Department of Health and Human Services
National Institutes of Health
National Center for Advancing Translational Sciences

25th Meeting of the
Cures Acceleration Network Review Board

Minutes of Virtual Meeting
December 14, 2018

The National Center for Advancing Translational Sciences (NCATS) Cures Acceleration Network (CAN) Review Board convened a virtual meeting, in open session, at 11 a.m. ET on December 14, 2018. G. Lynn Marks, M.D., CAN Review Board chair, led the meeting. In accordance with Public Law (P.L.) 92-463, the session was open to the public.

CAN REVIEW BOARD MEMBERS PRESENT

Chair

G. Lynn Marks, M.D., Senior Research and Development Advisor, Biomedical Advanced Research and Development Authority (BARDA), Office of the Assistant Secretary for Preparedness and Response (ASPR), U.S. Department of Health and Human Services (HHS)

Vice Chair

Ronald J. Bartek, M.A., Co-Founder and Founding President, Friedreich's Ataxia Research Alliance (FARA)

Executive Secretary

Anna L. Ramsey-Ewing, Ph.D., Director, Office of Grants Management and Scientific Review, NCATS, National Institutes of Health (NIH)

Board Members

Katharine Ku, M.S.
Richard Kuntz, M.D., M.Sc.
Geoffrey Shiu Fei Ling, M.D., Ph.D.
Brad A. Margus, M.B.A.
Valerie Montgomery Rice, M.D.
Megan O'Boyle
Harry P. Selker, M.D., M.S.P.H.
Anantha Shekhar, M.D., Ph.D.

Ex Officio Members

Christopher P. Austin, M.D., Director, NCATS
Rachel Ramoni, D.M.D., Sc.D., Chief Research and Development Officer, Office of Research and Development, U.S. Department of Veterans Affairs (VA Research)
Frank F. Weichold, M.D., Ph.D., Director, Critical Path and Regulatory Initiatives, FDA

OTHERS PRESENT

NCATS leadership and staff

I. CALL TO ORDER AND OPENING REMARKS: G. Lynn Marks, M.D., Senior Research and Development Advisor, BARDA, and Chair, CAN Review Board; Ronald J. Bartek, M.A., Co-Founder and Founding President, FARA, and Vice Chair, CAN Review Board

Christopher P. Austin, M.D., extended a welcome to the 25th meeting to CAN Review Board members and others participating by telephone or WebEx. He introduced the CAN Review Board chair and vice chair, G. Lynn Marks, M.D., and Ronald J. Bartek, M.A., who called the meeting to order.

II. MEETING RULES AND CONFIRMATION OF DATES FOR FUTURE NCATS ADVISORY COUNCIL AND CAN REVIEW BOARD MEETINGS: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, CAN Review Board

Anna L. Ramsey-Ewing, Ph.D., reviewed the procedures for the meeting. In the discussion sessions following the presentations, only CAN Review Board members would be able to participate verbally, and they would have to dial in to participate by phone.

Dr. Ramsey-Ewing said other participants could submit questions or comments using the Q&A box in WebEx, or they could send an email.

Dr. Ramsey-Ewing then confirmed the schedules for the meetings of the NCATS Advisory Council and CAN Review Board in 2019 and 2020:

- January 10, 2019 (virtual meeting)
- May 16, 2019
- September 19, 2019
- December 13, 2019 (virtual meeting; CAN Review Board only)
- January 16, 2020
- May 14, 2020
- September 17, 2020
- December 11, 2020 (virtual meeting; CAN Review Board only)

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

Dr. Austin gave a brief update on administrative matters, policy, and legislative and budget issues. He noted that the upcoming joint meeting in January will be convened by WebEx as an experiment. The hope is that participation would be easier for all members, especially those who would have to travel long distances to attend in person. Virtual meetings will also make content more readily accessible to the public.

Administrative Updates

Dr. Austin announced that Joni Rutter, Ph.D., has been appointed deputy director of NCATS. Dr. Rutter's training was in human genetics, and her familiarity with opportunities in genomic medicine dovetails with NCATS' work in translational science. She has been the head of science

for the *All of Us* Research Program since its inception, having previously served as director of the Division of Neuroscience and Behavior at the National Institute on Drug Abuse. She will attend the next joint meeting of the NCATS Advisory Council and the CAN Review Board and come on board as deputy director in January. Dr. Austin expressed his gratitude to Danilo Tagle, Ph.D., M.S., who has been serving as acting deputy director for the past six months.

Program Updates

- Launched in April 2018, the NIH HEAL (Helping to End Addiction Long-term℠) Initiative is a trans-NIH effort to advance national priorities in addressing the opioid crisis through science. Dr. Austin stated Congress added funding of $500 million per year to the NIH budget for the initiative. He then reviewed the spectrum of HEAL programs approximately a dozen IH Institutes and Centers (ICs) are undertaking. NCATS is leading or co-leading the program on pre-clinical screening platforms and novel drug development, as well as the Pain Management Effectiveness Research Network (ERN). Dr. Austin updated the CAN Review Board on NCATS' work on pre-clinical development of new chemical structures to modulate novel targets as part of the ASPIRE (A Specialized Platform for Innovative Research Exploration) initiative, which was launched by and partially funded as a CAN program.[1] The hope is that the 3-D platform paradigm will prove useful in research in the opioid addiction, overdose and pain space.
- Dr. Austin showcased the extramural NCATS ASPIRE Design Challenges (NOT-TR-18-031) to develop innovative and catalytic approaches aimed at solving the opioid crisis. This prize competition will reward innovators who come up with promising designs. Prototypes are not required, and innovators may compete in one challenge or all five. The total prize purse for each challenge is $500,000. The challenge will begin on December 31, judging will take place in the summer of 2019, and winners will be announced in August. Dr. Austin hopes that there will be a follow-on stage.
- The Pain Management ERN is an example of the clinical side of NCATS' participation in the HEAL Initiative. Dr. Austin explained how resources of the Clinical and Translational Sciences Award (CTSA) Program will be brought to bear on the opioid crisis. The purpose is to evaluate effectiveness, not efficacy, of pharmacologic and nonpharmacologic therapies for a broad range of pain conditions. Funded research programs will generate real-world evidence to guide practitioners who are treating patients but have only sparse data to determine what pain interventions to use. The CTSA Program's Trial Innovation Network (TIN) will provide coordination and support for the studies to ensure that data can be harmonized across trials. Dr. Austin said the time to respond to the Request for Applications (RFA-NS-19-021) will be short, given the critical need for nonaddictive pain treatments, and all applications must be submitted by February 11, 2019.
- Dr. Austin announced that NCATS' *Assay Guidance Manual* group, the National Institute of Neurological Disorders and Stroke, and the National Institute on Drug Abuse will convene a symposium on February 7–8, 2019, focusing on improving reproducibility of models for developing pain interventions. Interested parties should register by January 11, 2019.

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[1] Sittampalam GS, Rudnicki DD, Tagle DA, Simeonov A, Austin CP. Mapping biologically active chemical space to accelerate drug discovery. *Nat Rev Drug Disc.* November 2018:1–2. doi:10.1038/d41573-018-00007-2.

- Dr. Austin said that on December 5, tissue chips were part of the payload aboard a SpaceX mission to the International Space Station, where the astronauts unpacked the chips and placed them in a laboratory incubator. The tissue chips were then frozen for safekeeping until they can be used to study aging of the immune system.

Ongoing CAN Programs, Fiscal Year 2019
Dr. Austin listed the ongoing CAN research programs:

- 3-D bioprinting
- ASPIRE
- Biomedical Data Translator
- Rare diseases research
- Tissue Chip Program

Subsequent presentations and discussion focused on identifying new areas that might merit CAN support.

Discussion
Mr. Bartek asked about the CAN budget. At the last meeting, Dr. Austin said that the CAN budget went from a hard ceiling of $25 million last year to a soft ceiling of up to $80 million this year. However, Congress added only about $25 million to the budget, although it would allow NCATS to transfer programs to CAN so that CAN's special authorities could be leveraged. The additional funds did allow some new research activities, including a new rare disease initiative, aspects of the Biomedical Translator Program and part of the ASPIRE program. Dr. Austin asked the Review Board to identify areas of scientific need to capitalize on available funds to start new programs. Perhaps some concepts will prove well-developed enough to form the basis of research programs, while others will require workshops to flesh out ideas and work up budgets.

Geoffrey Shiu Fei Ling, M.D., Ph.D., said that he would like to hear more about the deliverables for NCATS initiatives. Compared with other ICs, NCATS is more about the process of science, meaning that traditional research milestones, such as published papers, might not apply to NCATS projects such as the design challenges and the upcoming symposium. What does NCATS expect investigators to produce? What do program officers anticipate in terms of deliverables when a project ends?

Rachel Ramoni, D.M.D., Sc.D., said that in an effort to focus on firm deliverables as outcomes at VA Research, she has been reviewing the organization's staff to identify people actively involved in portfolio management. Dr. Austin commented on efforts to recruit staff to undertake such an effort at NCATS, noting that some people in the Division of Pre-Clinical Investigation have already been identified to take on this challenge.

ACTION ITEM: Dr. Austin agreed to add Dr. Ling's idea to the agenda for the January meeting. During his retrospective on NCATS' scientific endeavors, Dr. Austin will address the question of "So what?"

IV. CAN PROGRAM UPDATE: NCATS BIOMEDICAL DATA TRANSLATOR PROGRAM: Christine Colvis, Ph.D., Director, Drug Development Partnership Programs, Office of the Director, NCATS

Christine Colvis, Ph.D., provided an overview and update of the CAN-funded Biomedical Data Translator, noting that NCATS anticipatesthat by revealing connections in existing data in terms of genes, proteins, clinical trial results and environmental exposures, it should be possible to accelerate treatment development for many diseases.

Background

The challenge is not only the sheer volume of information but also language differences across and within domains, which Dr. Colvis characterized as "crossing the chasm of semantic despair." Basic scientists often think at a molecular or cellular level, or the model organism level. The language they use is very different from the language used in the clinic, where the focus is on using clinical laboratory reports, signs and symptoms to diagnose disease and identify a therapeutic. Communication across the divide is not easy because of the different languages on the two ends of the bridge.

To bridge the chasm, new analytical tools, ontologies, data, algorithms, shared standards and access to high-quality data are needed. Machines are good at mining massive databases, searching, ranking, sorting and storing data. In fact, as long as a human directs a computer on how to rank and sort, it not only executes these tasks well but faster than a human worker. Of course, humans excel at intuitive reasoning, accurate natural language processing and visual reasoning, but both computers and humans are good at filtering and logical reasoning, as long as the computing algorithms are set up properly. For the Translator, the aim is to use the computer to perform ranking and sorting tasks, then marry the strengths of computers and humans to achieve a whole greater than the sum of its parts.

What sorts of questions would we want to ask of a system such as Translator? Dr. Colvis said that some queries would be "lookup" questions that can be answered readily using databases. Other questions (e.g., why, how, what if) require more abstract thinking. The goal for Translator is to work toward answering complex questions using a combination of computing and human power.

According to Dr. Colvis, the Translator program has just passed its two-year anniversary. The team has been identifying high-value data and locations of the data, performing quality control checks of data and the outputs from the system, looking for integration barriers, identifying the types of queries the Translator could handle and specifying requirements for building the Translator system.

Dr. Colvis emphasized that Translator is a high-risk endeavor. Failure is, in fact, an option, and NCATS wants the investigators to find the edge and identify ways to move forward when they fail. Another important facet of the Translator program is using a team approach, as the project is large, exceeding the capabilities of a single research team. The program would therefore benefit from employing a community approach to develop a highly robust system.

Dr. Colvis explained that a portion of the budget for Translator would apply CAN's Other Transaction Authority (OTA), which is not a contract, cooperative agreement or grant. The OTA confers a great deal of flexibility compared with other federal funding mechanisms. Both

individuals and organizations are eligible to apply, and requirements for applications and their reviews can be adjusted. Dr. Colvis said that projects awarded should be complementary to help avoid redundancy and maximize use of the available funds.

Dr. Colvis reported that Noel Southall, Ph.D., a program leader in the Division of Pre-Clinical Innovation at NCATS, has assembled a team of informatics scientists to manage and implement the Translator program. The investigators have embraced the opportunity to collaborate under the oversight of NIH intramural scientists. Nine teams are determining the feasibility of building Translator by focusing their efforts on data integration and analysis. The teams adopted the names of colors as their monikers rather than using institutions' or investigators' names. Team Purple is NCATS.

Update

Since the last time Dr. Colvis addressed the CAN Review Board, five new awards and several new related contracts have been awarded, and the teams have met in person seven times. For each meeting, between 80 and 100 peopleattended— a demonstration of a very high level of engagement, which is "both demanding and intoxicating", according to Dr. Colvis. Teams also meet by phone several times per week to focus on different aspects of the programs. It is a very intense process, but productivity is high.

Dr. Colvis shared information about a Translator success with bridging pre-clinical and clinical data by accessing the Columbia Observational Health Data Sciences and Informatics system, which includes publicly available demographic information as well as prevalence and co-occurrence data derived from measurements taken from the electronic health records of 5 million patients. When the subject matter experts (SMEs), a group of practicing clinicians, reviewed the results, they were highly impressed by the possibility of using such data.

This advance inspired the University of North Carolina at Chapel Hill Green Team, which is interested in environmental exposures. The Green Team's use case is asthma, and the members figured out a framework for sharing patient-level data while minimizing the risk of leaking sensitive information. The framework is regulatorily compliant and not subject to institutional review board oversight or data use agreements.

Another use case for the Translator is Fanconi anemia. Twenty-six different Fanconi-associated proteins are implicated in the disorder. Using a purely data-driven approach, one of the Translator teams identified TGF-beta as a candidate protein involved in disease development. Independent of that effort and using a different strategy, the Gray Team also identified TGF-beta as being implicated in the disease. These efforts did not rely on literature searches; the results were purely data-driven. This example showed how Translator could provide new insights into pathogenesis.

For the May 2018 "Hackathon", SMEs suggested questions and proposed ways that humans might try to answer the questions. One group focused on Ehlers-Danlos syndrome. That group included the parents of a child with the syndrome, and the Translator informatics scientists found it highly motivating to sit down at a table with both the SMEs and the parents.

Questions for the Translator

Dr. Colvis presented the criteria for questions that could be asked of Translator:

- The Google search engine cannot answer the question.
- The question must be relevant in the eyes of SMEs.
- Data are available to answer the question.
- "Ground truthing" can confirm the Translator's answer.
- The question provides opportunities for collaboration and integration.

The idea is that a question such as "What are some potential treatments for [common condition] based on knowledge of related rare conditions?" could be broken down into a series of simpler questions. The teams then "bid" on the questions based on their resources and tools (i.e., query decomposition and bidding). The goal is to have one team hand off their output to another team and from there to a third team. The output from one step becomes the input for the next step.

What's Next?

Dr. Colvis recalled that during the last CAN Review Board meeting, a concept was cleared to move forward with developing Translator. Work continues on templating questions in such a way as to increase the autonomy of machines and reduce the need for human input. The teams will also work with SMEs to evaluate the quality of Translator's answers. In addition to adding new tools to Translator, Dr. Colvis would like to continue building the culture and community that have been established. Since initial demonstrations have shown that Translator can provide useable results, efforts will start to focus on building a user-centered design for the interface.

Looking ahead, Dr. Colvis said that feasibility testing will continue for one more year, and then applications will be solicited for developing the actual Translator.

Discussion

Dr. Ling enthusiastically praised the work on the NCATS Biomedical Data Translator, saying that the program has used the OTA to great advantage. He also encouraged the teams to continue meeting weekly. By creating a remarkable new ecosystem, the teams are now cross-pollinating, and that approach will lead to new insights. What will be the next application of this model?

In terms of other programs that could benefit from this type of approach, Dr. Austin suggested that ASPIRE will use this sort of a mechanism and require similar input. By bringing people with disparate expertise together, we can close knowledge gaps. A recent editorial by the Biomedical Data Translator Consortium published in *Clinical and Translational Science* describes the "sociology" of the program, which is effective because of the way the program is run, brings people together, manages expectations and insists upon deliverables. That said, the model is not completely replicable, because it requires frequent telephone calls and because current hiring controls limit availability of NCATS staff to manage this high-touch program. The hope, then, is that the model will work and achieve breakout productivity, allowing NCATS to leverage additional resources to hire more staff and replicate the model.

Dr. Ramoni referred to the Undiagnosed Diseases Network and hypothesized that it could also benefit from having a high-touch team to bring together teams with diverse expertise to make projects highly effective. This approach would be a challenge due to hiring limitations; nevertheless, investigators appreciate the input of program managers and scientists from the funding agency. Could funders issue recommendations to leaders about novel team science and its effectiveness?

Mr. Bartek asked about dissemination techniques for possibly replicating the Translator model in other institutions without direct involvement of NCATS staff. Dr. Southall said that dissemination would be challenging, but Dr. Colvis spoke about the architecture of the model and the potential to bring in new data and new groups in a modular fashion. Her sense is that the model could become self-sustaining but would always need intensive involvement at the beginning.

Frank F. Weichold, M.D., Ph.D., commended the program leaders and underscored the importance of having SMEs available at the funding agency. The Food and Drug Administration (FDA), for example, funded 90 successful projects through its Centers of Excellence in Regulatory Science and Innovation that differed significantly from typical NIH-funded projects. Dr. Weichold also emphasized the critical need for having data security people on the team to provide continual monitoring to identify breaches and inappropriate data use. Data security requires both personal accountability and an integrated team approach. Dr. Weichold added that data interoperability and metadata (i.e., data provenance) are critical for understanding the strength of evidence used for any scientific process. Acceptance of data by SMEs depends on their evaluation of data quality and provenance. Dr. Southall agreed, saying that data security and quality requirements are important considerations as the system's capabilities are built out.

Megan O'Boyle supported the inclusion of caregivers for patients who have Ehlers-Danlos syndrome at a Hackathon event. Dr. Colvis highlighted other existing opportunities to promote patient and family involvement in Translator projects. Several Translator investigators, including Maureen Hoatlin, Ph.D., and Matthew Might, Ph.D., are involved in the rare disease research community and able to provide real use cases. Dr. Southall further noted that patients and their caregivers can provide context for raw data. For user-centered designs, people affected by the disease of interest can provide input to confirm the relevance of Translator questions. However, it is important that families and patients understand that Translator is not yet a functioning system. Ms. O'Boyle recommended that Translator projects tap into community members who have scientific knowledge, perhaps through work at NIH or in the pharmaceutical industry.

V. PRESENTATION AND DISCUSSION OF POTENTIAL NEW CAN PROJECTS

G. Lynn Marks, M.D., Senior Research and Development Advisor, BARDA, and Chair, CAN Review Board; Ronald J. Bartek, M.A., Co-Founder and Founding President, FARA, and Vice Chair, CAN Review Board; CAN Review Board Members

Dr. Marks invited the members of the CAN Review Board to think about ideas for new projects that could be brought to the January joint meeting with the NCATS Advisory Council for a vote. Dr. Marks outlined the project selection criteria, as recommended by the CAN Review Board:

- Collaboration
- Discrete and measurable outcomes
- Broad and significant impact
- Focus on a compelling disease (or diseases)
- Timeline less than five years from start to completion of the project

Brad A. Margus, M.B.A., asked about the rationale for requiring that CAN-supported initiatives be collaborative in nature. Mr. Bartek said that in this case, issues with gene therapy are so

broad and complex that no single individual or institution could come up with a solution, especially in the requisite time frame (less than five years). The hope is that CAN could make a positive contribution to gene therapy research in just a year or so.

Further discussion about the requirement for collaboration led to a recommendation that collaboration not be a "hard" requirement for CAN funding. Because the CAN Review Board created the requirement for collaboration, the Review Board could change it. Furthermore, waiting for collaborations to form might slow down projects. Mr. Bartek said that if an exceptional proposal were received from one individual or institution, the CAN Review Board could probably find a way forward.

Dr. Marks provided an overview of the process for developing CAN projects. It could involve, for example, convening workshops to develop and refine focus areas and concepts.

Gene Therapy

Dr. Marks said that he and Mr. Bartek believe that gene therapy is one area where CAN could help academia and industry make great progress by eliminating common barriers. Advances in gene therapy could potentially have a great impact on therapeutic development for many diseases, and the CAN Review Board is unique in terms of its OTA, which could even allow partnering with industry.

Dr. Marks said that the idea came to them during a two-day conference co-chaired by Dr. Austin and Wilson Bryan, M.D., of the FDA's Center for Biologics Evaluation and Research. According to Mr. Bartek, hundreds of trials of gene therapy are underway. During the conference, presenters from academia and industry outlined barriers that all programs encounter that cause delays and drive up costs. Rather than wait for all these programs to develop solutions independently and then not share them broadly due to intellectual property issues, NCATS could try to advance the translational science needed to solve the issues and provide the platforms needed.

Mr. Bartek outlined the five key issues that are common to all gene therapy programs. All of the barriers seem to lie squarely within the CAN Review Board's mandate to accelerate development of high-need cures. In no particular order, these are:

- *Development of standardized predictive measures/assays of neutralizing or particle-clearing antibodies to major serotypes.* Every gene therapy program has trouble deciding whom to include in trials based on exposure to viral vectors.
- *Immune response, suppression, transduction attenuation and re-dosing.* Validated assays might be used for determining doses appropriate for antibody levels. Also, one must keep in mind that immune responses are likely to be more nuanced in the eyes and central nervous system, which are mostly isolated from immune responses.
- *Assays for potency, biodistribution and filled particle quantitation.* The FDA has issued draft guidance to industry on potency assays.
- *Manufacturing.* Market forces may have to resolve these issues, but market forces operate slowly, and few solutions would be shared among manufacturers. The few manufacturers already operating in the space for gene therapy compounds are using antiquated technologies (e.g., ultracentrifugation), resulting in huge queues and exorbitant prices. Large volumes are needed for clinical trials, and a magnitude larger

volume would be needed for compassionate use protocols. More advanced technologies and higher-yield systems are critical needs.

- *Scientific tools to inform clinical trial design, selection of initial subjects and dosing levels.* Gene therapy involves only a single dose; therefore, should we question the usual dose escalation approach? Should initial trials start with more severely affected patients? Should safety profiles be established in older patients before enrolling younger patients? The FDA has already outlined essential considerations for clinical trial design.

Mr. Bartek asked whether the CAN Review Board or NCATS could work with the FDA to help accelerate progress broadly by leading a workshop or a series of workshops to work on clinical trial design applicable for many disease groups. Next steps in the very near term could include convening of workshops to refine the candidate list of issues and recommend initial attempts to identify approaches for solving them. Multistakeholder consortia would probably be necessary to provide solutions for the identified common challenges.

The initial recommendation was to convene a very broad workshop initially with all the stakeholders — industry, government, patient advocates and academics — to ensure that all priority issues are identified. Next would be a workshop to set priorities within the issues and discuss potential solutions. Other workshops could address clinical trial platforms and establish consortia to take on the issues. The hope is to solicit applications in fiscal year (FY) 2019 so that the funded projects could begin in FY 2020.

Dr. Austin suggested giving some consideration to the question of whether some issues should take precedence or be worked on simultaneously.

Dr. Marks and Mr. Bartek volunteered to draft a document to be the foundation for a presentation to the NCATS Advisory Council for its January 10, 2019, meeting.

Discussion

Mr. Margus thought that getting NIH — NCATS and CAN in particular — involved in dismantling barriers to gene therapy trials could have a major impact.

Dr. Weichold said that the FDA concurs about the nature of the priority areas causing delays in gene therapy. He noted that single-cell characterization is also an active area of research. The technology has really improved, and NCATS and the FDA could make real progress in figuring out why hundreds of experimental products are inactive or only sporadically active.

Dr. Ling suggested adding another priority area: nonviral approaches to gene therapy.

ACTION ITEM: Add a gene therapy focus area for development of nonviral approaches (e.g., gene editing, nanoparticles) for delivery of genes.

Anantha Shekhar, M.D., Ph.D., thought that gene therapy was an excellent focus area for the CAN Review Board. He noted that several Good Manufacturing Practice (GMP) viral vector facilities are funded by NIH. Could those Institute-funded facilities be enlisted to help manufacture products for this program of research? Dr. Austin recommended inviting investigators from the funded institutions to the workshop. Mr. Bartek agreed, saying that academicians have mentioned their institutions' facilities and would be interested in obtaining

resources to bolster their capabilities. Mr. Bartek pointed out that this funding initiative would not support development of brick-and-mortar facilities, however.

ACTION ITEM: Ensure that investigators who run NIH-funded GMP facilities are invited to the workshop.

Ms. O'Boyle recommended extending workshop invitations to some patients who have undergone gene therapy, both successfully and unsuccessfully.

Ms. O'Boyle also suggested generating, refining and prioritizing research questions online using a platform such as the Codigital Ideas Engine to get broad participation.

Repurposing of Nonpatented Drugs

Harry P. Selker, M.D., M.S.P.H., spoke about the national interest in bringing down drug prices. One way to do so would be to use existing data to support new indications for nonpatented drugs. There are probably many good drugs that will never be tested for safety and efficacy in many diseases because of the lack of financial incentives. CAN might be able to serve as a platform by bringing together data the FDA has used or collected by various mechanisms. The idea is to identify inexpensive drugs that have already undergone toxicity testing and might offer public health benefits but lack financial incentives.

Dr. Weichold observed that data liberation and interoperability are required to understand the data that exist. If those requirements are met, then experiments could begin. The effort is not so much repurposing of drugs as it is repurposing of information.

Dr. Ramoni spoke of the challenges of health data interoperability and suggested that a role may exist for the Biomedical Data Translator platform.

Dr. Bobbie Ann Mount, a program officer with NCATS' New Therapeutics Uses program said that discussions are underway with the FDA about holding a meeting, but the idea of a meeting has not yet been presented to the Advisory Council. Heather Stone, M.P.H., of the FDA's Office of Medical Policy at the Center for Drug Evaluation and Research, has been focusing on the development of a repurposing database to capture information on the global experience of repurposing FDA-approved products for neglected tropical diseases and emerging threats. Dr. Ramoni spoke of data stored at the Oak Ridge National Laboratory that would allow VA Research to be a data contributor.

Dr. Selker asked about including the Centers for Medicare & Medicaid Services (CMS) in the discussion. CMS staff are typically very enthusiastic, but CMS mechanisms are very cumbersome. Dr. Weichold thought that the Center for Medicare & Medicaid Innovation may have more freedom to operate.

Stephen Groft, Pharm.D., currently a contractor who provides advice to the NCATS Director, former director of the Office of Rare Diseases Research at NCATS, said that repurposing of nonpatented products requires a great deal of planning and a great many resources, but it can be done with a systematic approach. He suggested a pilot project within Translator.

ACTION ITEM: Dr. Selker will draft a framework for a one- to two-page proposal on repurposing of nonpatented drugs to be reviewed and revised by Dr. Colvis; Bobbie Ann Mount, Ph.D.; Dr.

Ramoni and Dr. Weichold. The proposal will be presented during the next joint meeting with the NCATS Advisory Council in January.

Platform Trials
Dr. Weichold mentioned that a strength of platform trials is real-time data review, possibly cloud-based. That could be set as an expectation to change the existing culture.

ACTION ITEM: Dr. Weichold volunteered to draft a proposal on platform trials to present at the next joint meeting of the CAN Review Board and the NCATS Advisory Council.

ACTION ITEM: Any CAN Review Board member who has additional thoughts about the proposals discussed or who would like to suggest other ideas for CAN activities should forward them to Mr. Bartek, Dr. Marks and Dr. Ramsey-Ewing as soon as possible.

VI. ADJOURNMENT OF THE CAN REVIEW BOARD MEETING

Dr. Austin expressed his appreciation to the CAN Review Board.

Dr. Marks and Dr. Ramsey-Ewing thanked the participants and presenters for their time and engagement, and they acknowledged the work of the NCATS staff in organizing the meeting. They adjourned the meeting at 1:52 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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G. Lynn Marks, M.D. Date
Chair, Cures Acceleration Network Review Board,
and
Senior R&D Advisor, Biomedical Advanced Research and Development Authority (BARDA), ASPR/HHS

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Anna L. Ramsey-Ewing, Ph.D. Date
Executive Secretary, Cures Acceleration Network Review Board,
and
Director, Office of Grants Management and Scientific Review, NCATS