Department of Health and Human Services  
National Institutes of Health  
National Center for Advancing Translational Sciences Advisory Council  
and  
Cures Acceleration Network Review Board  

Minutes of Joint Meeting  
September 3, 2015

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 8:00 a.m. ET on Sept. 3, 2015, in Conference Room 6, Building 31, on the National Institutes of Health (NIH) main campus. Christopher P. Austin, M.D., NCATS Advisory Council chair, and Freda C. Lewis-Hall, M.D., CAN Review Board chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

Following the joint meeting, the NCATS Advisory Council met in closed session for the 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., Associate Director for Special Initiatives, Office of the Director, NCATS

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

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

*Ad Hoc Members*
None in attendance

*Ex Officio Members*
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.

*Vice Chair*
Geoffrey S. Ginsburg, M.D., Ph.D., Director of Genomic Medicine, Duke University Health System
CALL TO ORDER AND WELCOME

Christopher P. Austin, M.D., welcomed members and guests to the 10th meeting of the NCATS Advisory Council and the 12th meeting of the CAN Review Board. He reminded everyone that the open session was being videocast.

Danilo A. Tagle, Ph.D., M.S., informed the group that the CAN Review Board will meet by teleconference on Dec. 11, 2015. Joint meetings in 2016 are slated for January 14, May 12 and September 15.

New staff members who have joined NCATS since the last joint meeting, and existing staff members who have taken on new roles, were then introduced:

- **Keith R. Lamirande, M.B.A.**, is the Center's new associate director for administration and executive officer.
• Anton M. Simeonov, Ph.D., has been named scientific director for NCATS and director of the Division of Pre-Clinical Innovation (DPI). Dr. Simeonov formerly served as the acting director in both of these roles.

• Petra Kaufmann, M.D., M.Sc., has been appointed head of the Office of Rare Diseases Research. She will retain her role as director of the Division of Clinical Innovation (DCI).

• George J. Coy will be taking the reins as the new budget officer for the Center.

• Artisha Y. Eatmon, Nyron M. Rouse and Julia T. Shriner are joining NCATS as grants management specialists in the Office of Grants Management and Scientific Review.

• Christine A. Livingston, Ph.D., and Maria D. Lourdes Ponce, Ph.D., are joining NCATS as scientific review officers in the Office of Grants Management and Scientific Review.

• Tania B. Lombo Rodriguez, Ph.D., will be serving as program manager for the Extracellular RNA Communication program at NCATS.

• Sabine C. Alexander has joined the Council Management Group.

• C. Taylor Gilliland, Ph.D., a fellow with the Office of Policy, Communications and Strategic Alliances, will be serving in a permanent position within the Office of Science Policy.

Dr. Austin then announced that Frank Douglas, Ph.D., M.D., and Victoria Hale, Ph.D., had completed their terms of service on the NCATS Advisory Council and the CAN Review Board.

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 held on June 18, 2015, were approved as written.

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

Christopher P. Austin, M.D., presented meeting materials that showcase selected NCATS activities and advances, such as:

• A feature on partnering between disease foundations and NCATS experts to develop assays for high-throughput screening or for repurposing applications;

• A paper summarizing NCATS Chemical Genomics Center (NCGC) research on developing small molecules for target qualification and drug development;

• The Assay Guidance Manual — made possible through an NCATS and Eli Lilly and Company collaboration — helping to disseminate information from experts around the world on the best methods of producing and validating chemical probes;

• A Commentary co-authored by Dr. Austin and published in Nature Chemical Biology outlining the promise and peril of many existing chemical probes, and offering some potential solutions.

Austin also unveiled a new seven-minute virtual tour video of the NCATS intramural laboratories.

Selected Translational Innovation Highlights

Austin presented examples of progress in early-, middle- and late-stage development along the translational science spectrum:

• Early-stage translation:
  o Comprising 19 genes, the family of aldehyde dehydrogenases offers a number of attractive targets for small molecules. A collaborator at Yale University proposed working on inhibitors to aldehyde dehydrogenase 1A1, which is involved in stem cell generation. The effort has yielded assays and a demonstration of efficacy of two highly
potent 1A1 inhibitors in cancer stem cell models (3-D spheroid and organoid) of a leading form of brain cancer, glioblastoma multiforme. Animal efficacy studies are ongoing.

- NCATS collaborated with Eli Lilly and Company to bring systems pharmacology approaches into the public domain. NCATS’ DPI expertise and 2,500 approved drugs from its pharmaceutical collection were made available for the effort. The compounds were tested for their relevance to several major diseases through Lilly’s Open Innovation Drug Discovery partnership. The data are available through PubChem and an article published in *PLOS ONE*.

**Mid-stage translation:**

- The National Institute on Drug Abuse partnered with the NCATS Bridging Interventional Development Gaps (BrIDGs) program and Signature Therapeutics, Inc., to come up with an abuse-resistant, oral oxycodone formulation. The opioid component is released only after exposure to trypsin in the stomach. The FDA approved the Investigational New Drug application; a clinical trial is planned.

- Four new projects within the Discovering New Therapeutic Uses for Existing Molecules (New Therapeutic Uses) program are underway to explore new indications for partially developed investigational drugs.

**Late-stage translation:**

- The Clinical and Translational Science Awards (CTSA) Program’s Recruitment Innovation Centers (RICs) and Trial Innovation Centers (TICs) are intended to eliminate the need to rebuild trial components for each multisite study funded by NIH. In addition, a series of new collaborative awards will support three or more CTSA Program hubs working together on an area of translational science.

- Collaborative initiatives involving DCI and the Office of Strategic Alliances include an NIH and NSF pilot program, which has made the I-Corps training program available to selected Phase 1 Small Business Innovation Research/Small Business Technology Transfer projects, and the creation of an NSF-CTSA I-Corps program. Ten CTSA Program hubs will pilot the program, which was among the initiatives announced by the White House during Demo Day on Aug. 4, 2015. Petra Kaufmann, M.D., M.Sc., attended the White House event.

- Through the CTSA Program Common Metrics Initiative, NCATS is exploring ways to measure the success of the CTSA Program in a hypothesis-driven way. The goal is to develop a data-driven, strategic management tool for the CTSA Program principal investigators (PIs) and NCATS to measure the impact of clinical and translational research conducted through the CTSA Program.

- Through its Office of Rare Diseases Research, NCATS supported a study conducted by the Rare Lung Diseases Consortium in conjunction with Pfizer and the LAM (lymphangioleiomyomatosis) Foundation that resulted in the first approved treatment (sirolimus) for LAM. LAM is an often-fatal condition that affects mainly women of childbearing age.

**Policy and Legislative Updates**

- The fiscal year (FY) **2016 NCATS budget request** was for $660.1 million, an increase of $27.4 million above the FY 2015 enacted level. FY 2016 begins on Oct. 1, and if no budget is passed, Congress will need to pass a continuing resolution bill to avert a government shutdown.

- The House passed the 21st Century Cures bill, which includes an NIH Innovation Fund of $8.75 billion over five years.
The Senate released an [Innovation for Healthier Americans] report; NCATS participated in a related hearing. There may be a draft bill in the fall of 2015. The 90-day public comment period for the proposed [update of the Common Rule] begins on September 8.

Discussion
Robert J. Beall, Ph.D., asked about the mechanism whereby people, companies and other organizations can engage with the NCATS pipeline. Austin responded that nearly all of the programs on the intramural side (e.g., BrIDGs, NCGC, Therapeutics for Rare and Neglected Diseases) issue public solicitations to assemble joint project teams. NCATS now is working on an NCGC solicitation for probe development. Regarding the Common Rule, Harry P. Selker, M.D., recalled that among the central issues in prior iterations was reliance upon central or shared institutional review boards (IRBs). Austin said that NIH is instituting a policy that will require central IRBs for all NIH-funded multisite studies. The CTSA Program is ahead of the curve in this regard.

Eric D. Kodish, M.D., spoke about the potential effect of the proposed Common Rule on biorepositories. In some quarters, there is hope that requirements for informed consent would become less stringent, but the proposed rule appears to be even more limiting. Austin said that the proposed rule appears to require specific consent for any use of a biospecimen. Use of old stored samples would be allowed. Dr. Kodish pointed out that advances in science have made permanent “de-identification of samples” impossible.

Geoffrey S. Ginsburg, M.D., Ph.D., applauded the CTSA Program Common Metrics Initiative and asked about incorporating metrics that the public and Congress could use for forecasting and evaluating CTSA Program accomplishments. Kaufmann clarified that the initiative is not intended to serve as a basis for evaluating the program; rather, the idea is to create a strategic management tool for CTSA Program investigators and NCATS. Dr. Ginsburg suggested that the initiative could be illuminating for the stakeholders; he also suggested creating a publicly accessible dashboard.

IV. NIH STRATEGIC PLANNING: Lawrence A. Tabak, D.D.S., Ph.D., Principal Deputy Director, NIH

Lawrence A. Tabak, D.D.S., Ph.D., explained that the Continuing Resolution enacted on Dec. 16, 2014, requires the NIH to submit a five-year scientific optimization no later than one year after enactment of the resolution (i.e., by Dec. 16, 2015).

The goal is to create a living document to help NIH fulfill its mission across a horizon of five years. The strategic plan should articulate approaches and opportunities that are both forward-looking and inspirational. It should identify major trans-NIH themes that will advance biomedical research. It is intended neither to delineate all the important things that NIH does nor to reflect all the priorities of the individual Institutes, Centers and Offices. However, it will link to the strategic plans of the individual Institutes and Centers (ICs), as appropriate.

Dr. Tabak outlined the process for developing the strategic plan. NCATS has three representatives on the strategic plan working group. NIH staff have contributed more than 80 callout examples of scientific advances, some of which could be highlighted in the plan. NIH has met twice with the Advisory Committee to the Director, which recommended emphasizing the interconnected nature of research and the inclusion of information on clinical methodologies, data science and workforce retention. NIH Director Francis S. Collins, M.D., Ph.D., has had meaningful input and oversight into the document.
Tabak reviewed the draft framework for the plan, which will open with an overview. The sections will be organized according to three areas of opportunity that apply across biomedicine: fundamental science, treatments and cures, and health promotion and disease prevention. Each section will describe emerging opportunities and recent breakthroughs and will include research callouts. Examples of callouts could include CRISPR (clustered, regularly interspaced, short palindromic repeats) genome-editing technology and the influence of the gut microbiome on the immune system. The concluding Underlying Principles section will explain how we set priorities at NIH and how we enhance stewardship of public funds. It will also highlight the unique role of NIH within the Department of Health and Human Services (HHS) and its alignment with the overarching HHS strategic plan.

A number of mechanisms were set up to garner input on the draft strategic plan. A request for information (RFI) collected 460 comments. More than 700 individuals participated in a series of webinars to engage the community.

Tabak said that the outline is being presented to 20 NIH advisory councils. October 15 is the proposed deadline for briefing HHS on the plan. Tabak also encouraged all present to send him comments via e-mail: lawrence.tabak@nih.gov

Discussion
Meryl Weinberg, M.A., said that she was glad to see the emphasis on patient involvement and partnerships. She suggested adding language to involve patients with multiple chronic conditions in clinical trials. Harry P. Selker, M.D., supported this idea, noting the importance of comparative effectiveness research and studies of clinical effectiveness.

Anantha Shekhar, M.D., Ph.D., asked about strategic opportunities to streamline cross-IC activities in terms of reducing duplication of networks and infrastructure by establishing strategic alliances for better utilization of resources. Tabak said issues such as these are examples of what will be included in the stewardship section. He explained that NIH can apply analytic tools to identify areas of overlap across NIH. Also, the community realizes that there is power in commonalities. Some ICs are discussing ways to enable institutions to share core facilities to increase efficiency.

Lawrence A. Soler, J.D., said that the best strategic plans not only describe opportunities but also are clear about activities that might be eliminated or de-emphasized over time. Tabak said that how NIH sets its priorities and makes decisions will be addressed in the Underlying Principles section. He acknowledged the importance of avoiding redundancy and harmonizing decision making, but one must also recognize that each IC is unique and the plan will not dictate the ICs’ priorities.

Geoffrey S. Ginsburg, M.D., Ph.D., said that science is becoming more global. Tabak agreed, saying that partnerships include other countries, with the Fogarty International Center being the point of intersection for most global activities.

Dr. Ginsburg also noted that the arrows in the diagram showing the relationship among the sections of the draft report symbolize important science. For example, NCATS is encompassed in the arrow between fundamental science and treatments. Tabak said that this will be described in the plan, but perhaps it should be captured graphically as well.
Pamela B. Davis, M.D., Ph.D., spoke about including interfaces with other government agencies (e.g., the FDA) and with the private sector.

Margaret A. Anderson, M.A., observed that the ultimate audience for the strategic plan is Congress, which will be seeking the answers to such questions as the following: Has NIH evolved? Is it spending its money wisely? Is it staying on course? NIH has been challenged in the past when people were under the impression that NCATS was developing drugs and competing with private businesses. The FasterCures organization developed a database of consortia called Consortiapedia to help characterize the phenomenon of public-private research partnership.

Ms. Anderson recommended speaking with stakeholder groups — including detractors — outside NIH. She volunteered to facilitate connections between NIH and external stakeholders. Frank Weichold, M.D., suggested adding language about advancing regulatory science. FDA is increasingly seeking patient feedback, patient preferences and patient-reported outcomes to incorporate into its regulatory decisions and risk-benefit analyses. Dr. Weichold also underscored the power of fundamental science, which is NIH’s greatest and most unique strength.

Robert J. Beall, Ph.D., recommended increasing the emphasis on accelerating the development of treatments and cures. The strategic plan should help Congress understand that delays have consequences. Congress needs to understand our sense of urgency.

V. EX VIVO FEMALE REPRODUCTIVE TRACT INTEGRATION IN A 3-D MICROPHYSIOLOGIC SYSTEM:

Teresa K. Woodruff, Ph.D., Director, Women’s Health Research Institute, and Chief, Division of Obstetrics and Gynecology-Fertility Preservation, Feinberg School of Medicine; Professor of Molecular Biosciences, Weinberg College of Arts and Sciences, Northwestern University

Freda C. Lewis-Hall, M.D., introduced Teresa K. Woodruff, Ph.D., who pointed out that NIH is at a pivotal point; new policies (NOT-OD-15-102) are calling for the inclusion of females in basic science, both in animal studies and in cell lines derived from female tissue. This is a time for the transformative power of science to revolutionize how tomorrow’s patients are treated by ensuring that new drugs are safe and effective for both males and females.

Presenting on behalf of the team working on FemKUBE, a model of the female reproductive tract “in a box,” Dr. Woodruff said that this project has been highly successful. The system integrates the ovary, fallopian tube, cervix and uterus in an integrated, dynamic, microfluidic system. The ovary component is a physiologic source of female steroid hormones, recapitulating the 28-day menstrual cycle. The EVATAR™ model integrates the liver with the reproductive tract model for the metabolism of steroids and other compounds.

Woodruff explained the contributions of the individual teams involved in the project. The hope is that reproductive tract toolboxes will lead to earlier discovery and better safety by identifying early off-target effects on the reproductive system. In addition, these systems may provide definitive evidence as to whether certain contraceptives act as abortifacients or as anti-ovulatory agents. Environmental health toxins could be evaluated in terms of their effects on reproduction. The devices could promote the development of new vaccines against cervical cancer and allow investigations of infection pathways.
The hardware and software are ready for implementation. The pumping technology can accommodate a 28-day cycle and allow signals to move in real time from organ to organ. The systems are easy to use, portable, free of materials that bind steroid hormones and capable of long-term stable operation. Patients undergoing hysterectomy are being asked to give informed consent for the use of their tissues in the devices. The goal is to replace such tissues with induced pluripotent stem cell (iPSC) technology in the future.

Other ideas — DudeKUBE (male reproductive system), PregoKUBE (pregnancy) and MyKUBE (cancer tissues) — are in the works. PregoKUBE could aid in drug development as a way to test the safety of drug candidates during pregnancy and also could serve as a method of studying the disproportionate effects of certain diseases (e.g., H1N1 influenza) on pregnant women.

Discussion
In response to a question about variations in the menstrual cycle, Woodruff acknowledged that these variations are important factors to include in research. A woman’s cycle can vary widely, especially if fibroids or endometriosis are involved. The ex vivo systems are flexible enough to accommodate studies with different cycle lengths.

Eric D. Kodish, M.D., commented that menorrhagia is of interest. Could the platforms reflect the interface between the female reproductive tract and the hematologic/coagulation system? Woodruff responded that another tissue-chip investigator is modeling the vascular system, which will be important for studying the endometrium and changes in spiral arteries.

S. Rao Kosaraju, Ph.D., asked about the length of time that the chips remain fully functional. Woodruff said that more than a million cycles have been run on each of the pumps. The membranes and springs have not failed with media only.

Geoffrey S. Ginsburg, M.D., Ph.D., inquired about the tissues’ somatic sequences at the beginning and the end of the 28-day cycle. This experiment has not been done, but Woodruff thought that there would certainly be endocrine-stimulated changes. It would be interesting to look at genetic consequences throughout the cycle in tissues on the platform.

Scott J. Weir, Pharm.D., Ph.D., asked about using the systems to study the interaction between certain genetic defects (e.g., Turner syndrome) and the interplay with the cardiovascular system, for example. Woodruff thought that Turner syndrome and premature ovarian insufficiency would be very intriguing use cases for the platforms. Dr. Weir recommended thinking about business plans and building a use case for each tissue in the platform — especially since no pharmaceutical company has women’s health as its portfolio. Woodruff was enthusiastic about setting up a partnership to work on a business plan.

Weir also discussed uterotropie effects of endocrine-disrupting compounds (EDCs), noting that fat should be included in the system because these chemicals traffic with fat.

In response to a question from Lawrence A. Soler, J.D., about interactions with the FDA, Woodruff said that there is not really a way to apply these tools for drug approvals unless the pharmaceutical industry sees a need to reduce animal studies. These experimental systems are probably better positioned for early-stage discovery and testing for EDC toxicities. NCATS is very progressive in bringing forward entrepreneurial ideas and technologies, but it is not yet clear where this type of research resides in the developmental pipeline.
Dr. Ginsburg encouraged Woodruff to deliver her presentation to other ICs. This model system could be very helpful in many different contexts.

Pamela B. Davis, M.D., Ph.D., asked about using iPSC technology to develop personalized systems to replace costly, painful and time-consuming testing for infertility. Woodruff thought that infertility assessment would be an ideal use case.

Frank Weichold, M.D., acknowledged that the platforms could be real game changers. He also said, “Regulatory hurdles, most of the time, are actually scientific questions that no one can address.” He recommended framing this model system in terms of personalized medicine. The FDA has a toxicology council, coordinated by the Senior Science Council.

Another idea suggested by Dr. Weichold was to explore testing of generic drugs for equivalency and nutritional supplements for efficacy.

Christopher P. Austin, M.D., asked Woodruff about the ethical, sociological and political issues involved in moving from mouse tissues to human tissues. Woodruff spoke about having an opportunity to help the public better understand reproductive health. We do not have good models to figure out how contraceptives work, for example. Regarding human tissues, patients undergoing hysterectomy can consent to the research use of their tissues. Going forward, however, the plan is to use iPSCs. With the NCATS partnership, a good, appropriate and ethical approach is being followed.

Dr. Austin also mentioned that certain conditions, such as LAM, intrauterine growth restriction and preeclampsia, could be amenable to study in these systems because other organs-on-chips could be linked via microfluidics.

VI. CONCEPT CLEARANCES

**Drug Repurposing Process Innovation Program: Christine M. Colvis, Ph.D., Director, Drug Development Partnership Programs, NCATS**

The purpose behind this set of proposed funding opportunity announcements (FOAs) is to provide support for pre-clinical studies, the planning of clinical trials, and early-stage clinical trials for which the hypothesis relies on a publicly available method or tool (e.g., crowdsourcing or computational algorithms) for identifying new indications for existing drugs. The goals are to assess a variety of methods for identifying drug-indication pairs and to improve the efficiency of clinical trials for drug repurposing studies. These FOAs are intended to complement the ongoing NCATS New Therapeutic Uses program.

Scott J. Weir, Pharm.D., Ph.D., remarked that it is challenging for academic investigators to identify drug-indication pairs. Sometimes the existing bioinformatics approaches do not pan out. Also, if a screen identifies a pair, what is the mechanism for following up? In addition, academic investigators often lack the expertise to conduct the translational research. Christine M. Colvis, Ph.D., said that the set of FOAs would include planning for clinical trials. Should following up on screening results be included in this process-oriented concept?

Jorge L. Contreras, J.D., had two comments. First, he thought that restricting the initiative to *publicly available* methods and tools seems unwarranted. The focus should be on *innovative* methods. At the
end of the program, the methods or tools should be publicly available, but this should not be a requirement at the outset. Dr. Colvis explained that using published methods would eliminate the need to evaluate both the method for identifying a drug-indication pair and the use case. Mr. Contreras’ second comment was that the first two goals would apply to very different applicant groups. Would they be competing against each other?

Other points that were raised in discussion included the following:

- Frank Weichold, M.D., suggested capturing information about off-label use, which would be helpful to the FDA.
- Another participant recommended referring to “methods or tools” in the description of the concept.
- Geoffrey S. Ginsburg, M.D., Ph.D., recommended including industry representatives as application reviewers.

Danilo A. Tagle, Ph.D., M.S., called for a vote to approve the concept clearance. A motion was made and seconded, and the motion was passed.

**Translational Research Informatics and Operations Support: Michelle A. Culp, M.P.H., Director, Office of Clinical Trials Operations and Management, NCATS**

This concept would be a contract solicitation for providing coordinated and comprehensive scientific technical support for NCATS translational and clinical research operations and management in order to harmonize and centralize activities across the Center. The contractor would assist NCATS staff in managing clinical and operational activities and would provide information management of NCATS’ clinical activities. The awardee would also provide support for ensuring human subjects safety and for quality monitoring of NCATS’ clinical studies.

Harry P. Selker, M.D., said that having an excellent contractor will be critical to helping the Center serve as a beacon for the rest of NIH and the CTSA Program hubs. Anantha Shekhar, M.D., Ph.D., also expressed his strong support for the concept.

Comments on this concept included the following:

- Pamela McInnes, D.D.S., M.Sc.(Dent.), confirmed that some major contractors have both a commercial side and a government side.
- Dr. Shekhar recommended optimizing feedback loops with help from the CTSA Program PIs rather than instituting a top-down approach.

Dr. Tagle called for a vote to approve the concept clearance. A motion was made and seconded, and the motion was passed.

**Ethical, Legal and Social Implications of Biomedical and Translational Research: Elaine Collier, M.D., Senior Advisor, Office of the Director, NCATS**

This concept is for a collaborative trans-NIH initiative to support investigator-initiated research on high-priority ethical challenges and issues in biomedical and translational research. Ethical challenges arise across the entire spectrum of translation, across domains of all ICs, and occur at any stage of research. Many ethical issues require empirical data to address the question; development of normative or conceptual frameworks also is valuable.
Results of the supported research would be expected to contribute knowledge that will enhance the ethical conduct and the social value of biomedical and translational research. Applications would undergo dedicated review in the Center for Scientific Review.

Eric D. Kodish, M.D., remarked that the extramural community has been in dialog with NIH about a perceived lack of action of the NIH on ethical matters. This FOA will stimulate ethics research and ensure the integrity of NIH-funded research. NCATS, being disease agnostic, is a good lead for this collaborative NIH initiative.

Louis J. DeGennaro, Ph.D., said that NCATS has proven itself to be a real leader, especially when it comes to process improvement. In his view, the summary of the concept is overly broad and vague, which could hinder the creation of a focused program. He suggested emphasizing high-priority points and identifying means to track progress. Elaine Collier, M.D., said that discussions are underway with other ICs to identify the specific areas of focus for the initiative. The concept, as presented, allows NIH ICs to identify priority areas across the broad spectrum of biomedical and translational research that NIH supports.

Contreras observed that research on legal challenges should also be included in this initiative, focusing on ethical, legal and social implications (ELSI) of biomedical and translational research. Dr. Collier agreed, saying that many bioethics departments include lawyers, ethicists and a diverse group of experts from other fields; however, the scope of the initiative should be expanded so its ELSI focus is explicitly clear.

Lawrence A. Soler, J.D., and Robert J. Beall, Ph.D., asked whether NCATS is the right home for this effort, suggesting that the NIH Office of the Director (OD) might be more appropriate. Collier stated that no NIH ethics office exists within the NIH OD. In response to the recommendation for an NIH ethics office from a task force a few years ago, Francis S. Collins, M.D., Ph.D., established a trans-NIH Coordinating Committee for Bioethics Research and Training. This committee, co-chaired by Collier from NCATS and Christine Grady, M.S.N., Ph.D., from the NIH Clinical Center, is charged to coordinate and stimulate bioethics research and training at NIH. Under the umbrella of this committee, NCATS would coordinate and work with the ICs to refine the objectives of the initiative and move projects into their correct homes and would keep the OD informed and involved.

Other comments included the following:

- Dr. Selker said that improvement is needed in the informed consent process, which affects the conduct of research.
- Myrl Weinberg, M.A., sought clarification about the use of the term “bioethics” as opposed to “ethics.” She recommended using the latter term because the focus is on ethical issues that affect biomedical research.
- Mary L. Disis, M.D., supported NCATS’ taking a lead in this area of research. In light of the forthcoming changes in the Common Rule and the possibility of further restrictions on biorepositories, she stated we need to take steps now to keep research going to benefit patients.
- Dr. Kodish said that the “social value of biomedical research” is a new and very important concept.

Dr. McInnes summarized, saying that she heard general support for the concept, provided that the suggestion to assure ethical, legal and social implications research are included in the title.
Tagle called for a vote to approve the concept clearance with proposed changes. A motion was made and seconded, and the motion was passed with one abstention.

VII.  NCATS STRATEGIC PLANNING: Dorit Zuk, Ph.D., Director, Office of Policy, Communications and Strategic Alliances, NCATS

Dorit Zuk, Ph.D., explained the process for developing the NCATS Strategic Plan. The goal is to have a plan in about eight months. Several thematic areas evolved from discussions with NCATS staff and a series of focus group discussions, which included some Advisory Council/CAN Review Board members. After incorporating feedback from the Advisory Council and CAN Review Board, NCATS will publish a Request for Information (RFI), hold a series of town hall webinars and analyze stakeholder feedback. Listed below are the proposed thematic areas and possible topics for the RFI:

Improving the Drug Development Process
- Achieving interoperability of bioinformatics systems
- Integrating patient data into pre-clinical research
- Focusing on the precompetitive space.
- Expanding therapeutic modalities beyond small molecules.

The members of the Advisory Council and CAN Review Board offered several comments on this thematic area:
- Scott J. Weir, Pharm.D., Ph.D., suggested checking a list of barriers developed as part of an Institute of Medicine (IOM) project on mapping the drug development process.
- Anantha Shekhar, M.D., Ph.D., asked whether NCATS should take action in the chemical space as opposed to the biomedical space.
- Dr. Weir remarked that a concern in the public and private sectors is the fact that clinical pharmacologists are becoming extinct in academia. Clinical pharmacologists are being trained on the job at the FDA or in industry, rather than in academic settings.
- Harry P. Selker, M.D., advised against focusing on drugs to the exclusion of other treatment modalities. He recommended changing the term “drug development” to “diagnostics and therapeutics development.”
- Margaret A. Anderson, M.A., suggested asking about the role of NCATS and/or NIH in the precompetitive space. Industry might have some interesting ideas to contribute. Freda C. Lewis-Hall, M.D., agreed, saying that greater specificity is needed in the definition of “precompetitive space.”
- Geoffrey S. Ginsburg, M.D., Ph.D., noted that the theme does not mention acceleration of clinical trials.
- Regarding rare diseases, Robert J. Beall, Ph.D., recommended adding language to generate new ideas about trial design.

Pre-Clinical Innovation: Testing and Predictive Models
- Approximating the human condition in models
- Determining the range of data needed for robust models
- Establishing innovative mechanisms for data collection and analysis
- Engaging the patient community in study design

The members of the Advisory Council and CAN Review Board offered several comments on this thematic area:
• Dr. Shekhar suggested adding something about personalized medicine.
• Dr. Selker noted that the term “predictive model” refers more to the clinical space, less so to the pre-clinical space.
• Dr. Ginsburg recommended adding “discovery and usability of biomarkers in pre-clinical study and potential relevance in clinical trials.”

Re-engineering the Clinical and Translational Process
• Connecting research and researchers along the translational science spectrum (i.e., breaking down silos)
• Measuring innovation in translation
• Determining skill sets and core competencies needed in translational science
• Defining and developing clinical informatics

The members of the Advisory Council and CAN Review Board offered several comments on this thematic area:
• Pamela B. Davis, M.D., Ph.D., thought that the reference to “clinical informatics” in the fourth bullet point should be broadened to include “-omics,” as well as data on the environment and locales, and she suggested rewording as “…developing a broader range of data science.”
• Dr. Zuk said that patient-driven research needs to come to the fore.
• Selker said that one of the “secret sauces” of NCATS is collaboration across disciplines. He suggested featuring that as part of “re-engineering.”
• Dr. Lewis-Hall commented on the lack of a tangible process map for clinical/translational processes. Once a map is generated, engineering or other expertise could be brought to bear to optimize the processes. Ms. Anderson pointed out that the IOM Forum on Drug Discovery, Development, and Translation (now part of the National Academy of Medicine) is working on such an exercise, but it would be worth bringing other entities into the discussion.
• Ginsburg suggested dividing up translation because research on dissemination is very different from the research involved in getting a drug or device from animals into humans.
• Dr. Shekhar recommended mentioning network science.

Repurposing Drugs
• Creating systematic approaches
• Establishing innovative partnerships to facilitate repurposing.
• Involving the community in repurposing efforts

A participant suggested adding a point about the hurdles yet to be overcome. The meeting participants discussed whether this theme should be combined with drug development. Many thought it was better to keep it as a separate thematic area.

Accelerating and Supporting Research on Rare Diseases
• Examining commonalities
• Defining rare diseases in an -omics era
• Engaging new partners
• Implementing patient-driven research

Selker said that the Patient-Centered Outcomes Research Institute (PCORI) has provided a broader view on how to garner patient input. We need alternative pathways to collect feedback from the general
public, not just from patient groups. Anderson said that this thematic area is a priority for patients and industry. There is much work to be done on the science of patient preference.

Anderson remarked on the need for greater synergy between NIH and the FDA.

**Partnerships with Stakeholder Groups**

- Engaging with the patient community: a bidirectional process
- Determining the nature of the on-ramp for interacting with stakeholders
- Establishing innovative partnership models
- Using modern communication and educational tools

The members of the Advisory Council and CAN Review Board offered several comments on this thematic area:

- Myrl Weinberg, M.A., observed that cultural barriers are not often well understood and suggested adding a point about training for stakeholders to understand better how to engage patients in meaningful ways.
- Lawrence A. Soler, J.D., spoke about the roles of professional societies and family groups, in addition to patient communities, as stakeholders.
- Dr. Davis spoke about difficult-to-reach groups, such as inner-city communities. How can we access these groups and make an impact on their health?
- Per Ms. Weinberg, additional stakeholders could include PCORI, the FDA, the biopharmaceutical industry, other NIH ICs, payers (e.g., Centers for Medicare & Medicaid Services, commercial insurance), and pharmaceutical companies.
- Dr. Beall suggested adding a point about the need to increase diversity in clinical trials.
- Christopher P. Austin, M.D., observed that legal, ethical and social ramifications were not mentioned.

Zuk asked all to help promote the RFI when it is published and to encourage their networks to respond to the RFI and participate in subsequent town hall webinars.

The meeting participants offered several overarching comments:

- Include ethical, legal and social considerations as an additional thematic area.
- Include devices and diagnostics, which are also in NCATS’ wheelhouse.
- Re-structure the RFI according to the early, middle and late stages of development. One could think about a matrix because certain themes are uniquely influential during certain stages of development and others cut across various stages.

**VIII. CTSA PROGRAM UPDATE:** Petra Kaufmann, M.D., M.Sc., Director, Division of Clinical Innovation and Office of Rare Diseases Research, NCATS

With regard to efforts to innovate multisite clinical research, Petra Kaufmann, M.D., M.Sc., spoke of efforts to innovate clinical trial implementation. One example is harmonization of research staff training: The CTSA Program is finding ways to implement, as a base, research training on Good Clinical Practice and then expand the training to additional translational science competencies.

For streamlined contracting, the CTSA Program investigators set up an Accelerated Confidential Disclosure Agreement. When a potential partner is interested in collaborating on a study, the agreement
would be ready to go, reducing the time needed for negotiations. Similarly, having an Accelerated Clinical Trial Agreement would facilitate interactions between industry and the CTSA Program hubs.

Efforts also are underway to accelerate subcontracting — a process that currently can take up to a year.

Having central IRBs will help speed up multisite clinical trials. An IRB reliance agreement establishes the relationship between two institutions. Through IRBrelly, the CTSA Program is providing methods, templates and tools for reliance agreements. A pilot test is underway with investigators at Duke University.

The application date for the TICs FOA is approaching. NCATS anticipates funding up to three awards at a total cost of $4 million, for up to seven years. The National Institute on Aging has committed to be a partner for this effort.

Another area of challenge in clinical research is recruiting research participants. CTSA Program investigators are integrating de-identified electronic health records to use the information in research participant recruitment with the goal to enable evidence-driven site selection. This initiative was led by the Accrual to Clinical Trials network in collaboration with many CTSA Program hubs. IRB approval was obtained, and a pilot query has been completed, with a rheumatoid arthritis study serving as a first use case. A total of 22 sites participated in six sets of queries.

An RFA for the RICs was issued in partnership with the National Library of Medicine. It is anticipated that two awards for up to five years will be funded.

Also, in terms of FOAs, the CTSA Program Collaborative Innovation Awards have been set up to encourage collaborations between investigators from at least three CTSA Program hubs. The scope is broad — across all aspects of translation — and open to different scientific areas. The initiative is set up as a phased program including X02s and then U01s or R01s, which involve a pre-review step. Groups that perform well in the X02 phase will be invited to submit applications.

Dr. Kaufmann also provided an update on the development of common metrics for the CTSA Program. Four working groups of CTSA Program PIs have provided input on metrics and operational aspects of the effort. The plan is to present the draft metrics at the next face-to-face CTSA Program annual PI meeting.

**Discussion**

Frank Weichold, M.D., inquired about how industry could access the CTSA Program for specific clinical trials for which CTSA Program involvement could make a difference. How well is that process known or worked out in terms of the approach and the application? Kaufmann responded that CTSA Program investigators have developed template agreements for which they have solicited feedback from several companies. The companies can reduce legal costs and initiate trials faster using the templates. The CTSA Program hubs can also help provide access to patient populations.

Freda C. Lewis-Hall, M.D., spoke about the need for a single point of contact for companies to access the CTSA Program trial network for trials, or for cohort or genetic studies. She recommended learning more about what sponsors need.

Pamela B. Davis, M.D., Ph.D., and Harry P. Selker, M.D., expressed interest in learning about the overall impact of the program (e.g., numbers of trials conducted in the United States). Kaufmann said that with
the new CTSA Program Common Metrics Initiative, the goal is to assess how each hub is functioning in the national context. This information will help the program administrators discern what works at which institutions.

**ADJOURNMENT OF JOINT MEETING**
Christopher P. Austin, M.D., thanked all participants for their input. He adjourned the meeting at 2:57 p.m. ET.

**CLOSED SESSION OF NCATS ADVISORY COUNCIL**
This portion of the Advisory 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).

Advisory Council members discussed procedures and policies regarding voting and the 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**
Christopher P. Austin, M.D., adjourned the closed session of the NCATS Advisory Council meeting at 3:30 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, M.S., Ph.D.                              Date
Executive Secretary, NCATS Advisory Council

Executive Secretary, Cures Acceleration Network Review Board

and

Associate Director for Special Initiatives, Office of the Director, NCATS

________________________________________________________  ____________
Freda C. Lewis-Hall, M.D.                                Date
Chair, Cures Acceleration Network Review Board

and

Executive Vice President and Chief Medical Officer, Pfizer Inc.