since that time, both programs have undergone a series of temporary extensions, with another temporary extension scheduled to take place on November 11, 2011. Legislators have been considering whether changes to the programs are appropriate; Dr. Rockey acknowledged that the extended temporary extensions have created uncertainty within the research community.

Management implementation for SBIR and STTR is rather unique. The Small Business Association (SBA) oversees and coordinates these programs for all eleven participating agencies, driving implementation and developing policy directions based on legislation, such as recently setting more restrictive ground rules for the inclusion of venture capitalists. The NIH Office of Extramural Research (OER) has a central office that is responsible for coordinating the program with the SBA and the IC, developing NIH policy, reporting information about the programs to the Administration and Congress, publishing parent funding opportunity announcements, etc. Each participating IC, in turn, has its own lead program and usually uses its Grants Management personnel as the point of contact for SBIR and STTR. In addition, NIH is a service agency for other federal agencies, including the Centers

for Disease Control (CDC), the Food and Drug Administration (FDA), and the Administration for Children and Families (ACF), providing review and other support for their SBIR programs.

Dr. Rockey briefly reviewed the budget allocations with NIH for FY 2011. Because contributions are based on current IC budgets for extramural funding, the National Cancer Institute (NCI), National Institute of Allergy and Infectious Diseases (NIAID), and NHLBI are the largest funding contributors to SBIR and STTR. $609 million was allocated to SBIR, and $73 million was allocated to STTR.

Dr. Rockey reviewed the phases of the SBIR and STTR programs, including the eligibility criteria, average amount, duration, and goal of each grant:

- *Phase I (Feasibility Study)*: The Phase I project period is six months for SBIR and one year for STTR. NIH regularly exceeds the SBA-recommended funding levels of $150,000 for six months for SBIR and $100,000 for one year for STTR. In FY2010, NIH gave average awards of $214,000 for SBIR and $200,000 for STTR grantees.
- *Phase II (Full Research/Research & Development)*: Applicants to Phase II compete for two-year awards for research and development (R&D). Once again, NIH regularly exceeds the SBA guidance levels of $750,000 for SBIR and $1 million for STTR (for two years), providing average awards of $1.2 million for both SBIR and STTR grantees in FY2010. Applicants with reasonably feasible projects can also take advantage of Fast Track, which combines the Phase I and Phase II application and review processes and saves a significant amount of time that would have been spent applying and awaiting approval for separate Phase II funding. Not all NIH ICs participate in the Fast Track funding mechanism.
- *Phase IIB (Competing Renewal/R&D)*: Many ICs offer competing renewal grants in the R&D phase. Funding varies but is typically around $1 million each year for up to three years. Not all ICs participate in this phase; generally this funding is directed toward clinical applications.
- *Phase III (Commercialization Stage)*: While NIH can offer grantees technical assistance as they try to commercialize their technology, the SBIR and STTR programs do not support research once it has reached the market, received R&D investments or research contracts, sold equity in the company, received investment from a third party, etc. At this point, the grantee must graduate to outside investment, other federal non-SBIR/STTR grants (primarily applies to DOD contracts), or support itself through the sale of its newly-developed product.

In March 2010, the SBA increased the funding guidelines for SBIR for Phase I to $150,000 for six months and $1 million dollars for two years in Phase II. STTR funding levels remain unchanged at $100,000 for one year for Phase I and $750,000 for 2 years for Phase II.

In order to qualify for the SBIR program, an applicant must be a for-profit small business concern (SBC) with 500 or fewer employees (including affiliates) and a principal investigator or project director whose primary employment is with the SBC at the time of the award and for the duration of the project period. Dr. Rockey noted that there are complicated constraints on SBC ownership in order to limit the involvement of venture capital: at the time of the award, the SBC must be at least 51 percent U.S.-owned by individuals and independently operated, or at least owned and controlled by another business concern that itself is at least 51 percent owned and controlled by one or more individuals.

Eligibility for the STTR program is similar except that it must be a formal cooperative R&D effort, with a minimum of 40 percent effort by the applicant SBC and at least 30 percent effort by a U.S. research institution, which can be a college, university, non-profit research organization, or federal R&D center. In addition, there must be an intellectual property agreement between the collaborators. The principal investigator or project director does not need to be employed by the SBC (as with SBIR) but must commit at least 10 percent effort to the project.

In summary, major differences between SBIR and STTR include the fact that SBIR permits partnering with a research institution whereas STTR requires it. In addition, the principal investigator for a SBIR grant must be primarily employed by the SBC, where as an STTR-funded principal investigator may be employed by a research institution or a small business concern.

Dr. Rockey reviewed the success rates for SBIR and STRR grant applications compared to R01 grants. The rates for SBIR funding went up in the early 2000s, correlating with a decrease in the number of applications. In 2010, there was a precipitous drop in SIBR grant funding success. She explained that this decline in success rate was largely due to changes during ARRA funding, including increased advertising of NIH programs available to small businesses. While NIH was exempt from the requirement to set aside ARRA funds for SBIR and STTR, two small business funding opportunity announcements were developed with ARRA funding: 1) a Phase I award for new entrants called the Small Business Catalyst Awards for Accelerating Innovative Research, and 2) the Biomedical Research, Development, and Growth to Spur the Acceleration of New Technologies (BRDG-SPAN) pilot program, designed to encourage translational medicine and third-party investment and bridge the valley of death between research and the commercial market. No formal evaluations have been done yet, but this program could serve as a model for encouraging translational research.

Dr. Rockey reported that applications can be submitted for review throughout the year, with deadlines in early April, August, and December. The standard review process for grants takes six to nine months. For a small business, this length of time can be a financial burden. She stated that NIH would like to find ways to streamline the review process. The Fast Track combination option for transition from Phase I to Phase II is important to optimize this process.

The SBIR legislation allows NIH to fund Technical Assistance Programs that offer discretionary technical assistance via an outside vendor. Approximately $4,000 per award (for both Phase I and Phase II awards) is set aside to help grantees make sound technical decisions, solve technical problems, minimize technical risks, and commercialize the SBIR product or process. One such program is the Niche Assessment Program, which advises up to 100 Phase I grantees each year and works to find alternative uses for their technology, identifies a competitive advantage, and develops market entry strategy. Another program is the Commercialization Assistance Program, which helps 40-80 Phase II grantees develop business and strategic plans, as well as help them build strategic alliances and investor partnerships.

Dr. Rockey described the Performance Outcomes and Data System (PODS), a Web-based tool that tracks SBIR and STTR outcomes by award and company and provides data on rates of commercialization by grantees. Outcome data for recipients of the Commercialization Assistance Program are tracked now, and in the future companies will be able to update their own commercialization data. Currently, these data are accessible only to NIH staff, but the intent is to

make the information public. PODS will assist in tracking the rate of commercialization for SBIR- and STTR-funded small business programs.

The Pipeline to Partnerships (P2P) program offers a Web showcase of SBIR, STTR, and NIH-licensed technologies. Dr. Rockey stated that P2P facilitates match-making between recipients and potential strategic partners and investors. It allows outside parties to search by application category (diagnostics, therapeutics, tool, etc.) and/or disease.

Dr. Rockey reported that 95 percent of SBIR/STTR awards are in the form of grants; the remaining 5 percent are in the form of contracts. This balance of grants and contracts is not required and could be reexamined. While most SBIR/STTR awards are investigator-initiated and are submitted to NIH's broad funding opportunity announcements (FOAs), 30 percent of all awards originate from targeted FOAs from ICs, which specify certain technologies or services that the ICs want companies to develop. NCI has a unique approach—using contracts for 25 percent of awards, setting up a Regulatory Assistance Program to help small businesses maneuver the FDA-approval process, and hosting an investor forum at which investors and venture capitalists can interact with small business awardees. Recently, SBIR has embarked on a Technology Transfer Program to develop new, exclusive license agreements for startup companies that are working with NIH intramural laboratories.

In 2002 and 2008, SBIR underwent an extensive evaluation that found that NIH is meeting its congressional goals. Seventy-five percent of the 2008 cohort has initiated commercialization, and companies grew under the program and hired new employees. A 2009 National Research Council assessment found that approximately 40-50 percent of SBIR-funded products were commercialized, the awards had positive effects on healthcare, companies grew and retained two full-time employees per project, and there is effective mission alignment between NIH and SBIR.

Dr. Rockey gave several examples of successful products that were developed with aid from the SBIR program. These include 1) a water-containing, ultrasound-visible marker in breast cancer imaging by Biopsy Sciences; 2) DeltaNu's small Ramon spectroscopic instrumentation for medical devices and material identification ($11 million in sales); 4) IntraLase's laser in corneal surgery; 5) Martek's omega-3 fatty acids for infant formula; and 6) the Sonicare toothbrush ($1.5 billion in sales and created over 500 jobs).

Dr. Rockey reviewed some of the benefits and challenges of the current structure of the SBIR and STTR programs. Benefits fall into the following categories:

- *Program flexibility*. Both grants and contracts can be used under the programs, multiple funding opportunity announcements are issued, ICs can tailor FOAs to their missions, due dates occur three times each year, Fast Track eliminates unnecessary steps, etc.
- *Application/review*. Review of SBIR and STTR applications is rigorous and follows NIH's standard operating procedures.
- *SBA oversight*. Oversight by the SBA is helpful in coordinating joint-agency FOAs and implementing best practices across agencies.
- *Re-authorization of programs*. Operating under congressional authorization provides stability.

Dr. Rockey noted challenges within those same categories, including:

- *Program flexibility*. The current restrictions on SBIR funding put a strain on centralized administrative support and management; currently, there is no mechanism to allocate money for NIH-level management. Review of management at the ICs and how it could be improved may be warranted.
- *Application/review*. The application review process takes six to nine months, which may be too long for a small business. The Small Business Administration is pushing to shorten the length of time from submission to funding, but this is challenging since NIH is expected to maintain its rigorous review process.
- *SBA oversight*. NIH sometimes has to educate SBA personnel about the unique needs of NIH and biomedical research. Other drawbacks include differences over the need for flexibility and delays in implementing new policies that are established by SBA.
- *Re-authorization of programs*. Lacking re-authorization for the past three years causes uncertainty and instability.

Dr. Rockey concluded her presentation by offering the SMRB several issues that they might want to consider in their deliberations. First, there may be ways to improve NIH processes for implementing and managing the SBIR program. Second, NIH might be able to expand its role beyond Phase I and II research toward helping awardees bridge the valley of death and reach commercialization. Third, the SMRB could consider how NIH can use the SBIR to best meet its mission.

Discussion

Dr. Cassell asked whether NIH would be part of an evaluation that is being initiated for National Aeronautics and Space Administration (NASA), DOD, and the National Science Foundation (NSF). Dr. Rockey responded that the last review took place in 2009 and can serve as a baseline for future reviews. Many changes are likely to be made as a result of the pending budget reauthorization. As a result, NIH has determined that it would be best to undergo re-evaluation after the reauthorization has been signed into legislation and after NIH has implemented the changes mandated in the reauthorization. It will be critical to assess the effect of these changes once they have been implemented.

The group briefly discussed the role of venture capital (VC) in drug discovery. Dr. Snyder noted that the majority of good small biotech companies are VC-funded, so if the SBA eliminated the rule on VC-funded companies, the programs would receive more and better quality applications. Dr. Rockey noted that while there are complicated rules regarding VC funding, companies with *some* VC backing can be eligible for SBIR and STTR funding. In addition, the House and Senate versions of the reauthorization give some relief to the existing stringent VC rules. She stated that an SMRB review of the different options and recommendations on this point would be helpful, as would a review of how the whole sector has changed in recent years. Dr. Rockey agreed that it seems odd to reject the very companies that are promising enough to obtain VC support or to exclude early-stage projects that do not themselves receive VC funding simply because the sponsoring company receives VC funding for other projects. Dr. Brody countered that perhaps it is best for government to remove itself once additional capital has been secured. He asked whether the government investment in these companies could be recuperated by getting equity for the government investment. Dr. Rockey explained that the grantee receives all the rights associated with Bayh-Dole, and in addition, equity arrangements described by Dr. Brody are not possible under the current legislative restrictions on SBIR and STTR

and under NIH's current intellectual property and investment policy regulations. She noted that the SMRB could take up this issue, which would require new authorization language if changes are to be made.

Dr. Shurin said that NHLBI has been actively trying to raise the quality of SBIR and STTR applications by identifying priorities that need to be addressed and publishing an increasing number of Requests for Applications (RFAs) and Requests for Proposals (RFPs) for SBIR and STTR applications that will address those gaps. Increasing the number of RFPs indicates that the work is a high priority and implies a high level of commitment to a project. Dr. Rockey added that participating ICs tend to use the programs primarily for IC-targeted research, but NIH should consider the proper mixture of IC targeting and company-initiated targeting. There should always be an avenue for companies with excellent ideas to apply for funding. Dr. Augustine mentioned the government-funded organization In-Q-Tel, which supports the intelligence community, invests in small startup companies, can take equity positions, and might be an interesting group with which to compare processes. Dr. Fauci noted that the In-Q-Tel model has been adopted in DHHS's Biomedical Advanced Research and Development Authority (BARDA), so making a connection with In-Q-Tel should not be too difficult. The Qualifying Therapeutic Development Program through the Internal Revenue Service was also mentioned as an example that allowed for grants or tax credits for small companies developing therapeutic products.

The group briefly discussed the length of time for the application process. Dr. Rockey conceded that the six-to-nine month timeframe is an issue for small businesses, but thus far that length has been necessary in order to allow the community to respond to requests for applications, study sections to review applications, and then for the appropriate council to assemble and approve applications. One favorable element is that the program has three deadlines each year, allowing companies to time their applications rather than wait for a single annual deadline. Dr. Rockey offered to provide any data the SMRB needs to make recommendations.

Charge to the SMRB
Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

Dr. Collins noted that, in light of the current economic situation and recent changes in the biotech and small business communities, this is an especially appropriate time to ensure that NIH is optimizing the SBIR and STTR programs. He observed that even the 2009 study of the programs may seem a little out of date given the significant changes in the community and in the limited patience venture capital now has for projects that are more than two or three years from commercialization. In addition, small business is an important driver of the overall economy, and NIH should ensure that the SBIR and STTR programs help to nurture that sector. Dr. Collins reported that ICs have differing attitudes about SBIR; some see it as an incredible opportunity and are integrating SBIR in very intentional ways, but others are still not as certain about how it fits their mission. He added that he is certain Dr. Rod Pettigrew at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) would describe the SBIR program as a great asset and good fit for NIBIB because small businesses can help to develop imaging and devices that are priorities. Currently, the SBIR requirement to set-aside 2.5 percent of funding is applied to each IC. Some ICs would like to spend more on the program and others might prefer to spend less. Dr. Collins explained that some ICs engage in unofficial "horse-trading" to match

funds with worthy applications, and the SMRB might want to consider ways to make this process more efficient.

Dr. Collins delivered the following charge to the SMRB on the SBIR and STTR programs:

- NIH requests that the SMRB recommend strategies for how NIH can optimize its utilization of the SBIR and STTR programs in keeping with the NIH mission.
- In addressing this charge, the SMRB should consider how the NIH can support the SBIR/STTR programs in ways that:
    - Foster innovation within small businesses that is in alignment with the priorities of the NIH ICs;
    - Attract quality proposals yielding the greatest potential for successful commercialization; and
    - Leverage resources and expertise to maximize support for ensuring the success of its grantees.

Dr. Collins said that, while the SMRB cannot change the legislation or reauthorization language, it could help NIH by reviewing areas of policy flexibility and advise NIH about how to operate the program most effectively and how to garner more interest from small businesses.

Discussion

Mr. Augustine announced that Dr. Snyder had agreed to chair a new working group assembled in response to Dr. Collins' charge. He asked that SMRB members interested in serving on this new working group contact Dr. Patterson or Mr. Augustine. He also suggested that the committee could be supplemented by relevant subject matter experts as needed.

Dr. Cassell suggested that the new working group should consult the report produced by the National Research Council because Congress paid attention to their recommendations.

Closing Remarks and Adjournment

Mr. Augustine noted that the next SMRB meeting would be held in December and asked whether members would like to discuss any other issues at this meeting or take up other topics for deliberation. He noted that it may be the right time to consider big changes that might not be acceptable in more prosperous times.

Dr. Cassell recommended that the SMRB allocate time during the December meeting for issues related to the scientific workforce, which Dr. Collins mentioned earlier in the meeting. Workforce issues include the size of the workforce, number of grants, grant size, etc., and results from the biomedical workforce survey should be made available, if possible. The under-representation of minorities in science should be part of that discussion.

Dr. Snyder inquired about the SMRB's decision to examine the organization of the NIH Intramural Research Program (IRP), which was originally raised for consideration at the first SMRB meeting. Dr. Collins acknowledged that the group had delayed deliberations regarding the broad topic of the IRP in order to focus on urgent concerns regarding the NIH Clinical Center. He stated that the IRP topic

could be revisited. Dr. Snyder said he had previously chaired a blue ribbon committee to evaluate the IRP at the National Institute of Mental Health (NIMH), and then-NIH Director Elias Zerhouni had expressed interest in setting up a similar committee for the entire NIH IRP. Dr. Collins reported that those evaluations did lead to substantial changes in how the IRP is reviewed; now every investigator is reviewed rigorously on a quadrennial basis, and poorly-performing investigators receive reduced funding and are encouraged to go elsewhere.

Mr. Augustine asked Dr. Brody if he wished to address an idea he had raised earlier with Dr. Collins. Dr. Brody responded that he thought that topic – discussion of NIH's support of extramural institutions and managing science in fiscally challenging times – had been determined to be outside of the SMRB's purview since it does not entail a structural change to NIH. Dr. Collins agreed, noting that determining which of NIH's advisory bodies should deliberate certain topics can be complicated, and the Advisory Committee to the Director and SMRB should not work on overlapping or competing projects. He stated that in this case, the issue is less about structure and more about NIH policy and priority-setting. NIH leaders have been discussing these difficult fiscal issues internally and with outside constituencies, and NIH may issue an RFI to get further input from the biomedical research community. Dr. Fauci recommended fine-tuning and narrowing the scope of the topic to avoid taking on subject matter that is too large and complex. Mr. Augustine suggested that one such topic could be the efficient management of the grants process. Dr. Green noted that the SMRB did not have a lot of topics for its next meeting and requested that topics for consideration on the December agenda be provided prior to the meeting so that SMRB members can gather information. He also suggested that intramural and extramural NIH grantees be polled for other structural changes that may be warranted.

Dr. Collins stated that by the SMRB's next meeting on December 21, 2011, NIH anticipates that the congressional Super Committee will have put forward budget recommendations. Congress must consider the recommendations and vote by December 23, 2011. Thus, the next meeting is on the cusp of whatever budget challenges NIH may be facing, which could influence the discussion of future needs and priorities.

Dr. Collins thanked the SMRB, particularly Dr. Snyder, for taking on the challenge of assessing the SBIR and STTR programs. He thanked Mr. Augustine and all of the SMRB members for their time and efforts. Dr. Augustine thanked Dr. Collins for his leadership, the members for their efforts, and the public for their interest and contributions.

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

_____ _____

Norman Augustine
SMRB Chair

Amy Patterson
SMRB Executive Secretary