

**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

January 16, 2014

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 January 16, 2014, in Conference Room 10, Building 31, on the National Institutes of Health (NIH) main campus. Christopher P. Austin, M.D., NCATS Advisory Council 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, Ph.D., M.S., Acting Director, NCATS Office of Grants Management and Scientific Review

Council Members

Margaret A. Anderson, M.A.

Jorge L. Contreras, J.D.

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

Louis J. DeGennaro, Ph.D.

Mary L. Disis, M.D.

Frank L. Douglas, Ph.D., M.D. (by
telephone)

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

Eric D. Kodish, M.D.

Freda C. Lewis-Hall, M.D. (by
telephone)

Bernard H. Munos, M.B.A.

Franklyn G. Prendergast, M.D., Ph.D.

Todd B. Sherer, Ph.D.

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

Paul G. Yock, M.D.

Representative Members

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

Robert I. Tepper, M.D.

Ex Officio Member

David Atkins, M.D., M.P.H., Department of Veterans Affairs

CAN REVIEW BOARD MEMBERS PRESENT

Chair

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

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.

Jorge L. Contreras, J.D.

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

Louis J. DeGennaro, Ph.D.

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Lawrence A. Soler, J.D.

Myrl Weinberg, M.A.

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Robert I. Tepper, M.D.

Ex Officio Member

David Atkins, M.D., M.P.H., Department of Veterans Affairs

INVITED PRESENTERS

W. Charles Huskins, M.D., M.Sc., Mayo Clinic

OTHERS PRESENT

Ronald J. Bartek, Friedreich's Ataxia Research Alliance

Harold Lee Brayman, Waters Corp.

Jason Ezzelle, PPD

Petra Kaufmann, M.D., M.Sc., National Institute of Neurological Disorders and
Stroke

Anastassios C. Koumbourlis, M.D., M.P.H., Children's National Medical Center

Andrew Peck, Waters Corp.

Sara Reardon, *Nature*

Michelle Rodrigues, M.B.A., SRI International

Rachel Tabakman, University of Maryland, Baltimore

York Tomita, Ph.D., Food and Drug Administration

Katherine Weber, Ph.D., American Chemical Society

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 fifth meeting of the NCATS Advisory Council. He advised those present that Dr. Lewis-Hall would open the sixth meeting of the CAN Review Board when she called in by telephone. He reminded attendees that the open session was being videocast.

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

The minutes of the joint meeting on September 16, 2013, were approved as written.

Dr. Tagle asked council members to sign the Confidentiality Agreement. He also announced that the next joint meeting of the NCATS Advisory Council and the CAN Review Board would be held on May 16, 2014. Council members will receive their travel reimbursement forms in advance of that meeting.

Dr. Austin introduced Dr. David Atkins, director of Health Services Research and Development at the Department of Veterans Affairs (VA), as an ex officio member of the Advisory Council and CAN Review Board. Austin remarked that NCATS has several mutual and overlapping clinical interests with the VA.

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

Dr. Austin welcomed Pamela McInnes, D.D.S., MSc. (Dent.), who became the NCATS deputy director on January 12, 2014, and Dorit Zuk, Ph.D., who will serve as director of the NCATS Office of Policy, Communications and Strategic Alliances starting January 26. Zuk then spoke about a few highlights of her career, including her four years of service as a science policy advisor in the NIH Office of the Director, and her seven years of work as a journal editor before that, most recently of *Molecular Cell*.

Austin announced the retirement of Stephen C. Groft, Pharm.D., effective February 8, 2014. Groft is leaving a 30-year legacy of advancing rare diseases research and improving the lives of patients with these conditions. McInnes will serve as acting director of the Office of Rare Diseases Research (ORDR) during the search for a new director.

Austin said that the recruitment for the position of scientific director of the Division of Pre-Clinical Innovation (DPI) is under way. In addition, NCATS continues to consider eligible candidates for the position of director of the Office of Grants Management and Scientific Review (OGMSR). McInnes currently is serving as the acting director of OGMSR.

Austin told the group that, if passed, the new federal “omnibus” fiscal year (FY) 2014 budget will return the NIH budget to nearly pre-sequestration levels. The entire NCATS budget for FY 2013 from all sources was \$615.9 million. If the Consolidated Appropriations Act 2014 passes as expected on January 18, all funding for NCATS programs will be included in NCATS’ \$633 million appropriation.

Regarding NCATS’ communications activities, Austin noted that NCATS’ disadvantage is that most people do not understand the term “translational science.” However, he said he hears much less skepticism about NCATS from external audiences than he did a year and a half ago. Austin said this change is thanks in part to [the NCATS overview video](#) and other communications efforts. NCATS also has received favorable coverage in mainstream publications, including *The New Yorker* and *Wired*.

Austin highlighted two pieces of legislation of interest to NCATS: the [Modernizing Our Drug and Diagnostics Evaluation and Regulatory Network \(MODDERN\) Cures Act of 2013 \(H.R. 3091\)](#), a recently reintroduced House bill, and the [National Pediatric Research Network Act of 2013](#), signed into law in November 2013. He mentioned that NCATS has participated in congressional briefings on pulmonary hypertension and the innovation pipeline.

Austin also reported on a new partnership between NCATS, the National Eye Institute and Organovo to create 3-D, functional retinas using a NovoGen Bioprinting platform that will be housed at DPI.

Austin provided several updates related to the Clinical and Translational Science Awards (CTSAs) program:

- NCATS awarded 15 new CTSAs on September 30, 2013, including a first-time CTSAs award to Dartmouth College.
- NCATS established an Advisory Council Working Group in December 2013 to work on the [Institute of Medicine \(IOM\)’s report on the CTSAs](#). The working group comprises experts in topic areas covered by the CTSAs program, and two of the three co-chairs (Dr. Disis and Dr. Weir) are NCATS Advisory Council members. At the May 2014 meeting of the NCATS Advisory Council, the working group will report on its efforts to devise success metrics — an IOM recommendation — for the CTSAs program.
- In December 2013, NCATS disbanded the CTSAs Consortium’s Steering Committee and Executive Committee and established a new NCATS Steering Committee following the IOM’s recommendation of a more streamlined system of oversight for the consortium. The committee is chaired by Elaine Collier, M.D., DCI acting director, and vice-chaired by Disis; members include Austin and diverse CTSAs representatives. The NCATS Advisory Council will hear more about the work of the Steering Committee at upcoming meetings.

Austin then provided several recent highlights of DPI work:

- Staff from DPI's Probe Development Program [published a collaborative study](#) in *Nature Communications* on the first small molecule agonist of RXFP1. NCATS is working on an agreement with a large pharmaceutical company to develop this agonist further. This project is just one of 200 ongoing collaborations between the Probe Development Program and outside investigators.
- DPI has successfully implemented genome-wide RNAi screening, a difficult challenge. DPI investigators and their collaborators [published a letter](#) in *Nature* that demonstrated the use of high-throughput RNAi screening to identify regulators of parkin upstream of mitophagy. The collaborators also [deposited their data](#) in the first public RNAi screening database, a major resource that will open up new avenues of research. Austin will arrange a presentation on the RNAi screening program at the next Advisory Council meeting.
- In partnership with Sage Bionetworks, NCATS and several collaborators in the Tox21 Consortium launched a set of two public challenges to analyze the vast amount of Tox21 data and to generate predictive algorithms. The winning group will publish its results in *Nature Biotechnology*. In addition, DPI and the Environmental Protection Agency have deposited the results of Tox21 screening into PubChem.
- A collaborative clinical trial of a centrally administered cyclodextrin for Niemann-Pick disease type C1 began at the Clinical Center in September 2013, facilitated by NCATS' Therapeutics for Rare and Neglected Diseases (TRND) program. A [10-part investigative series](#) in *The Wall Street Journal* described the collaboration between scientists and families of patients that led up to this trial.
- The Bridging Interventional Development Gaps (BrIDGs) program has announced several new projects, including investigations into acute radiation syndrome, beta thalassemia and cardiac arrest-induced acute brain injury.

Austin also provided updates on several other NCATS programs:

- ORDR has released funding opportunities for the Rare Diseases Clinical Research Consortia and for that consortium's Data Management and Coordinating Center. The Advisory Council will review these applications at its next two meetings.
- ORDR also is involved in several activities in the area of medical devices, including the trans-NIH Initiative for Biomedical Innovation, which is focused on medical devices, and, with the Food and Drug Administration (FDA), a needs assessment of medical devices for rare diseases.
- The Tissue Chip for Drug Screening program, funded in part by NCATS, is prepared to transition to the second stage of funding in 2014. Several publications have come out of the program recently, including a [special supplement](#) to volume 4, issue 4 of *Stem Cell Research & Therapy*.
- Several of the nine projects funded in 2013 through the New Therapeutic Uses program have begun human trials. Christine Colvis, Ph.D., NCATS program director, is working with the other NIH sponsors to secure a new set of compounds for the next stage of the program.

- The Extracellular RNA Communication trans-NIH initiative, led in part by NCATS, has funded several grants to examine the potential of extracellular RNA to serve as a therapeutic agent or as biomarkers. One such project showed promising results in identifying the role of secreted miRNA in promoting myelination and reducing oxidative stress.

Austin then described four topics under discussion at the most recent NIH Leadership Forum (a meeting of NIH Institute and Center [IC] directors and senior leadership), which was held the previous week:

- *An ongoing program to improve the structure of NIH scientific review.*
- *Alternative models for supporting science.*
- *Core facilities.*
- *Revising the investigator biosketch for grant applications.*

The group discussed the information provided by Austin. Dr. Sherer noted the difficulty of predicting the success of a project and remarked on the importance of program staff in controlling the variability of funding practices across study sections. Austin responded that NCATS is working to identify novel metrics of productivity for its grants. Dr. Kodish added that some ICs ask these borderline applicants to cut their budgets in order to be funded.

Dr. Douglas asked about the effect of a revised grant application review process on the tenure process. NCATS and the CTSAs are discussing this, Austin said. Trainees are concerned that participating in team science will result in less-impressive resumes, so it is important that NCATS and CTSAs develop different measures of success for translational scientists.

Dr. Beall asked about royalties for NCATS inventors. Lili M. Portilla, M.P.A., acting director, NCATS Office of Policy, Communications and Strategic Alliances, explained that the inventors receive a percentage of royalties, and the NIH IC receives the rest. She said she hoped to be able to work more closely with the NIH Office of Technology Transfer on these issues.

Mr. Munos said that some of his company's more innovative applications are rejected for funding due to the use of review criteria that he sees as irrelevant. Austin stated that in-house review of NCATS-funded grants would be helpful in addressing such problems.

IV. CAN REVIEW BOARD REPORT ON OTHER TRANSACTIONS: Freda Lewis-Hall, M.D., Chief Medical Officer, Pfizer

Dr. Lewis-Hall opened the sixth meeting of the CAN Review Board. She began by discussing the overlap between [NCATS mission](#) and the duties of the CAN Review Board, as described in its [charter](#). There are several opportunities available for the Board to

accelerate the work of NCATS, including the funding of research and providing outreach to important research partners.

Dr. Austin advised that the CAN budget is nearly the same as it was in 2013, and all of it is obligated to ongoing projects. However, Austin said it may be possible to make up the difference in funding to the Tissue Chip program if the CAN Review Board recommended moving \$2 million in FY 2014 funding from that program to a different program. It is faster to fund programs through “other transaction authority” (OTA) than through traditional grants, he said. NCATS again will request an increase for CAN in FY 2015, and the CAN Review Board should begin to think about ideas for FY 2015 projects.

Lewis-Hall reported to the CAN Review Board members on four types of projects that could benefit by OTA support from CAN:

- *Ongoing NCATS projects.* NCATS will provide the Board with a list of projects.
- *Ongoing [Big Think](#) projects.* The CAN Review Board is gathering information on this and the following two projects.
- *Outside projects that align with CAN’s charter.*
- *Projects that could be funded in partnership with other organizations.*

Dr. Sherer recommended that the Board support the most innovative research. Areas meriting funding might include outreach, regulatory support or registry projects in partnership with patient groups. Currently, there is no such large-scale coordination, and it could have a great impact. Austin asked the Committee on Patient Engagement to consider this suggestion and provide the CAN Review Board with its recommendations. Lewis-Hall agreed that it will be important to fund projects that have a disproportionately large impact, given the small amount of money available. Mr. Soler concurred with Sherer and advised that CAN use its funding in a way that NIH cannot. A partnership would demonstrate CAN’s value and possibly inspire future funding increases.

Lewis-Hall mentioned that representatives from the Defense Advanced Research Projects Agency (DARPA) recently discussed with the CAN Review Board DARPA’s experience with OTA. In particular, DARPA representatives said that OTA provides the opportunity to adopt commercial practices (which can reduce costs); exercise flexible intellectual property practices; and share costs, knowledge and resources between organizations.

In the ensuing discussion, Board members made the following points or suggestions:

- Austin requested the Board’s guidance on the ways in which NCATS can be most beneficial to the patient community. In response, Dr. Beall remarked on the difficulty of capturing patient data in rare diseases. Beall suggested that CTSAs create a shared system that would make data collection easier and de-risk involvement for pharmaceutical companies. Sherer and Lewis-Hall agreed with Beall’s assessment and remarked also on the redundancy and incompatibility

between systems created by different organizations. Sherer mentioned [Research Match](#) as one good existing option, but he suggested disease-specific overlays to motivate participation by particular patient groups.

- Dr. Davis spoke of the onerous reporting requirements that discourage the conduct of clinical trials. She remarked on the need for electronic clinical trials systems, such as one created at the University of Pennsylvania, that track patient data over time and generate adverse event reports in the correct formats.
- Dr. Groft promised to update the Council on the current status of the Agency for Healthcare Research and Quality's [Registry of Patient Registries](#) (RoPR), which recently was inactive.
- Ms. Anderson remarked that she would like NCATS' initiatives to transcend the boundaries of individual programs or organizations. Matching NCATS infrastructure with needs in clinical research will be a victory for the Center.

Lewis-Hall continued with her discussion of the meeting with DARPA. Key to DARPA's success with OTA is its identification of experienced project managers who can articulate the program vision to key stakeholders and the broader community. DARPA identifies awardees and provides funding only after building the program staff.

Lewis-Hall asked members of the CAN Review Board to consider how their idea of a patient registry could be implemented, given the limited funding. It is difficult to gather the expertise needed to create such a resource. She said that DARPA suggested that the Board consider how to identify the projects with the largest potential impacts and how to allow them to evolve as needed.

Further discussion included the following questions and comments:

- Mr. Soler asked whether NCATS, through CAN, could help convene NIH experts to participate in discussions with FDA, the pharmaceutical industry and patient groups, since FDA staff is often overwhelmed by the high-pressure decisions they face. He said that such participation would have accelerated the FDA's decisions on a project he worked on with the device group. Austin replied that this type of activity falls under the CAN authorization.
- Dr. Yock advised that several FDA sections are interested in particular breakthrough treatment pathways. Through CAN, NCATS could promote NIH partnerships with FDA as a means of advancing these FDA priorities.
- Davis remarked on the need for informatics tools that enable researchers to examine de-identified electronic health records to assess a proposed trial's feasibility. Support for bioinformatics companies through the SBIR program or a special NIH ombudsman would be a high-impact investment to facilitate clinical research.
- Dr. Atkins noted that RoPR was being re-competed. He also remarked on the potential for overlap between patient registries and clinical data exchanges. A common interface for these two systems would enable feasibility testing but not

patient contact. However, patient groups could help recruit these patients. Austin responded that the CTSA program had considered creating a clinical data registry. He asked how CAN's small amount of money could contribute.

- Mr. Munos suggested pursuing Yock's suggestion to facilitate NIH-FDA collaborations. Without a specific focus, CAN programs and initiatives may default to the same activities that NIH has pursued in the past. The CAN Review Board, he suggested, would find it easier to make good recommendations for which projects to support by first agreeing to focus on spurring the development of "breakthrough drugs," which he said should be carefully defined.
- Lewis-Hall stated that identifying barriers that hinder particular therapies from becoming breakthroughs would be valuable. For example, the tissue chip could revolutionize toxicity testing, a process that at present can hinder translation. Identifying these types of gaps would also provide a focus for CAN.
- Dr. Mahadevia remarked that CAN's greatest impact would come from building a resource for the research community, for example, a repository for safety data, rather than funding a specific activity.
- At Austin's request, Dr. Tepper spoke of the research community's need for well-characterized reagents. In fact, variability in off-target effects of reagents from different sources may explain some of the variability in published research results. If NCATS were to provide such a resource, along with an open database to house the results of studies, the research community would gain an important research resource, and data quality would improve.

Lewis-Hall thanked participants for their ideas on opportunities for projects and partnerships. The CAN Review Board should continue to collect and assess the ideas presented during the meeting, those that will be provided by NCATS, others already provided by Board members, and ideas identified by the IOM and patient advocacy organizations including FasterCures.

V. INTRODUCTION OF DEPUTY DIRECTOR MCINNES: Pamela M. McInnes, D.D.S., MSc. (Dent.), Deputy Director, NCATS

Dr. McInnes provided a summary of her background, training and experience, which include training in dentistry and materials science and research leadership positions at the National Institute of Allergy and Infectious Diseases and the National Institute of Dental and Craniofacial Research. She said her new role at NCATS is the culmination of her career-long passion for promoting product development. McInnes suggested that NCATS could lead NIH in creating novel clinical research designs, including patient-centered research. She thanked Austin for the opportunity to serve as deputy director.

McInnes said that she and James H. Doroshow, M.D., head of the National Cancer Institute's Oxidative Signaling and Molecular Therapeutics Group, had co-chaired the NIH Clinical Trials Working Group. The group was focused on improving the process of clinical trials at NIH, as recommended by an IOM report on the National Cancer

Cooperative Groups. The working group submitted recommendations to the NIH director for solving problems such as the loss of unpublished data, a lack of good training in clinical practices, and the proliferation of underpowered, repetitive investigator-initiated trials. McInnes remarked on the importance of high data quality, whether or not the results of a trial are positive.

VI. PROJECT OPPORTUNITY/NEED ANALYSES IN TRANSLATIONAL SCIENCE: Christopher P. Austin, M.D., Director, NCATS

Dr. Austin reviewed the language related to CAN in the “omnibus” federal budget bill for FY 2014 that was expected to be signed into law shortly. Austin asked CAN Review Board members to keep in mind that the bill requires NIH to describe the relationship of CAN activities to other NIH programs and the projected termination dates.

Austin reviewed four previous exercises at NIH that might help the CAN Review Board consider potential funding areas.

First, he described the ongoing IOM Drug Forum Visioning Process, which aims to identify gaps in the priorities and activities of organizations involved in drug discovery and development. Several CAN Review Board members are involved in the process, which will be completed in the next several months. The results will be shared with the CAN Review Board.

Second, Austin reviewed the 2010 NIH Common Fund Big Think, in which a panel of experts recommended ways for the NIH Common Fund to help solve the most pressing problems in clinical research. Austin asked the Board to consider which of the following Big Think recommendations could be catalyzed by CAN funding:

- Provide a “safe haven” for clinical research that frees investigators from some of the regulations that hamper them.
- Provide prizes to investigators who participate in clinical research or provide service to study sections. Austin suggested that such awards might be small (\$10,000 to \$25,000) but could have a great impact.
- Recognize the FDA approvals of grant applicants, not just their high-profile publications. Austin noted that this recommendation was one of the rationales for the NIH Leadership Forum to consider changing the biosketch format.
- Provide a common application for NIH funding and FDA approval.
- Revise rules on conflicts of interest for the participation of patent holders in trials. Austin noted that this must be undertaken on a higher level than NCATS or even NIH.
- Provide access to failed drug candidates, expand the Bridging Interventional Development Gaps (BrIDGs) program, and form a national network to select the top drug candidates for trials.

- Reinvigorate the pharmacological sciences in medical schools and provide more robust training for scientists who study human biology. Austin noted that this is one of the training areas on which the CTSA program focuses.
- Create tools to better understand human biology. Austin remarked that the CTSA program is creating tools for integrative biology and informatics.
- Improve the efficiency of the collection and analysis of human samples. Austin said the CTSA program is addressing this problem.

Third, Austin presented the five ideas that NCATS considered nominating for support from the 2013 Common Fund (below). He also suggested that the CAN Review Board keep in mind the [five questions for nominations to the Common Fund](#) as it considers the projects it might recommend.

- *In vitro* assay models to predict *in vivo* biology and toxicity.
- Diagnostic reagents and assays for rare and neglected diseases.
- Somatic cell models generated from stem cells.
- A public-private consortium to leverage Phase II pharmaceutical assets that have failed for efficacy or business reasons (this would be a larger, self-sustaining variant of the New Therapeutic Uses program).
- An innovative medical device initiative, similar to the TRND program, that would create partnerships among industry, academia and government agencies to develop biomedical devices.

Fourth, Austin highlighted several ideas that investigators commonly suggest to NCATS:

- Interoperable platforms for patient registries or phenotyping using a common ontology and procedures.
- Defining the pathway for biomarker identification, validation and early coordination for therapeutic development.
- A national library of human specimens, which may be too challenging now, but could be a useful and achievable alternative.
- Development and dissemination of induced pluripotent stem cell-driven efficacy models.
- Development and dissemination of computational modeling tools.
- Imaging.
- Devices and sensors to detect clinical outcomes.
- Multiplex, limit-of-detection and point-of-care diagnostic applications.

Austin asked the CAN Review Board to nominate ideas that could be funded in FY 2014 using the form that NCATS already had sent to Board members. The nominated ideas will be presented at the next CAN Review Board meeting.

Dr. Sherer asked what could be done to gain access to the less commercially promising, but still well-characterized compounds owned by pharmaceutical companies, which might be valuable for target validation and cross-disease laboratory research. Austin

replied that although this is a complex issue in the absence of revenue potential, NCATS would continue to encourage companies to share these data.

**VII. RARE DISEASES: THEN AND NOW — 30 YEARS OF ADVANCEMENTS:
Stephen C. Groft, Pharm.D., Director, ORDR, NCATS**

As a preface to Dr. Groft's presentation, Dr. Austin reviewed some highlights of Groft's career, which began in a drugstore pharmacy.

Groft presented a historical view of research on rare diseases and the development of orphan products, especially the alliances between public and private partners that led to the passage of key legislation, including the Orphan Drug Act of 1983 and the Rare Diseases Act of 2002.

One barrier to be overcome in future efforts is the dearth of accurate prevalence data on rare diseases. As many as 25 million people in the United States are suffering from one of more than 6,500 rare diseases. In addition, all rare diseases differ from each other and have unique product development trajectories. Although NIH supports more than 9,400 projects each year on rare diseases and orphan drugs, the field would benefit from NCATS support to collect more data on the incidence and prevalence of rare diseases.

Research activities in rare diseases are growing: In 1983, 26 drugs were designated by the FDA as orphan products and only two drugs were approved for rare diseases. In 2013, there were 258 designations as orphan products, and more than 450 drugs were available to treat rare diseases. Groft underscored the importance of incentives (such as market exclusivity, priority-review vouchers, tax credits and grant funding) to stimulate the development of treatments for orphan diseases. The most compelling of these incentives has been the FDA's protocol assistance to facilitate clinical trials.

Among the activities that have led to the increased emphasis on rare diseases and orphan products are research partnerships among globalized patient advocacy groups, industry and academic researchers; publicity about cutting-edge research and access to information on the Internet; a profitable business model; increased interest from NIH in translational research; improved capabilities in bioinformatics and genomic-based medicine; and the success of the Rare Diseases Clinical Research Network (RDCRN) in enrolling patients with rare diseases in trials.

Challenges remain, however. Groft said that it is still difficult for some patients to obtain a diagnosis and gain access to clinicians who focus on rare diseases. The CTSA, the RDCRN, and other networks might be well-suited to tackle this problem. Other challenges identified by Groft included recruiting patients and interested investigators, attracting public and private funding, demonstrating the value of natural history studies and patient registries, setting up central institutional review boards (IRBs) for multisite

studies using common protocols, designing clinical trials for small populations, and making the cost of orphan drugs affordable. However, optimism is not unreasonable, especially in some fields, because the amount of research activity in rare diseases and orphan products continues to increase, and many treatments now are in development.

Groft concluded by saying there is genuine hope for individuals with rare diseases. NCATS offers excellent opportunities for finding treatments and improving people's lives. He acknowledged his ORDR staff and expressed his gratitude to the patient groups that are committed to helping their constituencies. He also thanked Austin, who presented him with a plaque in honor of his 44 years of service to the U.S. government.

VIII. PEDIATRIC STUDY-RESEARCHER MATCHING: W. Charles Huskins, M.D., M.Sc., Professor of Pediatrics, Mayo Clinic

Dr. Huskins noted that the Pediatric Point Person Project was an initiative of the [CTSA Consortium Child Health Oversight Committee](#). The project was highlighted in the IOM's report on the CTSA program.

Point Persons (PPs) were research professionals at CTSA sites charged with reviewing and responding to collaborative opportunities in clinical research on child health using a central source in a structured format. The PPs also directed opportunities to the appropriate local investigators.

A one-year pilot project launched in 2012 was followed by an evaluation in which all the PPs at the 55 CTSA sites with child health programs were surveyed in order to compile a qualitative assessment of the PP process. Among other findings, the evaluation revealed that PPs typically were investigators themselves, with nearly three-quarters holding an M.D., a Ph.D. or both. Two-thirds of the PPs had been appointed by the CTSA Principal Investigator; however, only 15 percent received salary support for the activity and only 17 percent received administrative support. Forty-three percent reported receiving voluntary assistance from other research professionals.

For the PP project, protocol sponsors or proponents provided information in a structured form with fields for a study synopsis, target population, study objectives, key inclusion and exclusion criteria, enrollment details, and contact information for the sponsor or proponent. When a protocol information form came in, it was forwarded to the PP, who disseminated it to investigators at the local institution.

During the one-year pilot, 24 protocol information forms were submitted. Contract research organizations (CROs) submitted 15 of the forms, industry provided six, and individual investigators submitted two. Forty of the 55 CTSA institutions with child health components provided a total of 290 responses to these clinical research opportunities. Of these responses, nearly 75 percent indicated an interest in, or a need

for, more information. For the 15 protocols submitted by CROs, contact was made with 69 CTSA investigators, including 39 investigators new to the CRO.

In all, 16 CTSA institutions were involved in the selection, start-up or enrollment of at least one multisite clinical study as a result of the Pediatric Point Person Project. Huskins observed that early implementation of the PP process was by sponsors seeking to add new sites to ongoing clinical studies that were struggling with lagging enrollment. When protocols subsequently were presented, investigators were able to provide feedback that identified problems with the protocols as the reason for poor accrual.

The PP survey revealed that the pilot project led to better awareness of planned studies, and the central resource made it easier to disseminate information to investigators and to stimulate new collaborations. The challenges included identifying appropriate investigators, a lack of structured institutional support, highly specialized protocols and short response times for investigators.

Huskins reported that the project succeeded as a proof-of-concept to enhance connections between sponsors and potential investigators for multisite studies and to provide value added by identifying experts who could critique poorly performing clinical studies. Similar to other efforts currently under development through the CTSA networks (e.g., IRB reliance networks, streamlined consent forms, and biostatistical and design assistance), the project has the potential to improve the efficiency of clinical and translational research.

IX. REPORTS OF THE COUNCIL SUBCOMMITTEES

Partnerships with Pharmaceutical and Biotechnology Companies and Venture Capital Firms — Ankit A. Mahadevia, M.D., M.B.A., and Freda Lewis-Hall, M.D.

Dr. Mahadevia reported that this subcommittee's activities involve facilitating broader strategic recommendations and optimizing existing programs that already are showing success.

The subcommittee supports the idea of carrying out a systematic needs survey of pharmaceutical and biotechnology industry leaders. Subcommittee members conducted an informal survey of their colleagues in industry to see how business entities could best support NCATS. The survey responses reflected knowledge of NCATS and its programs, but also indicated that additional means could be used to deliver messages about NCATS activities and encourage more people in industry to become involved in NCATS initiatives. The subcommittee realized that additional external representatives could provide it with more diverse perspectives and identify additional ways to disseminate NCATS' messages.

During the May 2014 meeting, the subcommittee will present more detailed information and outline future plans. The subcommittee already is reaching out to potential new members in the NCATS Advisory Council, CAN Review Board and industry. Mahadevia asked Dr. Yock to suggest some potential new subcommittee members.

Medical Technologies (Devices and Diagnostics) — *Paul G. Yock, M.D., and Frank L. Douglas, Ph.D., M.D.*

Dr. Yock observed that the devices and diagnostics sectors seem to be a blind spot at NCATS, and yet devices and diagnostics represent about 40 percent of the life-sciences market. It is cheaper and faster to provide technologies to patients than it is to provide drugs to them.

Because the fields of devices and diagnostics are not highly represented in NIH training programs, a landscape analysis would be worthwhile. Notably, the National Institute of Biomedical Imaging and Bioengineering is very interested in such an analysis. The subcommittee is compiling questions for the analysis on (1) the proportion of total funding directed toward the development of medical technologies and diagnostics, and (2) the degree to which medical technologies are covered in NIH-supported education and training. It will take three to six months to finalize these questions. Yock added that the subcommittee also is interested in examining opportunities for industry collaborations.

Dr. Douglas added remarks on ongoing discussions about the similarities and differences in clinical research and translation for molecular therapeutics and medical technologies.

Dr. Austin remarked on the analysis underpinning a [2010 paper on research and development productivity](#) and asked whether a similar analysis for medical technology would be possible. Douglas replied that, although interesting, such an analysis might be impossible because the device field is so large and lacks a robust system for postmarketing surveillance.

In response to a question from Dr. Sherer, Yock said that the subcommittee is including drug–device combinations and also regenerative-type platform technologies.

Patient Engagement — *Margaret Anderson, M.A., and Myrl Weinberg, M.A.*

According to Ms. Anderson, patient engagement is an important, but daunting, activity in which NCATS could become involved. The Patient Engagement Subcommittee could help rationalize patient engagement or support infrastructure for patient registries, among other activities. The subcommittee made the following suggestions:

- While many sophisticated disease foundations are represented on the Advisory Council, many other organizations have a smaller size and impact. NCATS could help some advocacy groups and foundations that already engage with patient

- groups. However, many foundations are unclear about how to engage with NCATS; greater clarity of purpose is needed on both sides.
- An environmental scan across the different NCATS funding streams — especially the CTSA program — could reveal existing initiatives for patient (community) engagement.
 - NCATS could work more closely with other ICs. For example, NCATS could have a role in establishing infrastructure or best practices for patient engagement.

Dr. Prendergast asked for a more specific definition of “patient engagement” and suggested that NCATS clarify what it would like to achieve. He also recommended avoiding redundancy with social media platforms, such as [Smart Patients](#) and [Patients Like Me](#).

Disis suggested extracting information from CTSA grant renewals about the interactions between CTSA and patient groups. Follow-up with advocacy groups would provide a second perspective on a given CTSA-patient group interaction. She added that this information also could be used to draft best practices. Prendergast expressed concern that the CTSA’s information about community engagement might be pro forma and insubstantial, and he wondered whether CTSA’s use metrics to evaluate this engagement. Clear expectations of engagement would be useful.

Dr. Austin said the development of general and catalytic models for patient engagement would be the best fit for NCATS. The focus should be on the NCATS projects/programs that could help meet patients’ needs.

Prendergast asked how to learn more about what patients want to know about the research on their condition. CTSA institutions and patient groups focused on orphan diseases could serve as sources of ideas about best practices in patient engagement.

Dr. Beall commented on the need for creating a culture of participation in clinical trials and helping people understand these trials. According to Dr. Sherer, one main challenge for NCATS lies in trying to find a disease-agnostic approach for educating people about clinical trials and encouraging their participation in them. What works for some groups might not work for other groups. Dr. Davis commented on the [NetWellness](#) website developed by Ohio State University, which provides information on clinical trials. Through the “Ask an Expert” feature, physicians respond to questions that individuals submit through the site. Sherer suggested that a niche for NCATS might exist in terms of developing best practices for elucidating the risk-benefit concept in clinical science.

Mr. Soler emphasized the importance of ensuring that NCATS undertakes patient engagement activities to fill a specific need. He recommended asking foundations and other groups about their perceptions of patients’ needs. Dr. Groft remarked that the RDCRN has access to 95 patient advocacy groups; he also said that NCATS program officers have conducted surveys about patient engagement.

Anderson said the subcommittee will have more information to share at the May 2014 meeting.

X. CONCEPT CLEARANCE: PLATFORM DELIVERY TECHNOLOGIES FOR NUCLEIC ACID THERAPEUTICS: P.J. Brooks, Ph.D., Health Scientist Administrator, ORDR, NCATS

Dr. Brooks said that although his focus is on rare diseases, the ability to deliver nucleic acid therapeutics has far-ranging implications. This concept clearance involves issuing a Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) Funding Opportunity Announcement for platform technologies that deliver nucleic acid therapeutics. Although inserting genes into human cells in tissue culture now is routine, these capabilities have not been turned into effective treatments due to the technical challenges and threat of toxicity inherent in delivering nucleic acids into human cells. Platform technologies supported under this potential SBIR/STTR mechanism must be disease-agnostic and could include siRNAs, microRNAs, DNAs and mRNAs. Such a platform could have a major impact on the translation of treatments for monogenic disorders, cancer, infectious diseases and other conditions.

The following points were made in the discussion following Brooks' presentation:

- Dr. Prendergast noted the potential ambiguity in the terms "specific cell types" and "multiple diseases" in the concept. Brooks clarified that a delivery system for neurons, for example, could apply to a host of neurologic diseases. The platform should, in principle, be applicable to different nucleic acid sequences.
- Prendergast noted that it is relatively easy to deliver nucleic acids to the liver, and he also stated that the ability to deliver nucleic acids to certain tissues could vary according to disease state.
- Dr. Beall cautioned that much of the field is already covered by broad patents, thereby limiting the space for innovation.
- Dr. Tagle said that the funding amount and funding mechanism have yet to be determined, and that Dr. Brooks will take the Council's comments into account.

Dr. Austin called for a vote to approve the concept clearance. A motion was made and seconded. The motion was passed by voice acclamation.

ADJOURNMENT OF JOINT MEETING

Dr. Tagle adjourned the meeting at 3:06 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 3:50 p.m. ET.

CERTIFICATION

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

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

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

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