NIH SCIENTIFIC MANAGEMENT REVIEW BOARD

December 7, 2010

MEETING - SUMMARY

Board Members Present:

Norman R. Augustine, Chairman
Jeremy Berg, Ph.D.
Josie Briggs, M.D.
William R. Brody, M.D., Ph.D.
Anthony S. Fauci, M.D.
The Honorable Daniel S. Goldin
Eric Green, M.D., Ph.D.
Richard J. Hodes, M.D.
Stephen I. Katz, M.D., Ph.D.
Deborah E. Powell, M.D.
William L. Roper, M.D., M.P.H.
Arthur H. Rubenstein, M.B.B.Ch.
Susan B. Shurin, M.D.
Harold E. Varmus, 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. The minutes from the July 26, 2010, meeting were approved as written. Mr. Augustine stated that the Board would be addressing two important decisions: the Translational Medicine and Therapeutics (TMAT) report and the work of the Intramural Research Program (IRP) Working Group that was discussed at the previous meeting and was tabled.

Dr. Patterson reviewed the NIH Conflict of Interest Policy.

Mr. Augustine announced that the Board's first two reports are now available, the *Report on Substance Use, Abuse, and Addiction Research at NIH* and the *Report on Deliberating Organizational Change and Effectiveness*.

Dr. Collins thanked Mr. Augustine for his leadership and acknowledged the outstanding efforts of the members of the TMAT Working Group. He remarked that, although scientific advances are providing new insights into the molecular causes of disease at a dizzying rate, far too often promising diagnostics, devices, and treatments are not making it to market. He commented that the lack of economic incentives for rare and neglected diseases and uncertainty accompanying many new targets for common diseases have slowed the entry of potential therapeutics into the pipeline. He also stated that projects entering the pipeline encounter high failure rates at nearly every step. Dr. Collins said he thought structural changes are needed to ensure NIH capitalizes on new opportunities for translation, spends resources wisely, deploys new technologies efficiently, works effectively with the private sector and regulatory agencies in a new paradigm, and moves with all due speed to improve human health.

Dr. Collins asked the SMRB to complete its assessment of the potential value of a new entity focused on translation by December 2010 in order to ensure that any new proposal could be considered in the President's budget request to Congress for fiscal year 2012. Dr. Collins reviewed the TMAT charge he had issued to the SMRB and emphasized that it was not part of the SMRB's charge to determine in detail the consequences of this potential new entity on other Institutes and Centers (ICs) at NIH. He acknowledged that, if a proposal to create a new translation medicine and therapeutics entity at NIH was approved, a careful assessment of its consequences would be necessary. Dr. Collins thanked Dr. Barbara Alving of the National Center for Research Resources (NCRR) and Dr. Eric Green of the National Human Genome Research Institute, who have programs in their ICs that have been identified for potential inclusion in a new translational medicine entity. He also acknowledged the leadership of Dr. Jeremy Berg of the National Institute of General Medical Sciences, who will be leaving NIH this summer to become Associate Senior Vice Chancellor for Science Strategy and Planning in the Health Sciences at the University of Pittsburgh.

Presentation of the TMAT Working Group Recommendations and Report
Arthur H. Rubenstein, M.B.B.Ch.
Chair, Translational Medicine and Therapeutics Working Group

Dr. Rubenstein reviewed the charge to the TMAT Working Group and described its process, findings, and recommendations. He noted that despite a doubling of the investment in research and development by pharmaceutical companies over the past decade, there has been no corollary increase in FDA approvals. More recently, biotechnology and pharmaceutical companies have reduced their efforts in research and development because of a lack of available venture capital and shrinking resources. He reemphasized Dr. Collins' point that recent scientific discoveries and technological innovations have opened an unprecedented window of opportunity for accelerating the development of new therapeutics that could be enhanced by reorganizing TMAT programs within NIH.

The Working Group was charged with identifying the optimal attributes of a translational medicine and therapeutics program at NIH, determining whether a new organization could capitalize on the opportunities available, and broadly determining what programs, networks, and centers should be included in the program and how they should be organized. Dr. Rubenstein noted that the Working Group was also asked to consider how the Cures Acceleration Network (CAN) might fit into a translational medicine program. The Working Group considered current NIH infrastructure initiatives that are directly relevant and the methods that could be used to create synergy and avoid competition with both intramural and private sector programs. Inherent in the charge was the need to develop metrics and methodologies to evaluate change. Dr. Rubenstein emphasized that the TMAT Working Group remained committed to undertaking a transparent and deliberate process, and stressed that the SMRB's charge did not entail conducting an in depth analysis of all the consequences of creating a new translational medicine entity. He stated that the Board believed a subsequent analysis would be undertaken by those most knowledgeable of the specific details if NIH accepts a proposal to create a new TMAT center. He also reviewed the timeline of Working Group and full Board meetings held to deliberate TMAT research at NIH, including the stakeholder consultation held during the September Board meeting and a teleconference with the NCRR Advisory Council.

In accordance with the SMRB's framework for deliberating organizational change and effectiveness, Dr. Rubenstein reviewed the process for organizational change: assess the need for change, evaluate the options, and implement and evaluate the recommended changes. To assess the need for change, the Working Group asked whether TMAT research at NIH is capitalizing on existing scientific opportunities or whether reorganization could more effectively advance this research. The Working Group concluded that reorganization of several extant NIH TMAT-related programs would help the Agency to capitalize best upon emerging scientific opportunities.

In an effort to better optimize TMAT research, the Working Group considered new opportunities, new organizations, and new partnerships that could be pursued. Reorganizing TMAT activities would allow NIH to capitalize on emerging scientific opportunities and to expand and augment its efforts in developing new therapeutics. The aim of such a reorganization would be to leverage existing opportunities, support promising new areas of research, and enhance the synergy between public and private partnerships. The Working Group emphasized that a new effort should not duplicate the efforts of programs that are already effective. The Working Group identified the functional capabilities and activities of a TMAT research program at NIH. These included supporting and strengthening TMAT research; providing a central locus for related information on and access to resources, tools, and expertise; acting as a catalyst and convener for collaborative TMAT interactions and partnerships; expanding the precompetitive space; supporting training for translational research investigators; and enhancing communication amongst all TMAT stakeholders.

Dr. Rubenstein stated that the Working Group, after reaching a consensus that organizational change is warranted, evaluated the options for change by determining what kind of structure would best optimize TMAT research at NIH and which programs at NIH could accelerate this effort. The Working Group unanimously favored Option 2(c), which would involve creating a new center that would not directly include the Clinical Center, but would instead, support close functional ties between the two entities. The center would house the Molecular Libraries Program (MLP), the Therapeutics for Rare and Neglected Diseases (TRND) program, the Rapid Access to Intervention Development (RAID) program, the NIH and FDA partnerships, and the Clinical and Translational Science Awards (CTSAs). The new center should develop and provide research infrastructure for advancing translational medicine and therapeutics development; foster new and innovative strategies for TMAT research by advancing a process engineering approach to developing therapeutics, including strengthening and streamlining the process itself; and serve as a catalyst, resource, and convener for collaborative TMAT interactions and partnerships. It should also capitalize on the relative strengths of the extra- and intramural communities, private sector, government, and academia, to promote quick-win, fast-fail paradigms and further develop the precompetitive space. The activities of the new center should not duplicate, consume, or undermine the activities of other programs already underway at NIH.

Dr. Rubenstein reviewed the rationale for including some, but not all, of NIH's translational resources in a new translation-focused center. Of particular interest were TMAT-related activities, expertise, and resources that could be applied to a broad range of diseases and conditions, similar to those of the RAID and TRND programs, as well as the CTSAs. He stated that the aim was to identify programs critical in forming the framework of this new organization and empower it to be successful. He said that the CTSAs would be a great asset to the new center, because they share many of the same goals, such as accelerating the process of finding cures, training researchers, and serving as a resource for translational research.

Regarding implementing and evaluating the proposed change, it was noted that successful implementation will require strong leadership, clearly delineated tasks, and cooperation from affected parties. The new center should also be evaluated periodically to determine whether it is successful in achieving its intended goals. Dr. Rubenstein stated that the Working Group discussed the need to collect outcome measures for evaluation; in terms of long-term success, it would be important to see that the center contributed to the development of new products and treatments (as well as prevention, community outreach, and comparative effectiveness research) and that it broadly enhanced translational research. In addition to long-term goals such as drug development, short-term evaluations could include increased breadth and depth of TMAT research and increased interdisciplinary and cross-sector collaborations. Dr. Rubenstein noted that NCRR programs could play a significant role in this new center and stated that NIH should conduct a more detailed inventory to determine whether some of the other NCRR programs were germane to the scope of the new center. He added that NIH may consider adding new resources and services to help speed the translation of basic science discoveries into FDA approvals. In conclusion, he noted that the center should be created as soon as possible because of budget

issues and the need to find a home for CAN, although there should be no delay in creating this new center even if funds for CAN are not appropriated.

The Working Group recommendation reads as follows: "NIH should establish a new Center devoted to advancing translational medicine and accelerating therapeutics development. The new Center should incorporate MLP, TRND, RAID, CTSAs, CAN, NIH-FDA Partnerships, and other existing components or new resources to be developed (as appropriate)."

Role of the CTSAs in the Proposed New Center
Barbara M. Alving, M.D.
Director, National Center for Research Resources

Dr. Alving stated that NCRR's mission is to accelerate translational research by creating and providing access to essential resources needed by NIH-supported investigators. Although they may appear to be disparate, NCRR programs are in fact complementary, synergistic, and span the entire range of translational research. NCRR is composed of multiple resource centers that are essential for supporting the research conducted by NIH-supported investigators. The articulated objectives of the proposed new center comprise only a subset of the NCRR mission, which covers the full range of translational research.

NCRR is viewed by its academic health centers as providing transformative technologies, unique animal models, animal resources, training of veterinarians, access to deep multidisciplinary expertise, opportunities for minority-serving institutions, and direct hands-on training. Dr. Alving discussed the development and status of the CTSA Consortium. The CTSAs promote proficient translation from laboratory to community, enhance clinical research, and improve the efficiencies of IRBs and accrual to clinical trials. Dr. Alving highlighted the Institutional Development Award (IdeA) program and its interactions with the CTSAs. She also gave an overview of the budgets for MLP, RAID, TRND, and the CTSAs.

Dr. Alving recommended that the SMRB develop a financial and impact report, as directed by its founding legislation. She also recommended engaging in dialogue with stakeholders, including the other NIH ICs. She added that NIH should consider incorporating MLP, RAID, and TRND into NCRR after a careful review of the budgetary implications and with input from an expert advisory panel that includes industry representatives. She finished by noting NIH will need to recruit a director for the new center that will continue to address the full spectrum of translational medicine.

Discussion

Dr. Rubenstein stressed that the TMAT Working Group recommendations, with the exception of the CTSA program, do not address concerns regarding NCRR programs. Additional analyses regarding NCRR should be undertaken.

Dr. Katz emphasized that the TMAT Working Group did discuss the budget and budget implications of reorganization, although he acknowledged that these discussions were not extensive. He also pointed out that the current understanding of which programs will remain in the Common Fund and which will be incorporated into an IC may evolve.

Dr. Collins underscored how much NIH values the people and programs of NCRR, and that the potential to empower and strengthen connections is one of the appealing aspects of what is being proposed. Regarding budget considerations, he said future budget increases are unlikely and NIH will have to consider how to leverage its funds. He offered a clarification about the TRND program, noting that it is a congressionally approved program at its current budget level. Dr. Collins emphasized that it will continue to be an important

program because of Congress's enthusiasm for translational work focused on rare and neglected diseases.

Public Comment

David Anderson spoke on behalf of the National Primate Research Center (NPRC) program. The NPRC consortium supports the world's preeminent array of nonhuman primate resources and supports research at most of the NIH ICs, as well as the Centers for Disease Control and Prevention, the Department of Defense, and the National Science Foundation. These nonhuman primate resources are essential to the therapeutic discovery process, and the NPRCs are a critical resource for NIH translational research. The NPRCs believe that their resources, which comprise the finest nonhuman primate medical research structure in the world, will have the most impact by being collocated with the other components of the NIH TMAT program. Collocation with the TMAT program will facilitate effective collaborations among programs that are focused on therapeutics development.

Dr. William Talman, of the University of Iowa, provided comment as the President of the Federation of American Societies for Experimental Biology (FASEB). Dr. Talman stated that FASEB supports efforts to improve translation research in the U.S. and understands that the speed with which the TMAT proposal is moving is a deliberate effort to make bold strides in this enterprise. However, he stated that it is not clear whether a new IC would actually facilitate translation and the creation of a new bureaucratic structure could actually delay the process. Because the extramural scientific community has not weighed in on the SMRB's deliberations, it is not clear what the impact of this new IC will be and how it will affect fundamental scientific support of translation in other ICs. The research community would appreciate more information on how the role of a TMAT IC will be balanced with translational research already supported by other ICs. Additionally, FASEB is concerned about the impact of this proposal on NCRR resources. FASEB recommended that the SMRB delay the transmission of its recommendations until it has had the opportunity to consider other elements affected by this proposal that were not deliberated during the initial discussions.

Dr. Mark Lively, professor of biochemistry at Wake Forest University and a member of the NCRR National Advisory Council, spoke on behalf of the Council. The Council urged the Board to proceed with caution in its recommendations and requested that additional consideration be given to the large volume of information the Board received recently. The Council feels that the input from stakeholders represented at the SMRB meeting has not been adequately considered by the TMAT Working Group and noted that consideration of this information was not part of the Working Group's charge. He said that the members of the Council hope that the decisions made at the meeting will not result in the extinction of valuable NCRR programs.

Marguerite Pappaioanou, Executive Director of the Association of American Veterinary Medical Colleges (AAVMC), commented that AAVMC recognizes the importance of the SMRB's TMAT proposal and commends the NIH on its support of interdisciplinary research. AAVMC appreciates the SMRB's position that extant programs related to the TMAT initiative should not be disrupted. The Association believes it is critical that the full value of all NCRR's programs be recognized and supported, because they serve as a foundation for the entire NIH research enterprise and create a pipeline for comparative medicine, veterinary medical science, and critical research support. NCRR's extramural programs enable discovery across the entire continuum of biomedical research, and the programs and resources supported by NCRR's Divisions of Comparative Medicine, Research Infrastructure, and Biomedical Technology are vital to the TMAT enterprise. Veterinary medical scientists have the expertise needed to understand and interpret interspecies comparisons and experimental findings in animal models that are essential elements of translational research. AAVMC wishes to help the SMRB develop a complete understanding of the role, functions, and need to maintain and enhance critical NCRR programs as NIH evaluates the optimal location and reorganization of the programs.

AAVMC member institutions recommend that the SMRB and NIH fully support all the programs currently

supported by NCRR. AAVMC also asks that the SMRB and NIH develop a stakeholders group to advise NIH leadership on the reorganization of NCRR's programs, which should include representatives of the veterinary medicine field.

Dr. James Fox, of MIT, commented on the NCRR comparative medicine program and its longstanding involvement in training veterinarians for biomedical research careers. Representing the directors of 45 veterinary institutional training grants supported by NCRR, Dr. Fox emphasized the value of the grants currently administered by the Division of Comparative Medicine, which are critical to the success of biomedical research and translational medicine. These grants support the biomedical research infrastructure by providing veterinarians with high-quality mentored training in comparative medical research. Regardless of the organizational fate of NCRR, its training pipeline is a critical element of the national research infrastructure and should not be lost or diverted. The comparative medicine/veterinary sciences training programs should be supported by a non-categorical mechanism, as the skills provided by these training programs exceed the purview of any categorical NIH Institute. The Division of Comparative Medicine and NCRR have contributed to translational medicine in the past and can continue to do so in the context of the new center. Dr. Fox recommended that individuals with appropriate comparative medical expertise should be involved in the development of the reorganization plans for NCRR programs. Additionally, the Division of Comparative Medicine and the programs it oversees should be maintained or be fully incorporated as a unit in future NIH configurations.

Dr. Mark Lutschavnig, Director of Governmental Relations for the American Veterinary Medical Association (AVMA), said that it was unclear to the AVMA what will happen to the programs in NCRR that are not recommended for inclusion in a TMAT program at NIH. AVMA urged the Board to recognize the ongoing need for the development of researchers with comparative medicine training as previously recommended by the National Research Council. AVMA recommended that the Board maintain the integrity of each NCRR division and program regardless of the final organizational structure recommended by the TMAT Working Group to ensure that current programs retain synergistic strength. AVMA also recommended that the Division of Comparative Medicine be placed as an intact unit in the proposed TMAT entity if it is approved, or within an existing but broad-based NIH IC.

Dr. David Moore, Senior Director for Government Relations at the Association of American Medical Colleges (AAMC), requested that the Board and NIH take into consideration two issues as they deliberate the TMAT recommendations. The first concern regards the focus and objectives of the CTSA program. AAMC believes the NIH's commitment to advancing the CTSAs' key objectives and emerging accomplishments should be incorporated into the new center. AAMC believes the promotion of community outreach and community based participatory research will be among the consortia's early successes if they are allowed to continue. Drug development should not be the only focus of the new center. The Board and NIH should affirm its commitment to the full spectrum of translational research, which the center should foster in the CTSAs and the entire medical research enterprise.

AAMC's second concern is that the TMAT recommendations would profoundly affect the other programs within NCRR. NCRR's expertise in assessing and supporting the research needs of the extramural research community must be preserved in any reorganization. AAMC believes that the impact of the TMAT recommendations on these valued resources should be considered. AAMC recommends that any discussion of adopting the TMAT proposal also include consideration of the best way to sustain NCRR's programs and ensure their continued focus, integrity, and effectiveness.

James Hoehn from the EPSCoR/IDeA Foundation, a nonprofit group that supports science activities in the 27 states that are eligible for IDeA-like programs across the federal government, commented that NCRR is home to other programs that serve the biomedical community, plays an important role in providing research resources

and infrastructure that serve the broader scientific community regardless of research area, and is a well-run organization. The institutions and researchers who participate in the IDeA program are well served by NCRR. There are concerns that the IDeA program may be affected negatively by the proposed changes; the Foundation's priority is keeping the IDeA program intact and it requests that this be considered.

Dr. John Markley, Principal Investigator (PI) of a Biomedical Technology Research Center (BTRC) at the University of Wisconsin in Madison, called the Board's attention to a statement submitted by a group of five PIs of NCRR biomedical research centers. Of the 48 BTRCs, 44 of the PIs have signed the statement. The BTRC program has been successfully and professionally managed for over four decades and is highly regarded and well-established as an incubator for the invention, optimization, and tailoring of new technologies. The BTRCs support more than 7,000 investigators who receive research support through peer-reviewed grant awards from 22 NIH ICs. He also mentioned the impact of the NCRR Shared Instrumentation Grant and High-End Instrumentation Programs, which are NIH's mechanisms for getting important instrumentation into the hands of researchers. If the Board recommends the formation of a new TMAT center, it also should recommend that a process be established to ensure that sufficient time and attention are given to determining the impact of reorganization on the important and unique elements of the NCRR portfolio. This might provide an opportunity to strengthen and expand these successful programs at a time when innovation is crucial to the national agenda.

Mr. James Jorkasky, Executive Director of the National Alliance for Eye and Vision Research (NAEVR), the privately funded friends of the National Eye Institute (NEI), said that NAEVR is a research advocacy organization that speaks about the accomplishments of NEI. Mr. Jorkasky had told the SMRB about NEI's translational collaborations at the Board's September meeting. Although NEI is a relatively small Institute, it has had numerous translational collaborations that have expanded its research dollars, and NEI's translational research has resulted in many products that reflect the promise of translational research. As the TMAT Working Group proceeds in its deliberations and recommendations and as NIH further studies the implications of a translational research center for the ICs, all involved should adhere to one of the main characteristics described by the TMAT Working Group for such a new center—that it promotes and allows flexibility in decisionmaking and priority setting. Although a centralized decisionmaking entity could provide additional opportunities and economies of scale, especially for mid- to small-size Institutes, it should not stifle the creativity of the Institutes pursuing innovative translational approaches.

Dr. Kathleen Conlee, Director of Program Management, Animal Research Issues, The Humane Society of the United States (HSUS), said that the relevance of the TMAT recommendations to NCRR and its programs presents a good opportunity to draw attention to a costly and ineffective NCRR program—the warehousing and use of chimpanzees in invasive research. One TMAT goal is to promote quick win/fast fail paradigms, but the chimpanzee model is the very antithesis of this. Chimpanzee research is expensive, of dubious effectiveness, and regressive. HSUS respectfully requests that the SMRB recommend that (1) NCRR's policy against the breeding of federally owned and supported chimpanzees be implemented NIH-wide immediately and be properly enforced; (2) chimpanzee research and warehousing in laboratories be phased out and all government-owned chimpanzees be retired to the National Chimpanzee Sanctuary System, starting with the 200 currently at the Alamogordo Primate Facility; and (3) oversight of the National Chimpanzee Sanctuary System and associated funding should be shifted from NCRR to the Office of Laboratory Animal Welfare. The adoption of these recommendations would not only free valuable resources for the development of effective therapies but would save chimpanzees from suffering and give them a life that they deserve after decades spent in laboratories.

Partnership Between the NIH Clinical Center and the Proposed New Center
John I. Gallin, M.D.
Director, NIH Clinical Center

Dr. John Gallin was asked to comment on the proposed partnership between the NIH Clinical Center (CC) and

the new center recommended by the TMAT Working Group. Implementing the SMRB's recommendations would link the CC and the proposed TMAT center, which would facilitate translational studies by NIH extramural and other outside investigators while enriching the NIH intramural program. The pending SMRB recommendations regarding the CC's vision, budget, and governance would provide a sustainable solution to longstanding budget and governance challenges, and the recommendations underscore the importance of clinical research as a distinct component of the NIH enterprise. Sound and stable governance and funding are essential to realizing the expanded vision of the CC.

Dr. Gallin noted that his vision for the CC has always been to provide a national model for clinical research with emphasis on two core strengths—first in human clinical studies and the investigation of rare diseases. Cultivating interactions with external investigators in the new center would entail developing new research partnerships, making special resources available, and expanding clinical research training programs. To support these interactions, the CC will work with each of the components of the proposed center. While exciting, working with the new center will require deliberate and careful planning both upfront and in an ongoing manner to create the appropriate synergy for resource use between the Centers. As part of its organizational planning process, the CC plans to include a new strategic goal of supporting the national translational research agenda through collaborative partnerships and new research programs to enrich clinical science. To meet this goal, the CC will develop a comprehensive plan for allowing external investigators to use CC facilities and will create a compendium of specialized resources available for use by external investigators and post it on the CC website. The process will include stakeholder input from the new center.

Dr. Gallin observed that it is critical to have a clear understanding of the capacity of the CC in order to ensure that expectations for access to the Center are realistic and equitable. Additionally, NIH must assess the resources needed to accomplish this change. In doing so, the first objective is to preserve the strong programs of the CC. Policies and procedures for external investigator access must also be developed that will include an application and review process for proposals to use CC resources, a financial model for costing and reimbursement, and plans for ongoing communication with the NIH extramural grant community. Dr. Gallin will work with the NIH Deputy Director for Extramural Research, Dr. Sally Rockey, on the planning process pending the outcome of the meeting.

Dr. Gallin concluded that the CC is committed to enriching a collaborative environment to ensure a strong continuum of clinical research. The necessary changes can be accomplished through partnerships among the ICs, the CC, the proposed center, and the outside community. Collectively, a more robust environment can be created to address the opportunities and changes catalyzed by the SMRB's important work.

Motion on Behalf of the TMAT Working Group and Discussion

Dr. Rubenstein stated that while there is enthusiasm for establishing this new center, legitimate concerns have been expressed about its potential impact on other important NIH programs. In drafting the motion on behalf of the TMAT Working Group, he was mindful of the concerns raised by stakeholders and SMRB members.

The TMAT Working Group motion was presented as follows: NIH should create a new translational medicine and therapeutic center as recommended in the TMAT Working Group report; the SMRB endorses and supports NIH’s commitment to undertake a more extensive and detailed analysis through a transparent process to evaluate the impact of the new center on other relevant extant programs at NIH, including NCRR; and NIH should report back about these findings to the SMRB at its next meeting in February or March.

Mr. Augustine emphasized the two-part nature of the TMAT motion.

Dr. Collins reaffirmed Dr. Rubenstein’s assessment that there was broad support for the proposed center and the

opportunities it presented, as well as concerns related to the fate of programs affected. In anticipating a possible SMRB vote in favor of the TMAT Working Group recommendations, NIH has already given some thought as to how stakeholder input could be collected. Dr. Collins has asked Dr. Lawrence Tabak, NIH Principal Deputy Director, and Dr. Alan Guttmacher, National Institute of Child Health and Human Development Director, to form a group that would, with considerable expert input from NCRR, survey programs currently in NCRR and conduct a detailed assessment to determine which programs might be scientifically appropriate to transfer to the new center. This is analogous to what NIH is already doing with the SMRB recommendation on Substance Use, Abuse, and Addiction, where the SMRB made a specific organizational recommendation but also charged NIH with doing a more detailed analysis of which programs would fit into the new institute and which might be relocated to other ICs. Assuming the SMRB votes in favor of the TMAT recommendations, the stakeholder input process is expected to be initiated immediately through conference calls to gather advice from NCRR staff, NCRR grantees, and CTSA PIs. The group co-chaired by Drs. Tabak and Guttmacher would consult with content experts to consider possible ways to manage programs connected with this decision, seek broad public input, and then bring a more refined proposal to the SMRB in about three months. Dr. Collins emphasized that the goal would not entail dismantling programs already in place at NCRR or elsewhere, but to ensure that NIH's structure and function are optimized. Dr. Collins agreed that it was a good idea for NIH to report back to the SMRB at its next meeting and that this process would serve as a continuation of the TMAT charge.

Dr. Berg asked whether the TMAT Working Group considered an organizational model in which the TMAT-related resources would be placed in an existing IC, such as NCRR, with additional restructuring, including perhaps recruitment of new leadership. Dr. Rubenstein stated that the Working Group's discussions were primarily focused on the new opportunities arising from this effort. The members did consider placing TMAT-related resources in an extant IC but ultimately did not support this model, as a bold, new effort would likely not be achieved with this approach. The CC was considered as a hub for TMAT programs, but for a number of reasons, it seemed clear to the Working Group that forming a new organization would be the best approach. Dr. Katz agreed with Dr. Rubenstein's assessment, adding that, from the outset, the new entity was meant to be distinct and have a very clear focus on translational medicine and therapeutics.

Mr. Goldin thanked everyone for the public comments that were submitted. He stated that he thought the process was conducted well and that the guidance of Drs. Rubenstein and Collins will allow for a very positive outcome. Dr. Rubenstein stated that the TMAT discussions were challenging because of the constrained timeline the SMRB was following. Despite these challenges, the input into the process was remarkable. The public comments were relevant to the TMAT deliberations and were very helpful. Dr. Rubenstein added that he was proud of the deliberative process.

SMRB Vote on the TMAT Working Group Recommendations and Report

Mr. Augustine made the following motion:

> A new translational medicine and therapeutics center be created as recommended in the TMAT Working Group report; the Board endorse and support NIH's commitment to undertake a more extensive and detailed analysis through a transparent process to evaluate the impact of the new center or other relevant extant programs at NIH, including NCRR; and request that NIH report these findings to the SMRB at its next meeting in approximately three months.

Dr. Brody seconded the motion. Dr. Fauci clarified that a study of the impact of the SMRB's recommendations on other extant programs, particularly NCRR, should be conducted by NIH, and then NIH will report to the SMRB. Mr. Augustine concurred with Dr. Fauci and noted that the SMRB recognized that the TMAT Working Group did not have the time or expertise to evaluate individual programs outside an understanding of the broad impact of the recommendations. A vote was taken, with show of hands in favor and show of hands opposed. The

motion passed 13-1.

Mr. Augustine said that the next step would be to update the report of the TMAT Working Group to reflect the discussions that have taken place at the meeting and the final vote on the recommendations. The updated report will be sent to each member of the SMRB by the following morning. Mr. Augustine suggested that Dr. Collins would benefit from having the final TMAT report from the SMRB in time for the NIH Advisory Committee to the Director meeting in two days so that he could discuss the outcome of this meeting at its proceedings.

Dr. Collins thanked the TMAT Working Group and the SMRB for the thoughtful way they conducted the process. He felt the outcome reflected the SMRB's effort to solicit input from many important perspectives. He especially thanked Dr. Rubenstein for all of his time and effort. Dr. Collins said that to make a decision, he would first consult with Secretary Sebelius and provide appropriate notification to Congress. Over the last several months, Secretary Sebelius had been apprised of the TMAT discussions and has been generally positive about NIH's goal to support translational research. In addition, having received this recommendation, NIH will begin an immediate effort to ascertain stakeholders' views, particularly regarding the effect of reorganization on NCRR. To gather input, separate teleconferences will be held tomorrow with NCRR staff, NCRR stakeholders (particularly grantees), and CTSA PIs. Drs. Tabak and Guttmacher also will begin their detailed assessment for the possible realignment of NCRR programs and grant portfolios.

Dr. Collins also announced the launch of the interactive "NIH Feedback" website at feedback.NIH.gov that will allow NIH to provide information in real-time about several SMRB recommendations. The website will be used as a venue for expressing concerns, answering questions, and providing updates. He commented that most of NIH's current 27 ICs have arisen from political considerations regarding the need to emphasize research in a particular area and that rarely have new ICs been created based on scientific rationale. Dr. Collins said that the SMRB has taken a bold step recommending the creation of a new entity founded on scientific opportunities, and he is profoundly grateful to all involved.

Afternoon Session

Mr. Augustine stated that the SMRB would discuss the Intramural Research Program (IRP) Working Group's report and recommendations during the afternoon session. The recommendations had been tabled during the Board's September meeting to take into consideration the findings of the TMAT Working Group.

Working Lunch:
Brief Recap of the IRP Working Group's Recommendations on the Fiscal Sustainability and Utilization of the NIH Clinical Center
Arthur H. Rubenstein, M.B.B.Ch.
Chair, Intramural Research Program Working Group

Dr. Rubenstein explained that the IRP Working Group's charge was to recommend whether any change in the organization or management of NIH intramural research could further optimize the opportunities available in a central research program at NIH and maximize human health and patient well-being. The group first considered issues relevant to the CC and completed its deliberative process in September. However, a vote on the CC report had been tabled in response to the TMAT charge, and the final recommendation of the TMAT Working Group was that the CC not be incorporated into a new TMAT center. Because of this recommendation, no changes were made to the original CC report.

Dr. Rubenstein stated that the Working Group considered three important issues relevant to the CC: vision and role, governance, and budget. Regarding its vision and role, the Working Group noted specific challenges pertaining to the perceived lack of prioritization and commitment to funding the CC. The Working Group also

was concerned by barriers to partnerships and the need to leverage and expand the considerable resources of the CC—particularly to investigators in the external community. The Working Group also considered issues regarding the recruitment, membership, and retention of investigators who could use the CC, which could help maximize the use of CC resources.

In terms of governance, the Working Group noted that there is a lack of a trans-NIH vision for setting priorities in clinical research, which is complicated by the enormous complexity of both the administrative approval processes and oversight of CC operations. With input from the CC leadership, the Working Group considered whether a more streamlined, simplified, and efficient oversight approach could be developed.

Regarding the budget of the CC, the Working Group acknowledged that the cost of running the CC is increasing and its current funding model (school tax) has been unable to keep pace with inflation. Cost shifting to support the CC has had unintended and undesirable consequences, some of which have resulted in reduced use of the CC by some IC's intramural programs. It was also noted that the current funding mechanism does not support use of the CC by external investigators.

Regarding the CC, the Working Group articulated three recommendations: position the CC as a national resource, streamline its governing structure, and alter its current funding strategy. The Working Group envisioned clinical research at NIH prioritized in a seamless, efficient, and cost effective manner; supported by a fiscal model that is sustainable, responsible, and responsive; and governed by policies that do not negatively impact clinical researchers and discourage CC use. The overall outcome of any changes should be enhanced programmatic planning. The IRP Working Group stated that by implementing some of their recommendations, the CC would enhance the TMAT program and that the two issues were complementary. Dr. Katz said that the goal is to ensure that the CC serves as a state-of-the-art national resource with resources optimally managed to enable both internal and external investigator use. One issue that needs further investigating is a funding mechanism for supporting extramural research within the CC. While a mechanism has been developed for investigators prospectively planning to use the CC at the inception of an extramural grant, this mechanism does not include utilization of the CC on an ad hoc basis after an extramural grant has been awarded.

The Working Group recommended that the governing board have a simplified structure capable of developing and overseeing a clear and coherent plan for clinical research and recommended that Dr. Collins propose the formation of a CC governing board composed of IC directors and others so that the Director receives a “budget reality test.” That is, if a recommendation is made that a 12 percent increase in CC funding is needed to keep up with inflation, but there is only a 1 percent increase in total NIH funding, the governing board can take into consideration the entire funding climate before making recommendations to the NIH Director.

The Working Group also recommended a stable, responsive budget underpinned by priority setting. The CC budget should be linked to a strong planning process, remain stable and equitable in distribution, be effective in attracting and supporting a high quality work force, and ensure efficient use. There was unanimous agreement that the budget should be a line item in the Office of the Director’s (OD) budget. In this model, there would be a onetime, budget-neutral shift of the CC funds from the intramural research program to the line item in the OD budget. For the yearly CC budget, the Advisory Board for Clinical Research would make an initial recommendation for any percentage increases that would then be evaluated by the CC governing board. The difference between the final recommendation and the overall percentage increase in the NIH budget would come out of the total NIH budget.

Discussion

Dr. Collins thanked Drs. Rubenstein and Katz for their contributions and commented that it was wise to delay the vote on the CC recommendations until the TMAT Working Group completed its work. He stated his comfort

with the proposed model and expressed his support for having a CC governing board of IC directors to assist in the process of making wise decisions about the annual CC budget. He reminded the group that managing resources derived predominantly from taxpayer support will remain a challenge, but that a line item in the OD's budget for supporting this resource is reasonable. He stated that he would ensure that its management reflects the input from all of the stakeholders.

Dr. Collins expressed enthusiasm about expanding CC resources to extramural investigators. It is unclear at this time how to best support this arrangement, that is, how the CC will be utilized, what kind of cost-sharing might be needed, and how protocols will be staffed. He said that many of these issues will receive further investigation if the Board recommends this option.

SMRB Vote on the IRP Working Group Recommendations and Report

Dr. Rubenstein motioned that the following recommendations be accepted: (1) the role of the NIH CC should be to serve as a state-of-the-art national resource with resources optimally managed to enable both internal and external investigator use; (2) the NIH CC governance should have a simplified structure capable of developing and overseeing a clear coherent budgetary and programmatic plan for clinical research; and (3) the NIH CC budget should be linked to a strong planning process, remain stable and equitable, and be effective in attracting and supporting a high-quality workforce and assuring efficient use. The recommended funding option is a line item in the OD budget. This motion was seconded and approved unanimously.

Mr. Augustine thanked Dr. Rubenstein and his Working Group for its efforts. Dr. Rubenstein said he appreciated the work of his colleagues and values the unique composition of the SMRB, with both internal and external scientists and administrators. He also thanked the staff, particularly Dr. Patterson, for their support.

Addressing the future of the SMRB, Mr. Augustine proposed resurrecting the Deliberating Organizational Change and Effectiveness (DOCE) Working Group that Dr. William Brody chaired previously. He noted that a change in leadership of this group may be considered. The charge to this group would include reexamining its original report in the context of what has been learned from the real-world examples the Board has studied to date. This group also would report back to the SMRB at its next meeting with a process for determining what types of issues should be addressed by the SMRB. Any SMRB efforts, however, hinge upon what Dr. Collins and his colleagues believe is most appropriate for the Board to pursue, as well as any ideas the SMRB generates on its own. He stated that the SMRB could decide at its next meeting how it would like to focus its future efforts.

Dr. Brody expressed concern that even the most optimistic forecast for NIH's budget is not bright and wondered to what extent the SMRB, with the support of Dr. Collins, might deliberate issues that involve how to increase the efficiency of the NIH budget. It would be a very difficult undertaking and, despite the fact that increasing budgetary efficiency is very challenging to do in a complex government organization, it is something that requires scrutiny, if not specific recommendations. Dr. Rubenstein concurred with Dr. Brody' assessment and said that the biggest challenge looming is how to sustain current levels of activity in the face of less money. The SMRB could consider how NIH could reorganize, redirect, and become more efficient in some specific areas, similar to the CC. Research institutions won't be able to maintain current activity levels structured as they are now. Dr. Varmus noted that because most NIH funds are spent at extramural institutions, how NIH and the institutions receiving NIH funding do business and what efficiencies both need should be considered. Dr. Rubenstein said the NIH is extraordinarily efficient, but extramural institutions count on more money from NIH in their budgets than they should. He also noted that the stimulus money provided a false sense of security. Dr. Varmus commented that many of Dr. Rubenstein's colleagues and administrators around the country met recently to talk about the need for increased indirect costs. Dr. Rubenstein said that everyone, but particularly participants in the extramural program, needs to come to terms with the fact that funds will not increase each

year and that this needs to be emphasized to researchers and programs.

Dr. Brody remarked that there were some disturbing trends in the way NIH has been allocating its resources externally, which are matched by some similarly disturbing funding trends at external institutions. The SMRB is here to help NIH and its Director, but it cannot become too granular in its efforts, because that would be inappropriate. If there are areas related to resource allocation the SMRB can help with, it is an important topic to cover. A change is taking place, but most external institutions have not recognized this, especially the faculty. Mr. Goldin noted that because of possible budget cuts, it is important not to create too broad of a charter for the SMRB or any other advisory group. He also said that it would be helpful to the SMRB if Dr. Collins and the IC directors identified specific areas at NIH that need to be addressed. He emphasized that the SMRB has been effective because it has been given focused tasks and that it would be helpful to break down the NIH budget problem into manageable pieces.

Dr. Collins stated that the challenge will be to determine what kinds of projects are best suited for the Board's deliberation, given the SMRB's role and its statutory mandate. He also noted that the NIH has many other advisory committees and must be thoughtful in the assignment of tasks. He noted that the SMRB has been incredibly effective in accomplishing its tasks so far, and it would be useful to spend the next few months thinking about what other efforts would be particularly appropriate for the SMRB to consider. One such task may be to return to the original charge of the IRP Working Group, which was to consider the optimal organization of the NIH Intramural Research Program.

Closing Remarks and Adjournment

Mr. Augustine emphasized the importance of the commitment to reactivate the DOCE Work Group and said that he and Dr. Collins would work closely with that group. An update should be available at the next meeting.

Dr. Collins emphasized his appreciation for the SMRB's hard work and its flexible manner in approaching challenging problems. He concurred with Mr. Goldin's assessment that the SMRB was successful because it was given circumscribed tasks that it could delve into in order to produce thoughtful advice. He thanked Mr. Augustine for chairing the Board.

Mr. Augustine said he was impressed with how the internal and external members of the Board worked together on the subcommittees. On behalf of the Board, he thanked the NIH employees who support the SMRB for their diligence 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.

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Norman Augustine
SMRB Chair

Amy Patterson
SMRB Executive Secretary