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 23, 2013

The National Center for Advancing Translational Sciences (NCATS) Advisory Council and the Cures Acceleration Network (CAN) Review Board held a joint meeting in open session, convening at 8:30 a.m. ET on January 23, 2013, in Conference Room 10, Building 31, on the National Institutes of Health (NIH) main campus. Christopher P. Austin, M.D., NCATS Advisory Council chair, and Freda C. Lewis-Hall, M.D., CAN Review Board chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

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

NCATS ADVISORY COUNCIL MEMBERS PRESENT

Chair

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

Executive Secretary

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

Council Members

Margaret A. Anderson, M.A.
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.
Eric D. Kodish, M.D.
Freda C. Lewis-Hall, M.D.
Bernard H. Munos, M.B.A.
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
Robert I. Tepper, M.D., Third Rock Ventures, LLC

CAN REVIEW BOARD MEMBERS PRESENT

Chair

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

Vice Chair

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

Executive Secretary

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

Board Members

Margaret A. Anderson, M.A.
Robert J. Beall, Ph.D.
Jorge L. Contreras, J.D.
Pamela B. Davis, Ph.D., M.D.
Louis J. DeGennaro, Ph.D.
Mary L. Disis, M.D.
Victoria G. Hale, Ph.D.
Eric D. Kodish, M.D.
Bernard H. Munos, M.B.A.
Todd B. Sherer, Ph.D.
Lawrence A. Soler, J.D.
Myrl Weinberg, M.A.
Scott J. Weir, Pharm.D., Ph.D.
Paul G. Yock, M.D.

Representative Members

Ankit A. Mahadevia, M.D., M.B.A., Atlas Venture
Robert I. Tepper, M.D., Third Rock Ventures, LLC

CAN Review Board Ex Officio Members Present

Dr. Leona Brenner-Gati represented Dr. Hamburg and FDA at this meeting.
Joel Kupersmith, M.D., Department of Veterans Affairs
Larry Sipos, M.B.A., Acting Deputy Assistant Secretary of Defense for Force Health Protection & Readiness

INVITED PRESENTERS

Elliott M. Antman, M.D., Brigham and Women's Hospital
Elaine Collier, M.D., NCATS
Donald E. Ingber, M.D., Ph.D., Wyss Institute
Michael R. Knowles, M.D., University of North Carolina School of Medicine
John C. McKew, Ph.D., NCATS
Alan K. Percy, M.D., University of Alabama at Birmingham

Stephen R. Seiler, J.D., AesRx
Lawrence A. Tabak, D.D.S., Ph.D., Deputy Director, NIH

OTHERS PRESENT

Jim Bernstein, American Society for Pharmacology and Experimental Therapeutics
Khaled Bouri, FDA
Josephine P. Briggs, National Center for Complementary and Alternative Medicine, NIH
Dane R. Christiansen, Health and Medicine Counsel of Washington
Renee L. Cruea, Coalition for Imaging and Bioengineering Research
Daryn H. David, Ph.D., NIH Office of Behavioral and Social Sciences Research
Bethany Dishman, Federation of American Societies for Experimental Biology
Cynthia Fiducia, Harvard Medical School
Ross Filice, FDA
JoAnne Goodnight, Lynntech, Inc.
Michael P. Holsapple, Battelle Memorial Institute
Lori Pellnitz, SRI International
Jordan Schell, Lovelace Respiratory Research Institute
York Tomita, FDA
Shimere A. Williams, Lewis-Burke Associates, LLC

NCATS leadership and staff

I. CALL TO ORDER: Christopher P. Austin, M.D., Director, NCATS and Freda C. Lewis-Hall, M.D., Executive Vice President and Chief Medical Officer, Pfizer Inc.

Dr. Austin welcomed members and guests to the meeting and explained that the meeting was being held jointly by the NCATS Advisory Council and the CAN Review Board because a number of members serve on both groups.

Dr. Lewis-Hall encouraged those in attendance to be forthcoming with ideas and comments. She said that this is an interesting and challenging time for these groups and for NCATS overall; work must continue to advance despite economic constraints.

II. CONSIDERATION OF MINUTES: Christopher P. Austin, M.D.

The minutes of the Council meeting held on September 14, 2012, were approved as written.

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

Dr. Austin reviewed the NCATS mission, underscoring the importance of the word "catalyze." In this context, "catalyze" means bringing about transformative change by providing critical technologies and paradigms that will advance the translational efforts

of all NIH ICs as well as the private and nonprofit sectors. A collaborative organization by design, NCATS is charged with developing innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

Austin showcased the significant changes in NCATS leadership since the September 2012 Advisory Council and CAN Review Board meeting. He expressed gratitude to the former NCATS acting director, Dr. Thomas Insel, who played a critical role in standing up NCATS along with Dr. Kathy Hudson, the former NCATS acting deputy director. Currently, the deputy director position is vacant. Austin also thanked Dr. Josephine Briggs, who had served as the Division of Clinical Innovation (DCI) acting director through December 2012.

He also announced the schedule of future meeting dates of the Advisory Council and CAN Review Board.

Regarding the status of the NIH budget, Austin reminded everyone that NIH has been operating under a continuing resolution and will continue to do so through March 27, 2013. The sequestration was temporarily averted, but if Congress fails to resolve the budget dispute, a new sequestration will be ordered by the President on March 1, 2013, and implemented on March 27. The potential reduction of NIH spending in fiscal year (FY) 2013 would be about 6.4 percent. NIH is planning to continue to fund noncompeting grants at 90 percent of the approved level, as it has always done when operating under a continuing resolution.

Austin also mentioned that the federal debt limit will be reached on or about February 28, 2013, when the Treasury Department's special measures will end and cause default unless Congress acts to extend the limit.

He then shared some key components of the Food and Drug Administration Safety and Innovation Act (FDASIA). The Act, which would be particularly relevant to the NCATS Therapeutics for Rare and Neglected Diseases (TRND) program, would enable the FDA to approve a drug based on Phase II data and then rely on post-marketing data to show full clinical benefit.

Also highlighted were the proceedings of the NCATS Policy Workshop, which was held on December 11, 2012, and which offered an opportunity for developing a proactive policy research agenda.

Austin then presented on the role of the NCATS Division of Pre-Clinical Innovation (DPI), which is to conduct and use both internal and contract resources to advance collaborative research projects across the pre-clinical phases of the translational science spectrum. He addressed the potential of the Clinical and Translational Science Awards (CTSA) program to improve the efficiency and effectiveness of the translational process — particularly the clinical and implementation phases.

Austin reviewed some highlights of NCATS programs to date:

- A trial (carried out with the assistance of two NCATS programs) was reported in *JAMA* on the safety and efficacy of a repurposed cardiac drug, mexiletine, for use in nondystrophic myotonia.
- The successful use of high-performance neuroprosthetic control was published in *Lancet* and featured on the television program *60 Minutes;* this technology was developed with collaborative support from NIH, the Defense Advanced Research Projects Agency (DARPA), the Veterans Administration and FDA.
- DPI scientists co-authored more than 100 papers and book chapters in 2012.
- In just 15 months, the TRND program has brought four drug candidates into human trials.
    - One of these TRND projects is an NIH clinical trial for a promising drug for treating for Niemann-Pick type C disease. The project team won a Federal Laboratory Consortium Award for Excellence in Technology Transfer.
- A pilot program for the NCATS "therapeutics discovery initiative" was able to gain access to 58 "rescued" compounds from industry. A total of 160 pre-applications for studying the compounds for different indications were received. Some of these resulted in applications which are being reviewed in advance of the NCATS Advisory Council's May meeting. Awards will be made in June 2013.

Austin also shared key characteristics of NCATS' initiatives. First, they need to address significant bottlenecks and hurdles in the process of translation. He asked that the Council/CAN Review Board members think about — and report to NCATS — barriers they have had to overcome to deliver therapeutics to patients. Second, NCATS' initiatives must be highly collaborative across NIH, other government agencies and the private sector. Third, they need to be rapidly responsive solutions to meet the needs of biomedical researchers.

IV. NIH UPDATE: Lawrence A. Tabak, D.D.S., Ph.D., Deputy Director, NIH

Dr. Tabak provided additional information about the implications of a possible federal budget sequestration on the NIH budget.

Tabak spoke about plans for implementing recommendations that Dr. Francis Collins, director of NIH, received from working groups of the Advisory Committee to the Director (ACD).

Regarding the future scientific research workforce, Tabak presented a model developed by the Biomedical Research Workforce ACD Working Group to depict the likely career paths of college graduates with scientific degrees. The model shows that it is becoming increasingly difficult to launch traditional, independent academic research careers, and yet current training programs offer little preparation for careers outside of academia.

The Biomedical Research Workforce Initiative calls for innovative training approaches, awards that encourage independence, NIH support for postdoctoral stipends and benefits and faculty salaries, and a tracking system for trainees. This year, the ACD will launch a new working group on clinician scientists, finalize plans for FY 2013 activities, and initiate implementation plans.

Tabak stated that the ACD also received recommendations to solve the problem of certain racial/ethnic groups being underrepresented in the NIH-funded research workforce. The proposed Diversity Initiative has two goals: 1) increase the diversity of the NIH-funded workforce because compelling evidence shows that this will help accomplish NIH's mission; and 2) ensure that all applicants are treated fairly in the peer-review system. The first step in implementing the Diversity Initiative will be recruiting a permanent chief officer for scientific workforce diversity, who would have a broad mandate and substantial resources. Planning grants will be issued this fiscal year.

Finally, Tabak said that the ACD's Data and Informatics Working Group recommended in its report that "NIH leadership must accept a distributed commitment to the use of advanced computation and informatics toward supporting the research portfolio of every IC [Institute and Center]." Two initiatives are being proposed: 1) The Big Data to Knowledge (BD2K) initiative to enable the biomedical research enterprise to maximize the value of biomedical data; and 2) InfrastructurePlus, which would encourage an adaptive and highly collaborative environment to sustain world-class biomedical research. Plans are in the works to constitute governing boards for the proposed data and informatics initiatives and to recruit an associate director for data science.

V. CAN REVIEW BOARD AGENDA — PRESENTATION OF THE REPORT BY THE INSTITUTE OF MEDICINE: Louis J. DeGennaro, Ph.D., Executive Vice President and Chief Mission Officer, Leukemia & Lymphoma Society

Dr. Freda Lewis-Hall introduced Dr. DeGennaro, who presented highlights of a report by the Institute of Medicine (IOM) based on a two-day workshop held on June 4–5, 2012. DeGennaro thanked his co-chair, Dr. Carolyn Compton of the Critical Path Institute, as well as the participants in the 2012 workshop, which was dedicated to exploring options and opportunities for the implementation of CAN.

DeGennaro reviewed the authorizing legislation that created CAN, noting the emphasis on "high-need cures" defined as "a drug, biologic, product or device that is a priority to diagnose, mitigate, prevent or treat harm from any disease or condition for which incentives of the commercial market are unlikely to result in its adequate or timely development."

CAN's greatest impact could be in accelerating translational science. Partnerships among institutions can help accelerate the rate at which new discoveries are translated into products that can improve health. CAN could incentivize, "de-risk" and facilitate

research at the interface of academia and industry. Planning on a programmatic, not episodic, basis will help facilitate overall effectiveness of drug development and the impact of CAN in improving and accelerating the development of cures.

CAN's matching authority, DeGennaro explained, is a unique incentive. Matching requirements, properly crafted, could engage companies early in development and secure their commitment across the whole spectrum of therapeutic development. Building milestones into the process could help maintain focus.

CAN's flexible research authority allows CAN to use this mechanism to develop innovative partnerships that cannot be accomplished using standard NIH grants and contracts. DARPA uses such authority to capitalize on novel opportunities to solve problems. This approach means CAN may be able to foster partnerships that otherwise might be impossible.

DeGennaro said that CAN's place within the drug development ecosystem needs strengthening. CAN's interactions with FDA will be critical, and because some CAN projects will be in the precompetitive product development space, issues such as conflicts of interest, antitrust provisions, data access, publication and intellectual property need to be considered.

The workshop signaled that CAN is positioned to break the status quo by supporting individuals and companies that are outside the mainstream. CAN's portfolio should focus not only on cures, but also on transforming the process that will lead to cures.

Dr. Austin suggested to Lewis-Hall that it would be helpful if a subset of the CAN Review Board established some priorities and metrics. He requested that a report be presented to the NCATS Advisory Council during the May meeting.

VI. RE-ENGINEERING TRANSLATIONAL SCIENCES — ORGANS ON CHIPS: Donald E. Ingber, M.D., Ph.D., Wyss Institute

Dr. Danilo Tagle, NCATS associate director for special initiatives, pointed out that NCATS' Microphysiological Systems Program aims to use human tissues in systems that mimic human physiology for drug screening. The effort is a collaboration between NCATS (through CAN) and DARPA, and also is supported in part by the NIH Common Fund. The FDA is contributing regulatory and toxicology expertise to the effort. The goal of the program is to develop *in vitro* systems that are physiologically relevant, genetically diverse and pathologically meaningful on a modular, reconfigurable platform.

Tagle introduced Dr. Donald Ingber, founding director of the Wyss Institute for Biologically Inspired Engineering at Harvard University. Ingber explained that the work is focusing on replicating organ-level function on the chips and thus replacing animal testing as a means of assessing safety and efficacy of drug candidates.

Ingber showed a video clip of a lung-on-a-chip system that is composed of a clear flexible polymer about the size of a thumb drive. The chip contains a central millimeter-sized hollow microchannel that is spanned by a porous membrane. Living human lung alveolar epithelial cells are cultured on the top of the membrane and air is flowed over their surface, while living human capillary endothelial cells are cultured on the opposite side of the same membrane with culture medium containing primary human white blood cells flowing over their surface. Application of a cyclic vacuum in side chambers causes the artificial alveolar-capillary interface to stretch cyclically, thereby mimicking breathing.

Other organ-on-chip devices are in development. The beating-heart-on a chip system, for example, which is being developed by Dr. Kit Parker at the Wyss Institute, currently uses rat myocardium; however, human iPS cells are currently being explored as an alternative source. Ingber spoke about linking the heart and lung chips to assess the cardiac toxicity of inhaled drugs. It is also possible to induce inflammation in the lung chip with tumor necrosis factor-alpha, to suppress it with glucocorticoid treatment, and to mimic the complex human disease process of pulmonary edema ("fluid on the lungs") on the chip. Ingber also has developed a human gut-on-a-chip, which exhibits villus and crypt formation, as well as mucus production, when stimulated with *in vivo*-like trickling flow and peristalsis motions.

Ingber concluded by saying that the FDA has been extremely supportive of this work. Discussions are under way about potentially using the chips as biomarkers in the future. If they are as good as or better than an animal model, the FDA might tell therapeutics manufacturers that they can use results from organ-on-chip studies as part of their submission for approval instead of data from animal studies.

VII. CLINICAL AND TRANSLATIONAL SCIENCE — EDUCATING THE CLINICAL/TRANSLATIONAL SCIENTIST: Elliott M. Antman, M.D., Brigham and Women's Hospital

Dr. Elaine Collier, DCI acting co-director, NCATS, remarked that all CTSA awardees engage in training, including curriculum and course development. Both predoctoral and postdoctoral training programs are supported through the CTSAs. Predoctoral training is mainly for medical students.

Collier introduced Dr. Elliott Antman, the director of education for Harvard Catalyst (the Harvard CTSA) and associate dean for clinical/translational research at the Harvard Medical School. Antman explained that therapeutics development is a complex task with a bidirectional nature, and he underscored the importance of training the workforce of the future, which will help make the process more efficient.

Antman showed how various careers can "plug into" the spectrum of clinical and translational research. He also provided some background on the four tiers of translational science — ranging from experiments with a high degree of control of

experimental conditions (e.g., clinical pharmacology, biomarker development) to epidemiologic studies and global health research, which have far less control. This is an important framing point for those embarking on a career in clinical/translational science.

One important new concept is that information can be acquired rapidly using technology. Thus, training can focus more on learning where the information resides, freeing people to think creatively to solve problems.

A searchable catalog of the 230 course offerings at the Harvard CTSA is organized according to core competency domains. Antman discussed an introductory course in clinical investigation and a two-week introduction to translational medicine. This spring, the programs are being integrated into one master's degree program in clinical/translational science. Unique at this CTSA is the grant review and support program, which is intended to help overcome the hurdle to R01 funding.

VIII. RARE DISEASE RESEARCH AND THERAPEUTICS: Stephen C. Groft, Pharm.D., Director, ORDR, NCATS

According to Dr. Groft, about 11.4 percent of the NIH research budget is dedicated to rare diseases. NIH supports about 9,400 research projects on rare diseases and about 1,650 investigations involving orphan drugs.

The Rare Diseases Clinical Research Network (RDCRN) comprises 17 Rare Disease Clinical Research Consortia and one Data Management Coordinating Center supported by eight collaborating NIH ICs. More than 95 patient advocacy groups participate with the consortia and a patient contact registry. Consortium investigators take on multiple diseases, preferably based on a common pathway or some other unifying principle. Each consortium is required to conduct a minimum of two clinical research projects (one longitudinal and one pilot or demonstration project), run a training component, maintain a website for educational and research resources in rare diseases, and collaborate with a patient support organization.

RDCRN Projects — Many Disorders, One Goal: Alan K. Percy, M.D., University of Alabama at Birmingham

Dr. Percy provided additional background on the RDCRN and spoke about three examples of scientific advances emanating from the RDCRN consortia:

- The Rare Lung Diseases Consortium conducted a clinical trial showing that therapy with sirolimus may be useful in selected patients with lymphangioleiomyomatosis, a progressive, cystic lung disease in women. The drug stabilized lung function, reduced symptoms and improved patients' quality of life.

- The Consortium for Clinical Investigations of Neurological Channelopathies carried out a randomized, double-blind, placebo-controlled crossover trial of mexilitene in patients with nondystrophic myotonias. The scientists found that the drug was effective therapy for symptoms and signs of myotonia.
- The Urea Cycle Disorders Consortium found that N-carbamylglutamate augments ureagenesis and decreases plasma levels of ammonia and glutamine. The drug may serve as an important therapeutic adjunct in the treatment of acute hyperammonemia in this disorder.

Percy explained that the RDCRN's patient contact registry is open to patients with diseases under study by the various consortia. It serves as an international online system for communication, recruitment and research. So far, 179 diseases are represented among 10,515 registrations.

The Coalition of Patient Advocacy Groups is an important partner of the RDCRN. Advocacy groups provide funding for pilot projects and training and assist with recruitment for studies.

Progress in Rare Diseases Through RDCRN — Genetic Disorders of Mucociliary Clearance: Michael R. Knowles, M.D., University of North Carolina School of Medicine

Dr. Knowles spoke about the ripple effect that RDCRN support can have and offered the example of rapid progress made by the Genetic Diseases of Mucociliary Clearance Consortium. The consortium started with four U.S. sites in 2004; now it is possible to perform clinical trials in the network of sites.

Airway host defense is primarily through mucociliary clearance and coughing. This function is impaired in primary ciliary dyskinesia (PCD) and cystic fibrosis (CF), both of which are characterized by inflammation, infection and airway obstruction.

As of 2004, no simple laboratory test existed for diagnosing PCD, and there was scant information on the clinical course of the condition. No treatment regimens had been established. In 2012, consortium scientists reported that PCD and CF patients tended to have very low levels of nasal nitric oxide; this finding might provide the basis for a useful diagnostic test. The scientists also learned that respiratory distress and hypoxia are very common in term neonates with PCD. Therefore, cilia are very important in clearance of lung liquid in the neonatal period. Genetic studies of PCD have revealed 18 PCD-causing genes. Sixty-five percent of PCD patients have biallelic mutations; it is hoped that genetic testing will soon be able to identify more PCD mutations.

Knowles reviewed the training and educational activities carried out by the consortium.

In closing, Dr. Austin discussed and compared "disease-centric" research to a more integrated approach for studying common genes and pathways. He suggested an

analogy to a jigsaw puzzle: The more pieces you put in place, the easier the puzzle becomes as you reduce the degrees of freedom. NCATS could have a role in this model for research.

IX. RARE DISEASE RESEARCH AND THERAPEUTICS: Christopher P. Austin, M.D.

Dr. Austin introduced Dr. McKew and also remarked on the new NIH logo. All Institutes and Centers are being encouraged to use the new logo to make it clear that NIH is the primary funder of biomedical research in the United States.

Therapeutics for Rare and Neglected Diseases Program — Mission and Solicitation Update: John C. McKew, Ph.D., Acting Director, Division of Pre-Clinical Innovation (DPI), NCATS

Dr. McKew explained the great burden imposed by rare diseases. Somewhat fewer than 7,000 diseases affect humankind, but only a small fraction is sufficiently prevalent to support commercial development of therapeutic agents.

The TRND program is a unique model that hinges on collaboration between DPI and extramural laboratories with disease-area or target expertise. He reviewed the criteria for TRND projects, which are driven by milestones. TRND also focuses on helping to develop new platform technologies. McKew emphasized that TRND support is not in the form of grants, but rather collaborations where NCATS provides research in kind. A collaborator generally receives a data package sufficient to advance their therapeutic, not funds for a laboratory. Entry into the TRND project can occur as early in the therapeutics development process as lead optimization or as late as pre-IND (Investigational New Drug) filing and early clinical development.

McKew reviewed the project selection process. After considering with due diligence which proposals should be moved forward, the TRND staff will present the selected projects to the NCATS Advisory Council for consideration and approval.

Since 2009, TRND has shepherded 14 projects through the pilot phase and issued two public solicitations. Four investigational drugs have entered first-in-human trials for such disorders as chronic lymphocytic leukemia, sickle cell disease, hereditary inclusion body myopathy and Neimann-Pick type C disease.

McKew presented the existing TRND portfolio. Collaborators include academic researchers, small businesses and several foundations and companies. McKew went on to introduce Stephen R. Seiler, J.D., founder and chief executive officer, AesRx, who discussed his TRND collaboration on a new treatment for sickle cell disease.

A TRND Collaborator's Perspective: Stephen R. Seiler, J.D., Founder and Chief Executive Officer, AesRx

Sickle cell disease is a genetic, autosomal recessive disorder of hemoglobin that causes red blood cells to deform into rigid sickle shapes that block capillaries. It is a global disease; unfortunately, the ability to pay for treatment is inversely proportional to the prevalence of the disease.

The Aes-103 compound was an attractive development candidate because it had a proven mechanism of action, because X-ray crystallography studies had demonstrated that it hit the molecular target, and there was available a large body of safety and toxicity data. Nevertheless, Seiler explained, there was no private funding for clinical development of Aes-103.

TRND funding catalyzed the Aes-103 project, and it attracted additional support from AesRx; the National Heart, Lung, and Blood Institute; the NIH Clinical Center; the NIH Clinical Center Pharmacy Department; and other entities. AesRx aimed to complete a comprehensive "industrial-strength" preclinical package and sought to undertake an early clinical trial to de-risk its asset by achieving clinical proof of concept. The AesRx/NIH collaborators met with FDA officials to clarify clinical end points and a regulatory path forward for AesRx.

An IND application for Aes-103 was filed in less than a year from the announcement of the AesRx/NIH collaboration. A Phase I trial in healthy African American volunteers was completed in 2012. It showed that Aes-103 is safe and well-tolerated. Further, it has biological activity consistent with its proposed mechanisms. The drug is currently in a Phase I/IIa trial at the NIH Clinical Center in Bethesda, Md. Next will be a Phase IIa trial to include clinical end points recommended by the FDA. Having crossed the "Valley of Death," Aes-103 will be positioned to generate development support from the pharmaceutical industry or venture capitalists.

X. CONCEPT CLEARANCE OF POTENTIAL INITIATIVES: Elaine Collier, M.D., Acting Co-Director, DCI, NCATS

Dr. Collier presented two concepts for potential initiatives for consideration by the NCATS Advisory Council:

Ethical Challenges in Translational Research: Evidence-Based Approach

Researchers face many ethical challenges in the translation of basic findings into clinical testing and, ultimately, implementation in the clinic. Some of these include:

- Integration of data from multiple sources, including clinical and genomic data, with increased risk of identification of individuals;

- Increasingly robust phenotyping of distinct disease subsets, such as those defined as “rare diseases;”
- How to assign patients to different treatment areas of a clinical trial for diseases with no effective treatments;
- Biospecimen studies; and
- Research in clinical care settings, such as what is recommended in the IOM’s Learning Health Care System report.

Ethical challenges affect all areas of science and all stages of translation. Evidence-based research is needed to provide data to inform solutions.

This concept proposes NIH-wide collaboration supported with bioethics funds from the NIH Office of the Director. The initiative would help the CTSA community and NIH-funded networks by integrating evidence-based ethics research with current research activities.

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

Increase National Capacity for Clinical and Translational Research

Industry, academia and regulatory bodies exhibit willingness to change the currently inefficient practices in translational research. However, all in the biomedical research community need a national environment that supports innovation. CTSA-funded institutions have developed effective partnerships at the regional, state and national levels. Working with NIH-supported networks and other stakeholders, academic leaders at CTSA institutions are well positioned to address national solutions to increase the efficiency, quality, safety and capacity to conduct translational research.

This potential initiative would provide opportunities to pilot expansion of innovative and effective practices, methodologies and technologies across multiple sites in real time to support a sustainable national capacity for translation research. The projects would provide data on impact and scalability for increasing national capacity, with clearly defined targets and milestones for each project.

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

ADJOURNMENT OF CAN REVIEW BOARD MEETING

Dr. Lewis-Hall adjourned the CAN Review Board meeting at 3:48 p.m. ET.

ADJOURNMENT OF OPEN SESSION OF THE NCATS ADVISORY COUNCIL MEETING

Dr. Austin adjourned the open session of the NCATS Advisory Council meeting at 3:49 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.

XI. APPLICATION REVIEW

The Council reviewed 258 applications (with total direct costs [excluding TRND] of $33,535,297). The Council concurred with the review of all applications.

ADJOURNMENT OF CLOSED SESSION OF THE NCATS ADVISORY COUNCIL MEETING

Dr. Austin adjourned the closed session of the NCATS Advisory Council meeting at 4:30 p.m. ET.

CERTIFICATION

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

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

_____ _____

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

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