

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

**Fifth Meeting of the
Cures Acceleration Network Review Board**

Minutes of Meeting

December 12, 2013

The Cures Acceleration Network (CAN) Review Board convened a virtual meeting by teleconference, in open session, at 11:00 a.m. ET on December 12, 2013. 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.

CAN REVIEW BOARD MEMBERS PRESENT

Chair

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

Vice Chair

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

Executive Secretary

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

Board Members

Margaret A. Anderson, M.A.

Robert J. Beall, Ph.D.

R. Alta Charo, J.D.

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

Louis J. DeGennaro, Ph.D.

Mary L. Disis, M.D.

Victoria G. Hale, Ph.D.

Eric D. Kodish, M.D.

Frank G. Prendergast, M.D., Ph.D.

Lawrence A. Soler, J.D.

Myrl Weinberg, M.A.

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

Paul G. Yock, M.D.

Representative Members

Ankit A. Mahadevia, M.D., M.B.A., Atlas Venture

Susan E. Siegel, M.S., healthymagination, General Electric

Ad Hoc Member

Kate Beardsley, J.D., Beardsley Law, PLLC

INVITED PRESENTERS

Christopher P. Austin, M.D., Director, NCATS
Scott R. Ulrey, Deputy Director, Contracts Management Office, Defense
Advanced Research Projects Agency (DARPA)
Barry Pallotta, Ph.D., Program Manager, DARPA

OTHERS PRESENT

Sarah Buchanan	Misrach Mitiku
Jordan Chapman	Lori Pellnitz
John Clerici	Mary Purucker
Lauren Gross	Yvette Seger
Bret Light	Huifeng Yun
Virginia Meehan	

NCATS leadership and staff
Others not identified by name on the WebEx system

I. CALL TO ORDER AND OPENING REMARKS

Dr. Lewis-Hall welcomed the participants to the fifth meeting of the CAN Review Board. This virtual forum offered an opportunity to discuss how flexible research authority through CAN could be exercised beyond the usual mechanisms (e.g., grants, cooperative agreements, cooperative research and development agreements [CRADAs], and contracts). The overarching goal, Dr. Ginsburg added, is to be prepared to launch projects and initiatives if funding becomes available.

II. CONFLICT-OF-INTEREST FORMS AND CONFIRMATION OF DATES FOR FUTURE MEETINGS OF THE NCATS ADVISORY COUNCIL AND CAN REVIEW BOARD: Danilo A. Tagle, Ph.D., M.S., Executive Secretary, CAN Review Board

Dr. Tagle reminded the CAN Review Board members to submit their conflict-of-interest forms. He also reviewed the 2014 meeting schedule for the CAN Review Board and the NCATS Advisory Council:

- January 16: joint meeting
- May 16: joint meeting
- September 19: joint meeting
- December 11: CAN Review Board only (virtual meeting)

III. RELATIONSHIP OF CAN AND NCATS: Christopher P. Austin, M.D., Director, NCATS

Dr. Austin reviewed the NCATS mission statement and explained that CAN's charge was established in the authorizing legislation (Patient Protection and Affordable Care Act), which directs NIH to accelerate the development of high-need cures. Originally, CAN was created within the NIH Office of the Director, but given the alignment of the NCATS and CAN missions, CAN was incorporated into NCATS upon NCATS' creation in December 2011.

CAN's genesis was in part due to a perception in some quarters of Congress that NIH was insufficiently focused on interventions to improve the health of its constituents and a sense that the agency was not connected sufficiently to venture capitalists, patient advocacy groups, regulatory organizations, research entities, and the pharmaceutical and biotechnology industries. By establishing CAN, Congress hoped that NIH could engage all of those groups and accelerate cures.

Austin pointed out that CAN may award up to \$15 million per project for the first fiscal year (FY). One type of award authorized under CAN is the Matching Funds Award; to receive such an award, an eligible entity must contribute \$1 in nonfederal funds for every \$3 awarded. Awards made using other transaction authority (OTA) cannot exceed 20 percent (\$2 million in FY 2013) of the total funds appropriated under CAN for each FY (\$10 million in FY 2013).

OTA agreements can take many forms to support novel arrangements with public and private entities. This authority allows the agency to attract nontraditional applicants because the Federal Acquisition Regulation, certain intellectual property and data-sharing restrictions, and federal cost principles do not apply. OTA is not a free-for-all, however; the agency involved must safeguard government interests and remain transparent. OTA agreements have not been commonly used at NIH.

Currently, two entities within NIH have OTA: NCATS and the Common Fund. Several years ago, the OTA mechanism supported a streamlined peer review of nanomedicine grant applications to NIH, and an internal working group has been exploring further use of OTA at that agency. The OTA mechanism is one of the many tools that are used by DARPA and by the Defense Threat Reduction Agency to establish unique collaborations.

CAN initially was authorized for annual appropriations up to \$500 million; however, no monies were appropriated for FY 2010 or FY 2011, and only \$10 million per year was provided in FY 2012 and FY 2013. The hope is that subsequent funding levels will be higher, reflecting Congress' enthusiasm about CAN, concern about health care outcomes, and interest in boosting biopharmaceutical and venture capital investment. CAN's current appropriation is supporting the [Tissue Chip for Drug Screening program](#), which is co-funded by NCATS (\$9.4 million via CAN) and the Common Fund (\$4 million).

Austin recommended that the CAN Review Board consider particularly projects to fund via OTA that could be accomplished with 20 percent of CAN's current budget of \$10 million per year. If a compelling idea is brought forward, it might be possible to underwrite it through the Common Fund. In addition, Austin encouraged the CAN Review Board to brainstorm projects to undertake in the event that Congress boosts appropriations for CAN. Should that happen, NIH would have to be ready to expend the funds in as little as six months using traditional funding mechanisms as well as OTA.

Discussion

Dr. Ginsburg asked Austin to explain how NCATS and CAN differ in terms of strategies and to identify points of overlap. Austin said the two entities are well-aligned in their overall missions and philosophies. CAN, however, is meant to be a venture space within NCATS to focus on new interventions. Austin also remarked on the overlap of membership on the CAN Review Board and the NCATS Advisory Council.

Dr. Weir noted that some funding sources for CAN projects could come from outside NCATS. Should the CAN Review Board think about providing strategic support to projects that will go into the clinic? If so, he suggested building upon the Therapeutics for Rare and Neglected Diseases (TRND) program or drug-repurposing projects to move promising drug candidates into clinical proof-of-concept studies. CAN support could help achieve measurable outcomes in terms of bench-to-bedside translation. Austin agreed that this would be a possibility and observed that the closer a project gets to testing in the clinic, the more likely it is that the private sector will get involved; perhaps this situation would be ripe for OTA co-funding of a public-private partnership for running clinical trials.

IV. EFFECTIVE USE OF OTHER TRANSACTIONS: Scott R. Ulrey, Deputy Director, Contracts Management Office, DARPA

Mr. Ulrey stated that he is responsible for contracts and grants for DARPA and reported that he was actively involved in the development of Other Transactions (OTs) in 1990. DARPA has applied OTs for many purposes, including commercial-military integration partnerships and support and stimulation activities for dual-use, commercial technologies.

Ulrey explained that the OT requirement for matching funds (to the extent practicable) leads to novel contractual arrangements. The process has encouraged the best sources from the scientific and industrial communities to apply for project funding, and it also reduces the administrative burden associated with more traditional funding mechanisms.

The advantages of OTs include the ability to create partnerships with industry, universities, nonprofits and national laboratories. The mechanism also confers flexibility when it comes to intellectual property, specifically patent rights. For example, the government could delay taking rights to an invention to give an entity a commercial jump given substantial prior commercial investment. Also, competition is only required to the maximum practicable extent; DARPA can directly approach an entity if this would be advantageous.

According to Ulrey, the main disadvantage of OTs is that negotiations can be protracted because everything (e.g., setting of milestones, articles of collaboration for a consortium, management structure, sharing of intellectual property) is negotiable.

Under OTs, project milestones must be based on measurable events, demonstrating meaningful progress. If milestones are tied to payment, they can help incentivize the performer. If difficulties are encountered, it is possible to adjust an expenditure-based approach or prospectively change subsequent milestones for a fixed priced approach.

Industry views OT agreements as fixed commitments from the very beginning; this is very different from the standard relationship between the government and contractors. DARPA does not manage these programs in the same way it would prime contractor/subcontractor relationships. Through OTs, DARPA may engage subcontractors directly and leverage resources to reduce risk with additional cost sharing. One criticism sometimes leveled at OTs is that not every element of cost is analyzed; note that DARPA focuses on technical value. On the other hand, there is an aspect of self-policing in consortium arrangements because all the members are looking at the expenditures of the other parties.

With OTs, vertical teaming tends to be more effective in achieving the aims of research and development. With horizontal teaming (i.e., team members have a common objective and are competitors), some members of the consortium might be reluctant to share “the jewel” with others. Ulrey shared several examples of organizational structures used for OT-supported research and development at DARPA.

How might OTs work for CAN? One idea Ulrey advanced was having pharmaceutical companies establish teams of university performers, such as immunology researchers at different universities. Everyone would share in the research and help the pharmaceutical company solve problems.

Discussion

Ulrey reported that DARPA’s average award using OTs is around \$2 million or \$3 million. In the late 1980s, awards tended to be larger (around \$10 million), but DARPA is now pursuing smaller projects, which has reduced the size of the average award.

A meeting participant asked whether OTs could be a means of creating an open innovation challenge. Ulrey said that DARPA has not used OTs for that purpose, but every government agency has prize authority. CAN or NCATS could set up challenges or competitions; DARPA has had excellent success with these approaches. An example is DARPA's Urban Challenge for Autonomous Vehicles in City Traffic, which started as a search for a technology to eliminate human drivers to reduce the dangers of improvised explosive devices (IEDs) in warfare. The resulting technology is now becoming a reality.

Ulrey urged the CAN Review Board members to avoid "boxing in" OT collaborators by setting unnecessary limits or restricting the types of solutions. OTs are an excellent way to find creative solutions when a particular contract or grant does not suit.

Dr. Ginsburg inquired about ways to identify top performers.

Another question posed by a participant involved DARPA's "[1040-EZ](#)" Small Business Innovation Research (SBIR) program. Ulrey responded that the 1040-EZ mechanism was originally an OT approach developed in conjunction with the White House Chief Technology Officer; he noted that SBIR awards require delivery of a prototype.

Dr. Austin pointed out that DARPA is able to make awards within 30 days using OTs; NIH typically requires nine months. Ulrey pointed out that DARPA is a small and agile organization; reviews can be accomplished quickly. Moreover, DARPA has minimal formal processes that must be followed.

V. MICROPHYSIOLOGICAL SYSTEMS: FROM CONCEPT TO EXECUTION: Barry Pallotta, Ph.D., Program Manager, Defense Sciences Office, DARPA

DARPA was created in 1958 in the aftermath of the success of the USSR's Sputnik program, a development that shocked much of the scientific establishment in the United States. Dr. Pallotta pointed out that DARPA's mission was to prevent technological surprises while developing the United States' capability to surprise its adversaries. Major accomplishments of DARPA have included the development of the Advanced Research Projects Agency Network (ARPANET, predecessor to the Internet), global positioning systems (GPS), and the Global Hawk unmanned surveillance aircraft. Pallotta explained that DARPA focuses on high-risk research that creates revolutionary advantages for the military; because of this risk-taking culture, DARPA is tolerant of failure.

Pallotta delineated the organization of the six DARPA technical offices and reminded the participants that DARPA does not have any laboratories or clean rooms on site to conduct research and has virtually no permanent staff. There are approximately 120 program managers who conceive the organization's programs, select who will work on them, and oversee the programs. The program managers are a heterogeneous group; they come from government, academia and industry. Program managers often are "on

assignment” from their home organization under the Intergovernmental Personnel Act and work at DARPA for three to five years.

The first stage of a program’s development is the incubation and maturation of a program manager’s idea. An idea can originate from DARPA program managers or from other government, academic and/or industry personnel approaching DARPA with their suggestions.

Pallotta explained that the next step in program development is to articulate the program concept to office directors and then to the DARPA director. Once the program is approved by management, the program manager issues a broad agency announcement (BAA) to solicit proposals from the scientific community. The proposals are scientifically reviewed by government personnel and are not ranked; rather, they are evaluated for their strengths and weaknesses with respect to the criteria published in the BAA. These criteria include the scientific and technical merit of the proposal, the proposer’s capabilities, the cost and schedule realism of the proposal, and the potential contribution and relevance to the DARPA mission. Milestones and metrics drive project performance and the programs have defined start and end dates.

DARPA and NCATS share several common research interests, including developing tissue-chip technology for predicting the efficacy and safety of drug candidates. DARPA and the Food and Drug Administration sponsored a workshop on preclinical platforms that helped Pallotta formulate the Microphysiological Systems (i.e., tissue chips) program and establish reasonable metrics and milestones for the five-year program. Pallotta articulated his idea to the Defense Sciences Office management and, once approved, pitched the program to the DARPA director and the directors of the other offices within DARPA. As evidence of feasibility, Pallotta relied on the recently published Modular IMMune In vitro Construct (MIMIC) surrogate human immune system and also Michael Shuler’s work at Cornell University using liver, tumor and bone marrow tissue constructs in a microfluidic system. Clearly, trying to recapitulate an entire human entails risk, but based on others’ accomplishments it appears that a tissue-chip system could be developed in a reasonable time frame.

Pallotta described the genesis of the DARPA/NIH partnership that is working to develop the tissue chips. Both DARPA and NIH want to encourage immediate adoption of the technology by NIH and industry researchers.

Pallotta concluded by praising DARPA’s capable technical team and financial managers. Were it not for the public investment in research infrastructure, projects such as the human tissue chip would not be possible. He also acknowledged NIH support of his own training and research through the years.

VI. DISCUSSION OF THE CAN REVIEW BOARD ON THE USE OF OTA AT NCATS

Tagle asked for research ideas that could be supported through CAN via OTA. Projects should be broadly enabling and paradigm shifting, with a reasonable possibility of providing a compelling disease application within an achievable timeline.

Dr. Weir asked for more information about projects in the TRND portfolio that could benefit from some support to advance to the clinic. He suggested that perhaps Dr. John McKew could present this information at the next joint meeting of the NCATS Advisory Council and the CAN Review Board.

Dr. Davis suggested developing a human tissue or organ chip to simulate the blood-brain barrier. Pallotta responded that some DARPA and NIH-supported investigators are working on a neurovascular unit on a chip. He offered to present more information about this at a future meeting.

Davis also recommended establishing a clearinghouse (e.g., a website) that could match ideas from academia with entities in the private sector to promote collaborations. Dr. DeGennaro reported on modest efforts of the Leukemia & Lymphoma Society (LLS) to pair academic and industry researchers, but he supported the idea of a matching system on a larger scale.

DeGennaro said that LLS has an internal staff with expertise in hematologic malignancies and drug discovery/development to establish a portfolio of LLS-funded grants. The staff tracks the progress of the investigators as their work migrates from basic science and moves toward investigational new drug (IND) studies. The staff has the latitude to identify projects and move them forward. The effort is capped with and managed by pharmaceutical industry-like quality management, with milestones, timelines and deliverables. Teleconferences with investigators occur at least quarterly.

In response to a question from DeGennaro, Dr. Pallotta explained the diverse sources of ideas for DARPA projects. Usually, DARPA program managers start by creating a research agenda based on gaps in knowledge or unmet medical needs. Pallotta offered the actual example of hiring a health research firm to work in a consulting arrangement to perform an environmental scan to see what NIH and industry were funding in terms of research into human blood malignancies. In this case, subcommittees of DARPA's medical and scientific advisory boards (composed of key opinion leaders) weighed in with their expertise on each of the malignancies.

Dr. Beall recommended that NCATS staff conduct a needs or gap analysis to identify high-priority scientific needs and illustrate the funding mechanisms available to best inform deliberations at the January 2014 joint meeting. The CAN Review Board could use the analysis to formulate research recommendations to present to NCATS. In addition, Beall asked NCATS staff to present some research ideas to serve as "straw

men” to which the CAN Review Board would react. Dr. Lewis-Hall agreed with the idea of developing a “hot topics list.” Dr. Yock asked whether the list could be made available before the January 2014 meeting, and he recommended that the CAN Review Board come up with some ideas of its own.

Lewis-Hall also suggested overlaying research ideas (from sources outside of NCATS) with existing NCATS program activities to identify areas of overlap. Dr. Austin speculated that this activity would be feasible, and he volunteered to work with Lewis-Hall and Dr. Ginsburg to make sure that the information provided by NCATS during the January 2014 meeting meets the needs of the CAN Review Board. Furthermore, Austin asked that the Board use the ideas as a jumping-off point and avoid considering them as another exercise in concept clearance.

Mr. Soler observed that CAN has only a small amount of money and suggested that the funds could be used to help others in their work. For example, the support of patient groups could engage many people and help build political support.

General agreement was voiced in terms of, first, leveraging projects that are already under way (e.g., drug repurposing, TRND projects) because of the modest funding available and, second, positioning CAN to have a ready source of initiatives to launch when a larger body of funds becomes available.

The participants discussed sources for gathering research ideas. Ginsburg recalled the Big Think meeting convened by the NIH director a few years ago; many ideas were gathered from academia and industry. The list developed through that meeting might be a source of ideas for CAN. In any event, the Big Think template could be an “idea-generation platform.” Austin volunteered to collect the input garnered at the Big Think meeting and to learn more about the sources of Big Think ideas.

Lewis-Hall advised undertaking a landscaping exercise as part of the CAN Review Board’s continuing work. Per the NCATS mission, landscaping should not be by disease category. She recalled the landscaping exercise conducted by the Institute of Medicine (IOM) that was quite general in its scope. The IOM identified areas for improvement in translational science and therapeutics development, then overlaid those needs with the names of individuals and organizations that were active in the various spaces. Lewis-Hall mentioned the IOM Innovation Collaborative and the IOM Forum on Drug Discovery, Development and Translation, as well as ongoing efforts to conduct a mega-landscaping exercise to identify areas of gaps or unmet needs. Lewis-Hall volunteered to try to get additional information on the IOM’s landscaping exercises, and she asked that others with access to similar efforts provide information if possible.

A motion to request that that NCATS staff develop a list of “straw men” or “hot topics” for the CAN Review Board to consider as research initiatives was made and seconded. The motion was passed by voice acclamation, with no abstentions or nay votes.

VII. WRAP-UP AND FUTURE DIRECTIONS

Lewis-Hall reviewed next steps:

1. Austin and his team at NCATS will assemble a list of research ideas, including recommendations from the Big Think meeting, for consideration as “straw men” at the January 2014 joint meeting.
2. Austin and his team at NCATS will learn more about how ideas were collected for the Big Think meeting, including the template used.
3. The CAN Review Board will consider conducting a “mini-landscaping” exercise to garner ideas about potential research projects.
4. CAN members who have access to the IOM’s and other entities’ landscaping exercises on research needs are requested to bring them for discussion.

Ginsburg closed by saying that the suggestions of the CAN Review Board will form a path forward to the January meeting, and the research ideas that will evolve could serve as a bridge between CAN goals and the limited funds available. Austin thanked Lewis-Hall, Ginsburg, and the entire CAN Review Board.

ADJOURNMENT OF MEETING OF THE CAN REVIEW BOARD

Lewis-Hall adjourned the CAN Review Board meeting at 1:45 p.m. ET.

CERTIFICATION

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

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

Date

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

Date