NCATS CAN Review Board Virtual Meeting

Friday, December 11, 2015
11 AM-2 PM ET

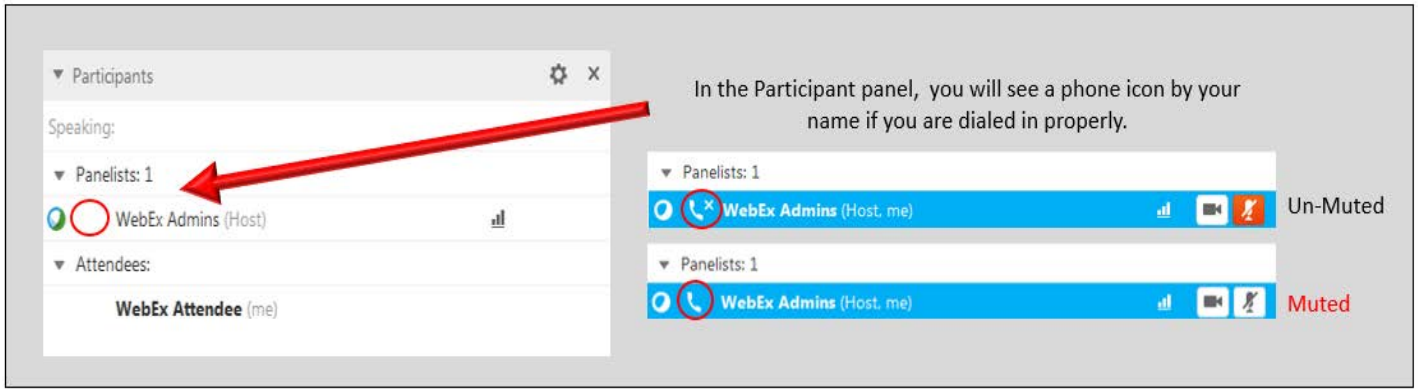
Please stay on the line, the meeting will begin shortly

13th Meeting of the NCATS CAN Review Board

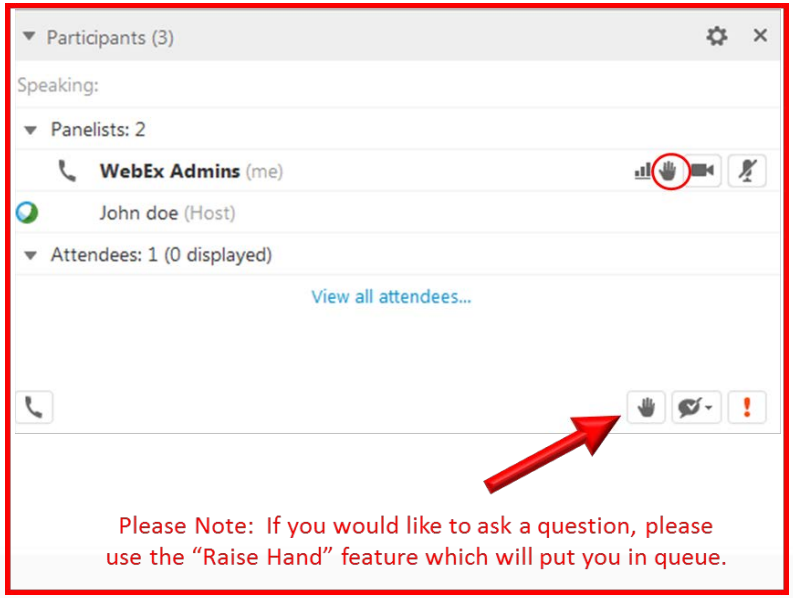
AGENDA

11:00-11:15 AM	**Call to Order and Opening Remarks**
	Freda Lewis-Hall, M.D.; Geoff Ginsburg, M.D., Ph.D. (CAN Review Board Co-Chairs)
11:15-11:20 AM	**Confirmation of Dates for Future NCATS Advisory Council / CAN Review Board Meetings**
	Anna Ramsey-Ewing, Ph.D. (CAN Executive Secretary)
11:20-11:30 AM	**Update on NCATS**
	Pamela McInnes, D.D.S., M.Sc. (Dent.) (Deputy Director, NCATS)
11:30-11:45 AM	**Previously Approved CAN Concept Clearances (3)**
	Dan Tagle, Ph.D. (Associate Director for Special Initiatives, NCATS)
11:45-12:30 PM	**New CAN Concept Clearances (4)**
	Dan Tagle, Ph.D. (Associate Director for Special Initiatives, NCATS)
12:30-2:00 PM	**Discussion of All Concepts**
	Freda Lewis-Hall, M.D.; Geoff Ginsburg, M.D., Ph.D. (CAN Review Board Co-Chairs)
2:00 PM	**Adjourn**

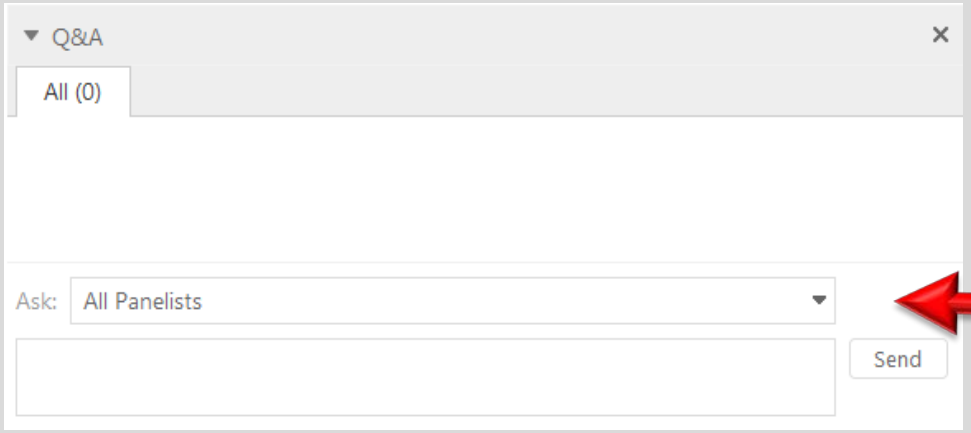
Today's Meeting Will Have a Discussion Session



- **Only CAN Review Board members will be able to participate in the discussion verbally**
- **To participate via phone, you must be dialed in properly**
- **<u>All other participants, please feel free to submit a question or comment via typing in Q&A box</u>**



TO ASK A QUESTION IN SPLIT SCREEN MODE:

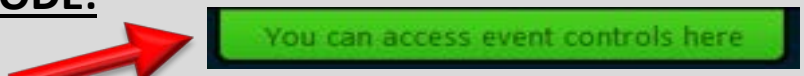


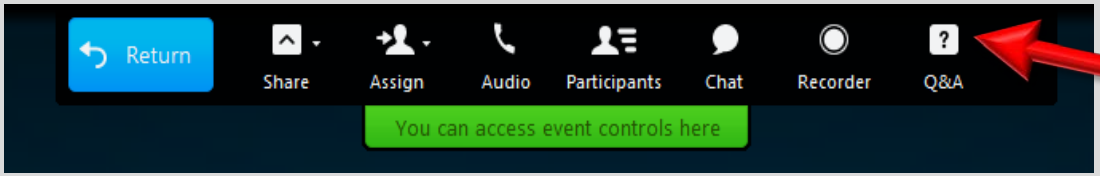
Type your questions into the text field in the **Q&A box**, located on the lower right side of your screen, and send to: **HOST (Christine Cutillo)**
*Please note: You will only be able to submit questions in the **Q&A** box **not** the Chat box*

Please note: You are only able to see the questions you have submitted, due to privacy concerns.

TO ASK A QUESTION IN FULL SCREEN MODE:

Hover over the green toolbar that will be at the top or bottom of your screen





Select the **Q&A** option, and a **Q&A** pop-up box will appear. Type your question and send to: **HOST (Christine Cutillo)**

Confirmation of Dates for Future NCATS Advisory Council / CAN Review Board Meetings

2016

January 14

May 12

September 15

CAN Review Board only (by phone): December 9

Update on NCATS

Pamela McInnes, D.D.S., M.Sc. (Dent.)
Deputy Director, NCATS

FY 2016 Budget Request

- On February 2, 2015, President Obama released the FY 2016 budget
  - NIH: request for $31.3B, increase of $1B over FY15
  - NCATS: request for $660.1M, increase of $27.4M over FY 2015
  - NCATS' Congressional Justification (CJ) and appropriation status is available at: https://ncats.nih.gov/about/center/budget

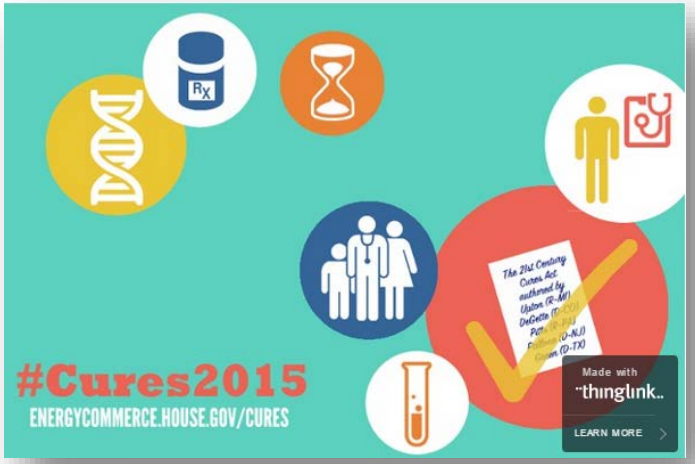
- House and Senate appropriation bills approved by committees, but never voted on by full chambers

FY 2016 Budget Request, cont.

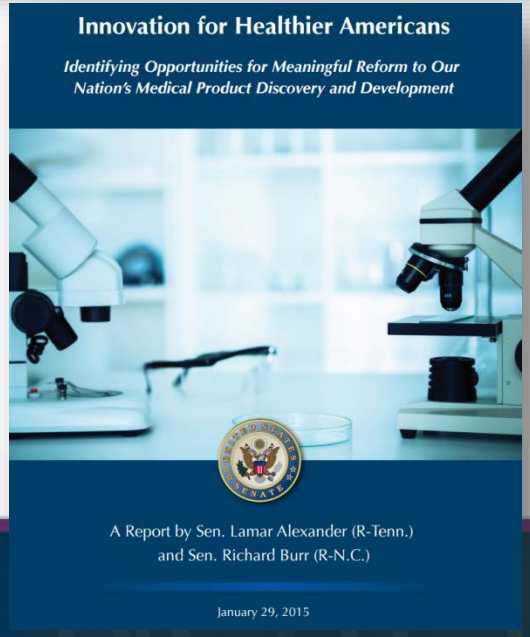
- At the end of October, Congress passed the Bipartisan Budget Act of 2015 (P.L. 114-74), which raised the Sequester caps for the appropriation bills
- Congress is working on revised appropriation bills, which could be included in an Omnibus bill for FY16
- Federal government is currently operating under a Continuing Resolution (CR) through December 11
- An additional CR, lasting through Wednesday, December 16, has been introduced

Congressional Authorizing Activities

- House – 21st Century Cures (H.R. 6)
  - July 10 – passed by large majority (344-77)
  - NIH "Innovation Fund" - $8.75 billion, over five years



- Senate – Innovations for Healthier Americans
  - Draft bill has not been released yet



Cures Acceleration Network Review Board

December 11, 2015

PREVIOUSLY APPROVED CAN CONCEPT CLEARANCES:

- 1) INCREASING ACCESS TO COMPOUNDS AND TOX DATA
- 2) PROOF OF PRINCIPLE (POP) AWARDS
- 3) SENSORS AND DEVICES TO DETECT CLINICAL OUTCOMES

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Concept Clearance

(1) INCREASING ACCESS TO COMPOUNDS AND TOX DATA

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(1) Increasing Access to Compounds and Tox Data

- Goal
  - Access compounds that did not have a safety signal in preclinical studies, but were later shown to have toxicity in humans
  - Investigate underlying mechanisms for the human toxicity and why preclinical tools failed
  - Incorporate this information into predictive modeling to benefit drug development
- Description of outcome
  - Develop new assays to fill gaps in the current predictive toolbox
- Potential impact
  - NCATS will work with multiple pharma companies, FDA, and companies that develop predictive tox tools
  - Understanding mechanisms of toxicity will have implications for all drug development

(1) Increasing Access to Compounds and Tox Data

- Criteria for evaluating success
  - Number of compounds in the program
  - Number of mechanisms elucidated
- Major obstacle to address
  - The underlying mechanism of toxicity discovered in or after Phase 1 trials is often not investigated
- Summary of ongoing research/activity in this area
  - New Therapeutics Use
    - Already has relationships with companies in place and process for establishing the collaborations between the academic researchers and pharma companies has been validated

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December 11, 2015

Concept Clearance

(2) Proof of Principle (POP) Awards

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(2) Proof of Principle (POP) Awards

- Goal
  - Program aimed at preclinical research projects that develop, demonstrate, or deploy interventions to improve human health; and have applied for NIH support but did not receive funding due to a lack of a specific piece of translational data
- Description of outcome
  - Generation of the specific piece of preclinical data to make a project more competitive for subsequent funding or otherwise move a project forward
- Potential impact
  - Strengthening applications for programs across NIH, and perhaps at a future stage, across the entire translational research enterprise
  - Applications funded will be those that potentially have a broad and significant impact
  - Each project will be completed in a short period of time

(2) Proof of Principle (POP) Awards

- Criteria for evaluating success
  - Success in obtaining the critical piece of translational data
  - Reports from awardees about subsequent progress (including any advancements such as creating IP, obtaining funding, preparing an IND package)
  - Outcomes of subsequent applications for NIH support
- Major obstacle to address
  - Experience with pre-clinical projects reveals that there are many applications which lack a critical piece of data that could make their projects strong candidates for other NIH programs
- Summary of ongoing research/activity in this area
  - NIH has a number of grant programs for limited amounts and short timeframes. However most of these programs are not:
    - Focused on projects that develop, demonstrate or deploy interventions to improve human health
    - Aimed at projects that have already undergone the NIH review process and received feedback indicating a lack of a limited yet critical piece of data

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December 11, 2015

Concept Clearance

(3) Sensors and Devices to Detect Clinical Outcomes

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(3) Sensors and Devices to Detect Clinical Outcomes

- Goal
  - Advance the integration of real-time data from multiple devices and sensors to meaningfully inform clinical outcome assessment
- Description of outcome
  - Requires diverse collaborative team (technology leaders, patients, data scientists, etc.) to uniformly collect and analyze sensors/devices data for assessing clinical outcome
- Potential impact
  - Resolution of engineering, technical, computational, social, and cultural barriers to adoption and utility of sensor and device data
  - Establish practices applicable to other disease domains

(3) Sensors and Devices to Detect Clinical Outcomes

- Criteria for evaluating success
  - Utilization of integrated data toward clinical outcome assessment / biological endpoint
  - Public dissemination of lessons learned and data
- Major obstacle to address
  - Many sensors and devices are available to measure physiologic, environmental, and patient reported information, however the clinical utility of these is limited by lack of integration of the data from multiple sources
  - This problem includes the collection, transfer, and management of data as well as various environmental measurements
- Summary of ongoing research/activity in this area
  - Many ongoing activities, including wearable technologies, but not standardized nor interoperable, and no concerted efforts to warehouse data
  - Opportunity to sync with efforts in Electronic Medical Records and Precision Medicine Initiative

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NEW CAN CONCEPT CLEARANCES:

- 6) SAME THERAPEUTICS: TARGETING SHARED MOLECULAR ETIOLOGIES UNDERLYING MULTIPLE DISEASES TO ACCELERATE TRANSLATION
- 4) 3-D BIOPRINTING OF HUMAN TISSUES FOR DRUG SCREENING
- 5) PROTEOMIC PROFILING FOR CLINICAL APPLICATIONS
- 7) TISSUE CHIP TESTING CENTERS: VALIDATING MICROPHYSIOLOGICAL SYSTEMS

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Concept Clearance

(6) SaME Therapeutics:

Targeting Shared Molecular Etiologies underlying multiple diseases to accelerate translation

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(6) SaME Therapeutics : Targeting Shared Molecular Etiologies underlying multiple diseases to accelerate translation

- Goals
  - Develop a matrix of diseases and molecular etiologies to identify shared molecular etiologies (SMEs) underlying multiple diseases
  - Stimulate the identification and novel clinical trials of SME-targeted drugs
- Description of outcome
  - A fundamental change in therapeutics development to focus on SMEs underlying multiple diseases, rather than clinical phenotypes of individual diseases
- Potential impact
  - Maximize the translational impact of NIH-funded science, and increase the number of patients who have effective treatments for their diseases

(6) SaME Therapeutics : Targeting Shared Molecular Etiologies underlying multiple diseases to accelerate translation

- Criteria for evaluating success
  - A matrix of SMEs and diseases, # of SME targeted therapeutics, # of clinical trials of SME-targeted drugs, # of traditional disease patients grouped into SME based clinical trials
- Major obstacle to address
  - Large number of human diseases, but too few with effective treatments. SaME Therapeutics provides a solution to this problem, consistent with NCATS mission to bring more treatments to more patients more quickly
- Summary of ongoing research/activity in this area
  - In rare diseases, druggable SMEs have already been identified (e.g. misfolded proteins, premature termination codons, lysosomal dysfunction, mTOR pathway). Also, a conceptually similar approach is being used in clinical trials of drugs that target SMEs underlying multiple cancer types

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Concept Clearance

(4) 3-D BIOPRINTING OF HUMAN TISSUES FOR DRUG SCREENING

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(4) 3-D Bioprinting of Human Tissues for Drug Screening

- Goals
  - Establish a multidisciplinary NIH-based Center that uses 3-D bioprinting to generate high throughput screenable assay models of human tissues for drug discovery
  - Access by extramural investigators to the NIH 3-D bioprinting core group to establish human tissue models and protocols for the generation and differentiation of human iPSCs to the tissue cells of interest
- Description of outcome
  - Catalog of reproducible, disease relevant, and screenable living human tissues using 3-D bioprinting with human patient iPSC cells that can be used for efficient drug discovery and development
- Potential impact
  - 3-D bioprinting of human live tissues derived from human patient stem cells is expected to provide drug efficacy data that is more predictive to those obtained in whole body responses
  - Decrease in clinical trials failure rates, and faster development times than those using the current simplistic in vitro and in vivo models

(4) 3-D Bioprinting of Human Tissues for Drug Screening

- Criteria for evaluating success
  - Create and make available to the scientific community a catalog of 3-D bioprinted human tissues that are robust and disease relevant for drug discovery and development
  - Reduce, remove or bypass system-wide bottlenecks in the translational drug discovery process by creating highly predictive assays for efficient and high throughput efficacy testing of new drugs
- Major obstacle to address
  - Rapid, scalable, and reliable fabrication of architecturally, physiologically and functionally defined human tissues using 3-D bioprinting technologies
  - Quantitative validation of 3-D bioprinted tissues in screening format
  - Foster effective multidisciplinary collaborations to leverage all the cutting-edge tissue bioengineering, iPSC and imaging technologies worldwide
- Summary of ongoing research/activity in this area
  - Ongoing research collaboration between NIH and Organovo
  - NIH is developing tissue models of the retina and skin using Organovo's NovoGen MMX Bioprinter®.

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Concept Clearance

(5) PROTEOMIC PROFILING FOR CLINICAL APPLICATIONS

(5) Proteomic Profiling for Clinical Applications

- Goals
  - Establish new clinical tests and protein biomarkers based on quantitative proteomics, phospho-proteomics, and validated antibodies
  - Optimize technical and analytical tools and easy-to-use resources and databases for physicians and clinical staff
  - Integrate analysis of genetic and proteomic data for decision-making in personalized health care
  - Better understanding and longitudinal monitoring of pathophysiology and drug effects by quantitative proteomic read-outs
- Description of outcome
  - New sensitive clinical tests, reliable panels of protein biomarkers, and quantifiable assays reflecting dynamically regulated proteins as the functional effector molecules in cellular systems to directly define phenotypes in monogenic and complex diseases
  - Mass spectrometry-based quantitative proteomics as a tool for evidence-based precision medicine, and its potential use in analysis of cellular biopsy material and bodily fluids
- Potential impact
  - Routine clinical analysis of human proteins and their posttranslational modifications will open up new opportunities for health care and precision medicine
  - Quantitative clinical proteomics will reduce human bias and increase success in the diagnostic and therapeutic process

(5) Proteomic Profiling for Clinical Applications

- Criteria for evaluating success
  - Routine analysis of selected protein markers or proteome-wide approach in the clinic
  - More clinicians utilizing the power of proteomics for decision-making and patient care
  - Bringing proteomics technology to the “bedside”
- Major obstacle to address
  - Standardize and simplify technical and analytical tools
  - Make clinical proteomic analysis as affordable and robust as genomic analysis and other clinical tests
  - Develop new high-throughput screening platforms to process many clinical samples in parallel
  - Characterize disease biology and drug effects by proteomics
  - Posttranslational modifications cannot be assessed by genomic methods but are often drug targets and critical endpoints (e.g. kinase inhibitors in oncology change protein phosphorylation, GPCR manipulation and downstream effects are dynamically regulated, channelopathies change proteins and phosphorylation signatures)
  - Increase the efficiency of translation by integrating genomic and proteomic data
- Summary of ongoing research/activity in this area
  - Mass spectrometry-based precision proteomics has dramatically improved over the last 10 years
  - Increased sensitivity and faster mass spectrometry allow reproducible and robust analysis of multiple clinical samples within a few hours
  - Human Proteome Organization (HUPO) has already established useful resources and guidelines, which can be further developed for clinical applications

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Concept Clearance

(7) TISSUE CHIP TESTING CENTERS: VALIDATING MICROPHYSIOLOGICAL SYSTEMS

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(7) Tissue Chip Testing Centers: Validating Microphysiological Systems

- Goals
  - Create Tissue Chip Testing Center(s) that will be responsible for the testing of a select group of compounds using pre-defined assays according to FDA and pharmaceutical industry standards
- Brief description of outcome
  - Independent validation of tissue chips to demonstrate functionality and utility
  - Dissemination of data through creation of a public tissue chip database
- Potential impact
  - Potential to more accurately reflect human responses when compared with current in vitro and animal models, and could have a substantial impact in the safety and efficacy testing of candidate therapeutics
  - Congruent with NIH efforts on increased reproducibility, rigor and robustness

(7) Tissue Chip Testing Centers: Validating Microphysiological Systems

- Criteria for evaluating success
  - Widespread use and adoption of tissue chips as tools for predictive toxicology and efficacy assessments of candidate therapeutics
- Major obstacle to address
  - Lack of better predictive tools in evaluating safety and effectiveness of promising candidate drugs
- Summary of ongoing research/activity in this area
  - Ongoing efforts across NIH, DARPA and FDA to develop tissue chip technology through a consortium approach
  - 1st Tissue Chip Partnership workshop held August 2015 bringing together consortium investigators with representatives from pharmaceutical companies and industry
  - Development of PPP with individual pharma partners, as well as with the IQ Consortium, to come up with validation set of compounds and standardized assays and biomarkers

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