

**Department of Health and Human Services  
National Institutes of Health**

**National Center for Advancing Translational Sciences Advisory Council  
and  
Cures Acceleration Network Review Board**

**Minutes of Joint Meeting**

**September 16, 2013**

The National Center for Advancing Translational Sciences (NCATS) Advisory Council and the Cures Acceleration Network (CAN) Review Board held a joint meeting in open session, convening at 8:30 a.m. ET on September 16, 2013, in Conference Room 6, Building 31, on the National Institutes of Health (NIH) main campus. Christopher P. Austin, M.D., NCATS Advisory Council chair, and Freda C. Lewis-Hall, M.D., CAN Review Board chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

Following the joint meeting, the NCATS Advisory Council met in closed session for review and consideration of grant applications.

**NCATS ADVISORY COUNCIL MEMBERS PRESENT**

***Chair***

Christopher P. Austin, M.D., Director, NCATS

***Executive Secretary***

Danilo A. Tagle, M.S., Ph.D., Acting Director, NCATS Office of Grants Management and Scientific Review

***Council Members***

Margaret A. Anderson, M.A.

Freda C. Lewis-Hall, M.D.

Jorge L. Contreras, J.D.

Bernard H. Munos, M.B.A.

Pamela B. Davis, M.D., Ph.D.

Todd B. Sherer, Ph.D.

Louis J. DeGennaro, Ph.D.

Scott J. Weir, Pharm.D., Ph.D.

Geoffrey S. Ginsburg, M.D., Ph.D.

Paul G. Yock, M.D. (by telephone)

Eric D. Kodish, M.D.

***Representative Members***

Ankit A. Mahadevia, M.D., M.B.A., Atlas Venture (by telephone)

Robert I. Tepper, M.D.

## **CAN REVIEW BOARD MEMBERS PRESENT**

### ***Chair***

Freda C. Lewis-Hall, M.D., Executive Vice President and Chief Medical Officer,  
Pfizer

### ***Vice Chair***

Geoffrey S. Ginsburg, M.D., Ph.D., Director of Genomic Medicine, Duke University  
Health System

### ***Executive Secretary***

Danilo A. Tagle, M.S., Ph.D., Acting Director, NCATS Office of Grants Management  
and Scientific Review

### ***Board Members***

Margaret A. Anderson, M.A.

Robert J. Beall, Ph.D.

Jorge L. Contreras, J.D.

Louis J. DeGennaro, Ph.D.

Frank L. Douglas, Ph.D., M.D.

Eric D. Kodish, M.D.

Bernard H. Munos, M.B.A.

Todd B. Sherer, Ph.D.

Lawrence A. Soler, J.D.

Myrl Weinberg, M.A.

Scott J. Weir, Pharm.D., Ph.D.

Paul G. Yock, M.D. (by telephone)

### ***Representative Members***

Ankit A. Mahadevia, M.D., M.B.A., Atlas Venture (by telephone)

Susan E. Siegel, M.S. (by telephone)

Robert I. Tepper, M.D.

Tadataka Yamada, M.D., Takeda Pharmaceuticals International, Inc. (by telephone)

### ***Ex Officio Member***

Margaret A. Hamburg, M.D., U.S. Food and Drug Administration

## **INVITED PRESENTERS**

Alan I. Leshner, Ph.D., American Association for the Advancement of Science

Sharon F. Terry, M.A., Genetic Alliance

## **OTHERS PRESENT**

Lee Brayman, Waters Corp.

Nadine Chien, Ph.D., J.D., Furiex Pharmaceuticals, Inc.

Rebecca M. Farkas, Ph.D., National Institute of Neurological Disorders and Stroke  
(NINDS)

Pamela M. McInnes, D.D.S., M.Sc., National Institute of Dental and Craniofacial  
Research

Priti Mehrota, Ph.D., National Institute of Allergy and Infectious Diseases (NIAID)

Judith Mun, M.P.A., American Association of Colleges of Osteopathic Medicine

Andrew Peck, Waters Corp.

Michael L. Salgaller, Ph.D., The Confay Group

Shimere A. Williams, Ph.D., Lewis-Burke Associates, LLC

NCATS leadership and staff

## **I. CALL TO ORDER AND WELCOME**

Dr. Austin welcomed members and guests to the fourth joint meeting of the NCATS Advisory Council and the CAN Review Board. He advised attendees that the open session was being videocast.

Austin remarked that Kate C. Beardsley, J.D., is still awaiting confirmation of her position as an ad hoc member of the NCATS Advisory Council and CAN Review Board. The *ex officio* position for the U.S. Department of Veterans Affairs remains vacant.

Dr. Lewis-Hall also extended a welcome to those in attendance. The members participating via teleconference announced themselves.

Dr. Tagle informed the group that the next joint meeting is slated for January 16, 2014, and Austin stated that the joint meetings will last one-and-one-half days beginning in 2015.

In addition, Austin noted that statutory language provides for four meetings of the CAN Review Board per year but only three for the NCATS Advisory Council. Therefore, only the CAN Review Board will convene by teleconference on December 12, 2013. This virtual meeting will be published in the *Federal Register* and will be open to the public. Council members are welcome to participate.

## **II. CONSIDERATION OF MINUTES: Danilo A. Tagle, M.S., Ph.D., Executive Secretary, NCATS Advisory Council and CAN Review Board**

The minutes of the joint meeting held on May 17, 2013, were approved as written.

## **III. DIRECTOR'S REPORT: Christopher P. Austin, M.D.**

Austin advised that he has informally made a modification to the NCATS mission statement to broaden its focus beyond diagnostics and therapeutics, to explicitly include medical technologies and behavioral interventions, and the demonstration that the interventions improve human health: "To catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of *interventions that tangibly improve human health* across a wide range of human diseases and conditions."

He then updated the group on progress in filling senior positions within NCATS. Candidates for the deputy director position have been interviewed, and negotiations are under way with a candidate for the Division of Clinical Innovation (DCI) director position. Candidates for the Office of Grants Management and Scientific Review director are being interviewed, and applications for the Office of Policy, Communications & Strategic

Alliances director are under review. There also is continuing discussion to refine the scientific director position parameters, and it is anticipated that recruitment will begin soon.

Regarding the financial picture at NIH and NCATS, Austin said NIH is still operating under a continuing resolution. Because of cuts to the NIH budget, including those resulting from sequestration, the budget appropriated for fiscal year (FY) 2013 is equivalent to the FY 2001 budget in constant 1998 dollars. In other words, despite the tremendous scientific opportunities available now, NIH has no more financial capacity to carry out research aimed at improving human health than it did in 2001.

Austin spoke of the impact of medical research on health in the United States in terms of gains in life expectancy and commensurate increases in productivity. Moreover, he stated that NIH-supported research has a substantial impact on the U.S. economy: In 2012, NIH funding supported more than 400,000 jobs at 2,500 institutions and small businesses nationwide and generated in excess of \$57 billion in new economic activity, amounting to a twofold return on taxpayers' investment.

Referring to a graph showing changes in spending on scientific research from 2012 to 2013, Austin pointed out that China, Germany, Japan and South Korea are all increasing their spending on research, while Canada and the United States are cutting theirs. The downward trend could indicate major challenges for the NIH intramural program in particular because its research relies on appropriations that could be reduced by as much as 30 percent. A Board member suggested finding out whether the United Kingdom is increasing or decreasing its spending.

Austin urged attendees to educate their communities about the multiplier effect of investing in biomedical research. He commented on a [fact sheet](#) about the effect of sequestration on NIH and showcased efforts of the NCATS Office of Communications to spread the word about the Center. For example, the [NCATS stakeholder e-newsletter](#) and [website](#) highlight advances made possible with NCATS resources. The Office of Communications also is reaching out to diverse audiences via social media, including [Facebook](#), [Twitter](#) and [YouTube](#). Several NCATS' initiatives and accomplishments recently have been covered in *The Wall Street Journal*, *Science*, *The Scientist*, PBS' *Nova Next*, and on CBS' *This Morning*.

Austin also mentioned that the Institute of Medicine (IOM) report on the Clinical and Translational Science Awards program ([The CTSA Program at NIH: Opportunities for Advancing Clinical and Translational Research](#)) stimulated a great deal of media coverage and positive publicity. He noted that the program represents about 85 percent of NCATS' budget.

Austin said the NCATS Office of Policy's recent activities have included publishing a notice in the *Federal Register* on May 15, 2013, at the request of congressional

appropriators as a way of ensuring that NCATS is not competing with the pharmaceutical industry. Fourteen responses were received. And, since the last meeting of the Advisory Council and CAN Review Board, NCATS has briefed members of Congress and their staffs on translational science, the intersection of NCATS and the pharmaceutical industry, and research on rare diseases.

With regard to FY 2014 appropriations, Austin said the Senate Appropriations Committee approved the Labor, Health and Human Services, and Education bill in July, which would have provided \$666 million for NCATS, including \$50 million for CAN. However, no bill was released by the House, making it likely that NIH will continue to operate under a continuing resolution.

Despite these budgetary limitations, Austin highlighted several key accomplishments of NCATS since the last joint meeting:

- Two teams in the Division of Pre-Clinical Innovation (DPI) received NIH Director's awards: the Therapeutics for Rare and Neglected Diseases (TRND) Niemann-Pick C Development team, which is investigating cyclodextrin as a treatment for Niemann-Pick disease type C, and the DPI Matrix Screening Group, which is seeking innovative ways to study combinations of therapeutics.
- DPI's Assay Development and High-Throughput Screening Technologies Group collaborated on a malaria vaccine clinical trial with researchers in the Vaccine Research Center at NIAID, results of which were recently published in *Science*.
- A recent paper described how the Tox21 robotic platform promises to improve the process for characterizing human hazards posed by chemicals. Also, representatives from the U.S. Office of Management and Budget spent a day at the Tox21 laboratory and were impressed by the interagency collaboration that makes the program possible.
- A Phase II clinical trial is now enrolling patients to test Aes103 for sickle cell disease. *BioWorld Today* provided excellent coverage of TRND's role in this story.
- Four new TRND projects were announced, including the program's first stem cell project (for retinitis pigmentosa) and its first collaboration with a large pharmaceutical company (Eli Lilly) to develop a parathyroid hormone analog for hypoparathyroidism.
- A collaboration involving NCATS' Bridging Interventional Development Gaps (BrIDGs) program, the National Institute on Drug Abuse, and Signature Therapeutics seeks to develop an oral prodrug formulation of oxycodone. The advantage of a prodrug is that common methods of tampering do not release appreciable amounts of the active opioid.
- NCATS co-hosted a Research & Development Day with Novartis in Cambridge, Mass. on September 12. The event featured 10 collaborative drug development projects from the TRND and BrIDGs programs that have been sufficiently de-risked to be suitable for adoption by biopharmaceutical companies or other organizations, which will complete the clinical development, registration and marketing of these agents. More than 100 representatives and venture

capitalists of the biopharmaceutical industry attended, expressing licensing interest in many of the projects.

- The Rare Diseases Clinical Research Network within the Office of Rare Diseases Research (ORDR) released a funding opportunity announcement for the Rare Diseases Clinical Research Network (RDCRN), which currently supports many collaborative consortia that undertake multisite clinical studies in groups of related rare diseases. Collaborators include 10 other NIH Institutes and Centers (ICs).
- ORDR is in the planning stages of several projects related to the development of medical devices for rare diseases.
- The Tissue Chip for Drug Screening program is a collaboration of the U.S. Food and Drug Administration, the Defense Advanced Research Projects Agency (DARPA) and NCATS. The program's first grants were awarded a year ago. The program is now in the stage of platform and engineering development. DARPA will integrate cells and/or organs onto the platforms. Each "tissue chip" is being developed as a module to allow it to be used in conjunction with others. The hope is to develop integrated systems for toxicology testing that would be acceptable to regulatory agencies for therapeutics approval. The program is ambitious but, importantly, remains *ahead* of preset milestones.
- In June 2013, NCATS announced nine Discovering New Therapeutic Uses for Existing Molecules (NTU) awards totaling \$12.7 million for the first year. The funding is supporting research on a selection of investigational pharmaceutical industry compounds to explore new treatments for patients in eight disease areas. The program's success will be gauged using several measures: whether the [template agreements](#) created by the program administrators speed negotiation time; to what extent the pilot advances disease understanding; and whether it results in promising new therapeutics. Christine M. Colvis, Ph.D., explained plans for the next round of the NTU program. She added that [NCATS' NTU website communications](#) helped spark discussion between academic researchers and pharmaceutical company representatives about additional opportunities for drug rescue and repurposing beyond the parameters of this program.
- The new Common Fund program that NCATS is co-leading with NINDS and the National Cancer Institute (NCI) on Extracellular RNA Communication is designed to investigate the roles of extracellular RNA (exRNA) in normal body fluids and as a biomarker in disease. Austin explained that RNA in vesicles had long been considered cellular debris, but recently it has been recognized that many organisms use exRNA for intercellular communication. The collaborative, cross-cutting program is supported by the NIH Common Fund and led by a trans-NIH team that includes NCATS; NCI; the National Heart, Lung, and Blood Institute; the National Institute on Drug Abuse; and NINDS. NCATS is administering 18 of the 24 NIH awards announced in August, which in total represent an investment of \$130 million over 6 years.

- Another Common Fund program that NCATS is co-leading with NIDDK, Illuminating the Druggable Genome (IDG), is focused on unannotated proteins from four gene families that encode regulatory proteins frequently targeted by marketed drugs, including the kinases, ion channels, G protein-coupled receptors and nuclear receptors. The goal is to establish a public, curated, searchable knowledge hub for the druggable genome. Because it takes a long time to go from discovery of novel genes to the development of a viable product, industry has dropped this line of research. Austin anticipates the release of a funding opportunity announcement this fall. A meeting participant commented on the pharmaceutical industry's efforts going back 10 or more years to develop platforms for well-known drug targets. The recommendation was to discuss those abandoned efforts with the drug companies to learn whether the data could be retrieved and placed in the knowledge base.

Following Austin's remarks, Dr. Contreras expressed an interest in learning how many patents are applied for or are jointly owned by NCATS-supported researchers. Lili M. Portilla, M.P.A., acting director, NCATS Office of Policy, Communications & Strategic Alliances, referred to the [NCATS website licensing page](#) on which NCATS' patents are listed.

In terms of intellectual property generated, Portilla asserted that NCATS' activity is on par with ICs twice the size of NCATS. For example, in 2012, NCATS held 20 percent of NIH Cooperative Research and Development Agreements (CRADAs), but it has only 2 percent of the agency's budget.

#### **IV. INITIATIVE TO ENHANCE REPRODUCIBILITY AND TRANSPARENCY OF RESEARCH FINDINGS: Christopher P. Austin, M.D., Director, NCATS**

At the urging of the NIH Director's Office, Dr. Austin addressed the issue of lack of reproducibility and transparency of published research findings. Many papers and articles have highlighted this problem in recent years. For example, three investigators with Bayer HealthCare published a [paper](#) showing that nearly two-thirds of in-house projects could not replicate data published by others. In-depth examination of this issue, particularly by NINDS staff, revealed insufficient reporting of methodologic approaches for pre-clinical (animal) studies. Only a small percentage of published studies used a randomized or blinded design, and no studies conducted calculations of sample size (power).

An ad hoc group of NIH IC directors was convened to address the challenge of poor reproducibility of research findings. Underlying problems were felt to include poor education, poor evaluation and perverse incentives. The group developed a set of five action principles and recommendations mapped to them. The five principles were:

1. Raise awareness in the community.
2. Enhance formal training.

3. Improve the evaluation of applications and require power calculations in the proposal.
4. Protect the integrity of science by recommending that journals adopt a more systematic review process for submitted papers.
5. Increase stability for investigators.

The recommendations and suggested actions issued by the group include the following:

1. Encourage ICs to discuss the issue with advisory councils and boards of scientific counselors, or hold workshops to call attention to the issue of reproducibility to stakeholder communities. (Maps to Principle #1)

**Action:** All ICs and offices of the directors will discuss the reproducibility and transparency of research findings with their stakeholder communities to alert them to the issues and solicit feedback by the end of the 2013 calendar year.

2. Integrate modules and/or courses on experimental design into existing required training courses and award terms and conditions. (Maps to Principle #2)

**Actions:** The Office of Intramural Research will create and pilot a new module on research integrity as it relates to experimental biases and study design to be included in the ethics training course required for NIH intramural fellows. Once this module is tested, the Office of Extramural Research will make it available on the Web and encourage its adoption (or equivalent) by extramural training programs for fellows and trainees.

3. Consider options for an evaluation process of the “scientific premise” of a grant application. (Maps to Principle #3)

**Action:** Select ICs will perform pilot evaluations of the scientific premise of grant applications.

4. Collaborate further with scientific journals and the scientific community on efforts to improve rigor. (Maps to Principle #4)

**Actions:** NIH will continue outreach to partner with journals and determine the value of recently adopted reporting guidelines; and NIH will evaluate the PubMed Commons Community Response Effort, which is a pilot program allowing scientists to post online comments about original research articles.

5. Adapt the NIH biosketch format to allow investigators to place their work in a functional context. (Maps to Principle #5)

**Actions:** Select ICs will perform pilot evaluations of biosketch modifications, including elements that could help frame the principal investigator’s work and clarify the applicant’s contributions to the publications cited. Select ICs also will pilot additional experiments to reduce perverse incentives. In addition, efforts by NCI to reduce perverse incentives will be evaluated. NCI recently developed an Outstanding Investigator Award to address perverse incentives by providing substantial, longer-term support to experienced investigators.

Two additional suggestions are:

1. Consider the use of guidelines and/or checklists to systematically evaluate grant applications. (Maps to Principle #3)

- Action:** Select ICs will pilot the use of a checklist to enhance systematic review of applications.
2. Consider the advisability of and approach to supporting replication/reproducibility studies or centers. (Maps to Principle #4)  
**Actions:** Select ICs will pilot additional use of supporting replication studies and evaluate ongoing pilot work by NINDS in the support of replication studies. In addition, there will be an evaluation of ongoing efforts of the National Institute on Aging in supporting the Interventions Testing Program, where pre-clinical studies are conducted with multisite duplication, rigorous methodology and statistical analysis.

Austin pointed out that, for the most part, graduate students and postdoctoral fellows are the ones carrying out the research; they need to be instructed properly. Also, having reviewers of applications check papers cited in applications would not be a trivial process. Journal editors are in a position to help make sure that poorly done research does not make it into print, but Austin observed that by the time a paper is submitted, it is too late — the project is already completed. Regarding the idea of providing support for replication/reproducibility studies, Austin questioned whether this would be a good use of scarce resources. The Animal Care and Use regulations already in place mitigate against duplicative research.

Austin clarified that, at NCATS, all DPI projects begin by reproducing the study results of the collaborating investigator. If this criterion is not met, the project does not proceed. Similarly, programs undertaken by the Office of Special Initiatives (e.g., exRNA, Tissue Chip, NTU, IDG) are all milestone driven with built-in cross-checks.

According to Austin, discussions are under way with regard to assessing the rigor and reproducibility of DCI programs — mainly carried out through the CTSA institutions — although this task is challenging because NCATS funds are supportive rather than project-specific. ORDR programs are similar to those of DCI in this regard.

Dr. Davis commented on the push to reduce the number of animals to a bare minimum, saying that the trend is not always in the best interest of the science. She cautioned that some models of human disease are very fragile, and research findings may depend on how the animals were transported and cared for.

Dr. Ginsburg remarked that journals could play an active partnership role by promulgating policies to increase transparency and reproducibility of published research. Austin recalled problems with spurious associations in early genome-wide association studies: Journal editors instituted a requirement that investigators had to have a replication set before they could publish, thereby reducing the problem greatly.

Ginsburg also said that NIH has a fiduciary responsibility and should begin by cleaning its own house first. At a certain point, however, NIH will have to think about how to engage

industry in this effort. Austin agreed that these issues are relevant to both industry and academia. Dr. Douglas said that in industry, reproducing study results is a *pro forma* part of the process.

Dr. Tepper spoke about the importance of having investigators base their work on a sound foundation of data. He said that perhaps a forum could be set up to enable an investigator's scientific peers to comment on the veracity of that foundation. Also, before publication, peers could undertake studies to ensure the findings are reproducible. With a proper incentive structure, reproducibility could be built into studies.

Dr. Lewis-Hall spoke of the widespread nature of this problem and suggested escalating to a more cross-cutting, collaborative, high-level effort to solve it. Ginsburg asked about the possibility of elevating this issue to an IOM initiative to bring these issues to the forefront and transform the whole of research.

Austin mentioned the Science Exchange as a possible way of testing reproducibility of a publication (or pre-publication).

Austin asked the Council and Board members to call or send in their ideas via e-mail.

**V. IOM REPORT ON CTSA PROGRAM: Alan I. Leshner, Ph.D., CEO, American Association for the Advancement of Science, and Sharon F. Terry, M.A., President and CEO, Genetic Alliance**

Dr. Leshner observed that the CTSA program has grown from the initial 12 sites to the current 61 in the seven years since its inception. The total program budget is \$461 million, making it one of the largest NIH programs. It does not directly fund or conduct large-scale research projects.

The IOM evaluation led to two overarching conclusions. First, the CTSA program has been successful in establishing CTSA as academic focal points for clinical and translational research and has begun to build a national network that will need to be fully integrated and collaborative to catalyze progress further. Second, the CTSA program is contributing significantly to the advancements of clinical and translational research and is, therefore, a worthwhile investment that would benefit from a variety of revisions to make it more efficient and effective.

The IOM committee articulated seven recommendations:

1. **Strengthen the leadership of the CTSA program by NCATS.** Originally, a steering group made up of the CTSA principal investigators ran the program. The IOM committee thought that NCATS needs to take a more active leadership role.
2. **Reconfigure and streamline the CTSA Consortium.** The Consortium should be chaired by NCATS with a principal investigator as co-chair. The CTSA program has

- a system of many committees involving many people. The entire organizational structure needs to be simplified and make clear that NCATS is in charge, in the view of the IOM committee. The CTSA Coordinating Center would benefit from clearer guidance from NCATS.
3. **Build on the strengths of individual CTSA across the spectrum of clinical and translational research.** Although the overall program should span the full gamut of clinical and translational research, the individual CTSA must build on their own idiosyncratic strengths and seek collaborations amongst themselves and with industry. The IOM committee envisioned opportunities for the CTSA to serve as academic focal points with broad collaborations and community involvement. Also recommended was the establishment of an innovation fund run by NCATS to be used as a set-aside mechanism to stimulate collaborative pilot studies.
  4. **Formalize and standardize the evaluation processes for individual CTSA and the CTSA program.** The IOM committee recommended a continuous process for distilling lessons learned and sharing them widely. The metric for evaluating the CTSA should not be the number of papers published; rather, it should be progress in translational science.
  5. **Advance innovation in education and training programs.** Translational research is an acquired skill. The CTSA institutions must avoid “cookie cutter” research and provide flexible and personalized training experiences.
  6. **Ensure community engagement in all phases of research.** Partnerships between CTSA institutions and communities develop over time. Community engagement is a learned skill; the CTSA institutions could share lessons learned and best practices, but not all CTSA will engage communities in the same way.
  7. **Strengthen clinical and translational research that is relevant to child health.** A focus on child health is required for NCATS programs, but the CTSA institutions need greater clarity about this: Do they all need to carry out pediatric research? Should CTSA with experience in child-health research adopt a leadership position and collaborate with other CTSA? NCATS needs to take charge to ensure that this requirement is covered.

Ms. Terry remarked on the need for communities and CTSA institutions to both benefit from community engagement. Advocacy groups are looking for real and meaningful partnerships that bring value. The CTSA have been operating mostly in a traditional academic role, but they also should be engaging communities to accommodate the changing landscape of translational science. A focus on community needs to be incorporated into all parts of research. In addition, the IOM report helped raise awareness about the CTSA program among various communities, including land-grant colleges, community health centers, and occupational and physical therapists.

Speaking as a principal investigator in a CTSA program and as a Council member, Dr. Davis said she found the IOM committee’s report to be fair and helpful. The committee structure of the overall CTSA program has been cumbersome. Developing appropriate

evaluative metrics to gauge success will be challenging. Having permission to reach out and collaborate is very exciting, but each partner must be strong and able to contribute. The CTSA's are ready to extend and participate in meaningful collaborations.

In response to a request for specific examples of CTSA successes, Leshner responded that the IOM report provides some examples, also noting that the CTSA's have contributed to their home institutions in terms of cross-collaborations. Notably, the REDCap system for capturing patient data at Vanderbilt University is now being used by several hundred institutions. He also mentioned I2B2 (Informatics for Integrating Biology and the Bedside), Harvard University's clinical trial and data-sharing system.

Regarding the organizational structure, coordinating 61 institutes would seem to be an impossible task. Leshner explained that it was outside the committee's charge to consider the size or the budget of the program. However, the strategic planning process should articulate goals and metrics, and the size of the program should be compared against those goals and milestones. The number of CTSA institutions should relate to the nature of the science to be done.

Dr. Ginsburg inquired about incentives and the recognition of team science and translational research. If NCATS leadership were to underscore the importance of developing metrics for translational accomplishment, that would carry some influence. Traditional academic metrics are not very useful if transformative change is what is desired. Terry remarked that the training section of the IOM report emphasizes the importance of team science and recommends instruction on team leadership. Incentives do need to be aligned to avoid stagnation.

A discussion ensued about dovetailing various programs of NCATS and other ICs with the CTSA's. For example, if a promising compound is identified through the TRND program, could CTSA resources be marshaled to test it in proof-of-concept trials? Other NIH initiatives, such as one on patient-centered outcomes, could be a basis for community engagement. Having CTSA leadership who can see the whole picture would be key to such efforts.

Dr. Douglas suggested that the CTSA's as a group might be able to tackle the issue of reproducibility of research findings. Leshner thought this was an excellent idea for tackling this widespread problem.

Dr. Austin said that if one looks at where the CTSA institutions spend their money, about half goes to support clinical research units. About 25 percent goes to training — altogether the program supports about 900 trainees. It is the largest training cohort of NIH. About 10 percent of these budgets support pilot programs and early-stage translational projects. The remainder goes to informatics, tools and so forth. At this point, the CTSA's are trained and their research engines are primed; they are ready to be deployed.

Dr. Beall recommended that the CTSA's work on improving the processes of clinical trials. Most trials in this country are underpowered in terms of patient numbers. How can we do trials better, faster and cheaper? Davis spoke about the usefulness of standardized protocols and reliance agreements among institutional review boards (IRBs). Electronic medical records can be used to identify potential study participants who may meet eligibility criteria and even give an indication of study feasibility. Austin envisions a true CTSA-based national network with a harmonized, federated IRB structure that could carry out trials very efficiently, to the benefit of industry and the CTSA institutions. The IOM has placed its imprimatur on these sorts of collaborations with industry.

Davis said that most CTSA's do not envision themselves running major, multisite trials. However, she expressed enthusiasm for the idea of the innovation fund, which could support pilot studies involving 10 or so participants to see if the process runs smoothly. The innovation fund could pay for training, laboratory support, skilled nurses and a biostatistician.

With regard to training, CTSA staff could train in industry laboratories or with entrepreneurial communities. Not all training is conducive to the online format; team building and leadership courses should be conducted in person.

The participants discussed the challenges of clinical trial enrollment. Only 5 to 10 percent of cancer patients are in clinical trials. With neurological diseases, the figure is only 2 percent. Referral rates are low. Ms. Weinberg suggested exploring the materials and messaging available through the Center for Information & Study on Clinical Research Participation, a nonprofit that encourages people to participate in clinical research. Other possible solutions discussed were community engagement and practice-based research networks.

Austin also remarked on the problem of investigator turnover: Too many investigators enroll only a few or no patients and then never do another trial.

Elaine Collier, M.D., acting DCI director, spoke about the need for better clinical outcome measures and improved cohort distinction.

Austin thanked Terry and Leshner for their contributions to the IOM committee and the report. NCATS is setting up a Working Group to address the committee's recommendations. Austin asked those present to submit nominations for the Working Group membership. Membership in the Working Group will not be restricted to members of the NCATS Advisory Council and CAN Review Board.

## VI. CAN REVIEW BOARD AGENDA: OTHER TRANSACTION AUTHORITY: Lili M. Portilla, M.P.A., Acting Director, Office of Policy, Communications & Strategic Alliances

Ms. Portilla presented the legislative history of CAN, which has three authorities: the amount of the initial award up to \$15 million, matching funds, and the flexible research authority (same as “other transaction authority”). Under the third authority, CAN may fund projects “in accordance with the terms and conditions of this section. Awards made under OT [other transaction] for a fiscal year shall not exceed 20 percent of the total funds appropriated under CAN for each fiscal year” (\$2 million for FY 2013, with the same expected for 2014).

According to Portilla, “other transaction authority” (OTA) is best described as what it is not. It is not a grant, a cooperative agreement, a contract or a CRADA. It is truly a unique mechanism and another tool in the “tool box” to establish unique collaborations under CAN. OTA provides flexibility for entering novel arrangements with nontraditional government partners in the public or private sectors. It can shorten the acquisition timeline for certain types of projects and encourage cost sharing between the agency and partner.

Portilla explained that OTA serves as a flexible means to achieve the goals of a collaboration. DARPA uses OTA as a way to engage nontraditional partners and deal with overcoming certain intellectual property issues. The NIH Common Fund also has this OTA. It was used for the NIH Common Fund Nanomedicine Initiative to conduct nontraditional NIH peer review of grants.

One challenge is the lack of a defined structure for engaging partners. Since each OTA can be a unique agreement, measures of success need to be developed for each one. The agency needs to have experienced personnel for developing and administering OTA projects as the mechanism requires certified personnel to negotiate and execute.

The NIH OT Work Group established a set of guidance principles for using OTA:

- **Partnerships:** OT could be used to eliminate barriers and establish unique partnerships.
- **Milestone-driven science:** OT is well suited for project team approaches, especially for large-scale projects.
- **Creative implementation:** Individuals supporting OT must be innovative and well trained in its use.
- **Constructing an OT agreement:** Develop a menu of vetted terms and conditions to be included in OT agreements; use templates from other agencies.
- **Evaluating success:** OT contracts/agreements need to include language on how each OT will be monitored, how risks will be assessed and how the project will be evaluated.

- **Speed:** In agencies using OT, the mechanism can move science initiatives and programs forward efficiently.

Portilla reported that early in the establishment of NCATS, DARPA was asked to help provide guidance to the Center on how to appropriately establish and implement OTA collaborations. DARPA was very receptive in providing this advice to NCATS.

Dr. Austin suggested that OTA could be used if NCATS wanted to engage in a true cost-sharing collaboration with a company. Such an arrangement could not be set up under other mechanisms. Portilla provided some examples of how OTA could be used (e.g., giving microgrants to companies to help them collect some data to prepare to apply to NIH grant programs). Dr. Beall thought that such arrangements could be beneficial for patients. There are many orphan diseases and some have therapeutic targets, but no resources are available for companies to collect pilot data to apply for TRND funding, for example.

Dr. Ginsburg inquired about using OTA to fund prizes for challenges. Portilla noted that the U.S. Department of Health and Human Services has prize authority.

Dr. DeGennaro explained the Therapy Acceleration Program of the Leukemia and Lymphoma Society. The program has accelerated pre-IND (Investigational New Drug application) studies and clinical trials as well. When partnering with small companies, it is necessary to make fast decisions. The companies cannot wait a year or more for a decision about funding.

Dr. Weir spoke about the possibility of a treatment coming in through the TRND program and then bridging it to a CTSA using CAN's OTA — that would be an important accomplishment for NCATS.

Ms. Anderson suggested being thoughtful about the projects selected for OTA. There should be a sound justification and rationale for using this avenue.

Austin asked the group to think about how CAN's OTA could be used effectively. The discussion will continue at the December meeting of the CAN Review Board. The participants requested that some information be provided to "seed their thoughts" prior to the December meeting:

- DARPA key projects, best practices and lessons learned with regard to use of OTA.
- Findings of the IOM panel that convened about two years ago on OTA.
- Case studies from DARPA or other entities using OTA to demonstrate the types of breakthroughs made possible with OTA.
- Ideas from NCATS staff about biomedical innovations that might be accomplished using OTA under CAN.

## **VII. REPORTS OF THE COUNCIL SUBCOMMITTEES**

### ***Patient Engagement***

*Margaret A. Anderson, M.A., and Myrl Weinberg, M.A.*

Ms. Weinberg introduced a five-step model for patient engagement in the research and development process: 1) setting of a research agenda; 2) development of research questions; 3) selection of outcomes and comparators; 4) recruitment; and 5) translation and dissemination of results. The model calls for partnering with patient advocacy, family caregiver, and consumer organizations. NCATS could serve as either an example or a pilot within NIH for demonstrating the value of patient engagement. The challenge lies in identifying where to start, targeting the most relevant areas within NCATS for patient involvement, and learning what the CTSA's are doing that might qualify as best practices. It would be important to incorporate the views of patients and patient advocacy organizations.

Patient engagement needs to be built into the research and development processes right from the beginning. Research questions need to be based on outcomes that patients want to have met. Recruitment also can be advanced with the help of patients and patient advocates.

Weinberg emphasized the importance of applying a systematic and well-documented process for patient engagement. The hope is that NCATS will develop some best practices.

As for how NCATS can interact with patients or those who work with patients, Ms. Anderson said that NCATS has much work to do. What are the core elements that NCATS needs to focus on to engage patients? For what purposes would engagement be useful? Weinberg mentioned the need for training to ensure that patients, consumers and the organizations that represent them can engage meaningfully with NCATS.

Dr. Austin said the Council is relying on the subcommittee to bring forward recommendations. He suggested being specific: "In this program, you should think about engaging this group of patients..." He also asked the subcommittee to think about terminology because not all research participants are patients.

### ***Partnerships with Pharmaceutical and Biotechnology Companies and Venture Capital Firms***

*Freda C. Lewis-Hall, M.D., and Ankit A. Mahadevia, M.D., M.B.A.*

Dr. Mahadevia stated that biotechnology companies and venture capital firms have a long history with NIH. He recommended continuing to streamline the process for contracts to garner some quick wins for NCATS.

Mahadevia observed that some NCATS projects are getting quite a bit of attention in the press, but it is important to ensure that perceptions match the reality. He also underscored the importance of connectivity: Biotechnology companies, venture capitalists and pharmaceutical companies must partner with academia and patient organizations. NCATS would be the perfect entity to bring these groups together.

Dr. Lewis-Hall offered some remarks about connectivity. Much of what we accomplish in collaborations is based on serendipity. Is there a system, process, format or platform to allow us to synthesize collaborations in a more directed way?

### ***Medical Technologies (Devices and Diagnostics)***

*Frank L. Douglas, Ph.D., M.D., and Paul G. Yock, M.D.*

Austin noted that few program people at NCATS possess expertise in devices and diagnostics. Dr. Yock said that NIH in general has lagged in supporting the development of devices and diagnostics, compared with biopharmaceutical companies.

Medical technology represents about 40 percent of the life sciences industry, which is dominated by U.S. companies. Medical technology has been very successful in terms of delivering care to patients.

The university landscape in medical technology is changing rapidly. Biomedical engineering departments are on the increase. The best engineering students are going into biomedical engineering. Proportionately, many more women are going into bioengineering than the other fields of engineering. It is a very dynamic workforce that NIH has not fully embraced.

The “valley of death” in medical technology is far less dire than in drug development. University discoveries with relatively small amounts of funding can segue to patient care.

What role could NCATS — particularly the CTSA program — take in medical technology? One theme discussed by the subcommittee dealt with affordability. Health care economists point to new medical technology as the greatest driver of health costs. There may be an important niche for affordable technology innovation.

Dr. Douglas observed that the United States’ lead in medical technology is being challenged. He recommended focusing on value-driven engineering. Every stage from design through manufacture offers opportunities to maximize clinical utility, cost savings and user-friendliness that could lead to breakthrough innovations.

Also, medical technologies lend themselves to combination products. It is possible to print tissues or materials impregnated with antibiotics to reduce surgery-associated infection. Douglas also mentioned the need for devices for the lymphatic system.

Douglas suggested identifying a niche on which to focus. Whether the research involves combination products or the biocompatibility or bio-absorbability of materials placed in the body, translation is the name of the game! A great deal of science and technology is ready for translation in the realm of devices and diagnostics. Douglas also acknowledged ORDR's Trans-NIH Medical Devices Initiative as an example of what can be done to foster this translation.

Austin thanked the subcommittees for their service to the Council.

### **ADJOURNMENT OF JOINT MEETING**

Dr. Tagle adjourned the meeting at 2:45 p.m. ET.

### **CLOSED SESSION OF NCATS ADVISORY COUNCIL**

This portion of the Council meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

Council members discussed procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during the discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent.

### **ADJOURNMENT OF CLOSED SESSION OF THE NCATS ADVISORY COUNCIL MEETING**

Dr. Austin adjourned the closed session of the NCATS Advisory Council meeting at 4:25 p.m. ET.

## CERTIFICATION

We hereby certify that, to the best of our knowledge, the foregoing minutes and supplements are accurate and complete.

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Christopher P. Austin, M.D. Date  
Chair, NCATS Advisory Council  
and  
Director, National Center for Advancing Translational Sciences, NIH

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Danilo A. Tagle, M.S., Ph.D. Date  
Executive Secretary, NCATS Advisory Council  
Executive Secretary, Cures Acceleration Network Review Board  
and  
Acting Director, Office of Grants Management and Scientific Review, NCATS

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Freda C. Lewis-Hall, M.D. Date  
Chair, Cures Acceleration Network Review Board  
and  
Executive Vice President and Chief Medical Officer, Pfizer