American Institute for Medical and Biological Engineering

AIMBE/NIH Summit on

Validation and Qualification of New In Vitro Tools and Models for the Pre-Clinical Drug Discovery Process

Lister Hill Auditorium, NIH Campus, Bethesda, MD

NIBIB

National Institute of Biomedical Imaging and Bioengineering

- Drug discovery costs too much and takes too long – especially pre-clinical

- How can AIMBE help with this problem?

- Advocate to get new technologies into the pre-clinical space to REPLACE existing methodologies – especially animals

- …the next generation of systems biology tools will be in vitro systems that are in defined, serum free conditions and composed of human cells…

  Lee Hood
  Days of Molecular Medicine
  Conference, May 7, 2009

- Geron Corporation and GE Healthcare establish agreement to create tools to test for toxic effects of drug treatments

  June 30, 2009

- Establishment of Regulatory Science Initiative between NIH and FDA

  February 24, 2010

- ….with earlier and more rigorous target validation in human tissues, it may be justifiable to skip the animal model assessment of efficacy altogether …..

  Francis Collins July 6, 2011
  Science Translational Medicine

- Authorization of NCATS

  February, 2012

- However, although it seems simple after much discussion with the NIH, FDA and industry it's a far more complex issue

- Recurring topic was validation and qualification of new technologies – especially for replacement of existing technologies

- Needs community to come together to explore the technology and the definitions of *validation* and *qualification*

Agreement on the Definition of Validation and Qualification for Our Purposes

- **Validation (this is something the technology developer must provide to the FDA or to Pharma clients or both)**

  Validation is documented evidence that provides a high degree of assurance that a human-on-a -chip assay will consistently produce a result that meets its predetermined specifications.

- **Qualification (this is something the FDA does with the developer)**

  A conclusion that within the stated context of use, the results of assessment with the human-on-a -chip systems can be relied upon to have a specific interpretation and application in drug development.

Workshops have established

- Community interested in validation and qualification
- Established that validation and qualification will be fundamentally different between toxicological evaluation and efficacy
- Fourth workshop established that toxicology is straightforward and the largest unknown is concerning context of use
    - already existing programs in Tox21, ECVAM, ICCVAM
- Efficacy was addressed in the fifth workshop but is a much more unknown field in terms of regulatory science and guidance but FDA is considering how to utilize these systems for this application

What COULD efficacy mean in terms of regulatory evaluations?

- Allow pre-clinical results to steer and/or limit clinical trial construction
- Reduce the number of people necessary for clinical trials, especially for Phase III, by creating human variants to represent uncommon genome profiles
- Allow in vitro clinical trials for rare diseases
- Better evaluations for children
- Better evaluation for aged individuals
- The ultimate precision medicine → individualized disease chips for each human

Developing guidance on validation of a human-on-a-chip technology for efficacy

- Guidelines for developers will need to be general because each system is different but all will need to show accuracy, specificity, stability, reproducibility, dynamic range etc.
- A standard set of compounds needs to be tested for each system and well defined endpoints should be established. Guidance on how many test compounds will be needed at how many concentrations against what gold standard should be developed.
- Limitations of the systems need to be identified.
- Demonstration that the technology is robust and transferable will be needed.
- Will need to determine whether the test method will allow for standardization.
- Justification for the technology vs. existing technologies should be made.
- Determining if the technology is cost effective is important.

Acknowledgements

Workshop Steering Committee

Co-chairs:

J Hickman, U of Central Florida (AIMBE Fellow)
Chris Kelley, NIBIB/NIH (AIMBE Fellow)
Dan Tagle, NCATS/NIH

Members

Sonja Beken, European Medicines Agency
Kaled Bouri, FDA
Federico Goodsaid, Vertex Pharmaceuticals
Anne Plant, NIST (AIMBE Fellow)
Tracy Chen, FDA

Logistical Assistance

Šeila Selimović, NIBIB/NIH
Matt Quade, NIBIB/NIH
Sarah Mandell, AIMBE

Thursday, May 25

8:00-8:30 AM	**Continental Breakfast and Check-In**
8:30-8:45 AM	**Welcome from the Organizers and Goals of the Workshop** *James Hickman, Ph.D., AIMBE Fellow and Professor, University of Central Florida* *Christine A. Kelley, Ph.D., AIMBE Fellow and Acting Associate Director, Extramural Science Programs, NIBIB/NIH; Dan Tagle, Ph.D., M.S., Associate Director for Special Initiatives, Office of the Director, NCATS/NIH*
8:45-8:55 AM	**Welcome from AIMBE** *Gilda Barabino, Ph.D., AIMBE President, Dean and Daniel and Frances Berg Professor, The Grove School of Engineering, The City College of New York* (confirmed)
8:55-9:05 AM	**Welcome from NIBIB and Perspective** *Dr. Kris Kandarpa, Ph.D., Director, Research Sciences and Strategic Directions, NIBIB/NIH* (confirmed)
9:05-9:25 AM	**NCATS Welcome and Perspective** *Christopher P. Austin, M.D., Director, National Center for Advancing Translational Sciences, NIH and Chair, IrDRC International Rare Diseases Consortium (Americas, Europe and Asia)* (confirmed)
Session 1:	***Moderator:*** **Khaled Bouri, PhD, MPH, Interdisciplinary Scientist, FDA/OC/ OCS/ORSI**
9:25-9:55: AM	**FDA/CDRH-- In Vitro Devices for Efficacy Link to What Happens When Diagnostics are Developed for Rare Diseases.** *TBD, Director Office of In Vitro Diagnostic and Radiological Health, FDA* (invited)
9:55-10:25 AM	**FDA** *Bill Mattes, Ph.D., Director, Division of Systems Biology, National Center for Toxicological Research (NCTR), FDA*
10:25-10:40 AM	***Break***
10:40-11:10 AM	**European Innovative Medicines Initiative (IMI) on In Vitro Prediction of Efficacy** *Sonja Beken, PhD, Belgian Federal Agency for Medicines and Health and the European Medicines Agency* (invited)

11:10-11:35 PM	**NIST – Convergence of Tissue Models and Regenerative Medicine** *Anne Plant, Chief, Biosystems and Biomaterials Division, NIST* (confirmed)
11:35-12:00 PM	**Patient Advocacy for Rare Diseases** *Dr. Chris Penland, Ph.D., Vice President of Research Cystic Fibrosis Foundation* (invited)
12:00-1:00 PM	***Lunch***
Session 2:	**Moderator: William E. Bentley, Department of Bioengineering, University of Maryland**
1:00-1:30 PM	**Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Overview and New Directions** *Warren Casey, PhD, DABT, Acting Director National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)* (confirmed)
1:30-2:00 PM	**Emulate Company Perspective** *Daniel Levner, Ph.D., Chief Technology Officer,* (confirmed)
2:00-2:30 PM	***Break***
2:30-3:00 PM	**Hesperos, Inc. Company Perspective** *Michael L. Shuler, Ph.D., President/CEO and Professor, Biomedical Engineering, Cornell University* (confirmed)
3:00-3:30 PM	**TissUse Company Perspective** *Reyk Horland, VP Business Development* (confirmed)
3:30-4:00 PM	**Insphero Company Perspective** *Dr. Jens M. Kelm, Chief Technology Officer, Co-Founder & Member of the Management Team* (confirmed)
4:00-4:30 PM	**GSK** *Brian R. Berridge, DVM, PhD, DACVP, Senior GSK Fellow, Head, WW Animal Research Strategy, Office of Animal Welfare, Ethics & Strategy* (confirmed)
4:30-5:00 PM	***AstraZeneca*** *Lorna Ewart, Ph.D., Head of IMED MPS Centre of Excellence* *AstraZeneca* (confirmed)
6:15-8:00 PM	***AIMBE Sponsored Reception-Share Wine Lounge***

Friday, May 26

8:00-8:30 AM **Continental Breakfast and Check-In**

8:30-8:45 AM **Goals of the Second Day**
James Hickman, Ph.D., AIMBE Fellow and Professor, University of Central Florida

8:45-9:15 AM **NCATS Rare Diseases Program**
Petra Kaufmann, DDS., Director, Office of Rare Diseases Research and Division of Clinical Innovation, NCATS (confirmed)

9:15-9:45 AM **FDA/CDER---Ideas on Efficacy for In Vitro Systems for Rare Diseases**
Paul Brown, Ph.D., OND IO, FDA (confirmed)

9:45-10:15 AM **Surrogate BioMarkers and Rare Diseases**
Federico Goodsaid, PhD, Senior VP Clinical and Regulatory Affairs, TOMA Biosciences (confirmed)

10:15-10:45 AM ***Break***

Session X: **Preclinical Rare Disease Models**

10:45-11:15 AM **European eRARE initiative**
Dr. Daria Julkowska, Coordinator, Agence Nationale de la Recherche - ANR
Health & Biology Department (confirmed)

11:15-11:45 AM **A Brain Microphysiological Model of Disease and Toxicity**
Thomas Hartung, MD, PhD, Johns Hopkins University (confirmed)

11:45-12:15 PM *Monicah Otieno, Ph.D., East Coast Head of Molecular & Investigative Toxicology, Johnson & Johnson, Janssen Research and Development* (confirmed)

12:15-1:15 PM ***Lunch***

1:15-1:45 PM *Gordana Vunjak-Novakovic, Ph.D., Mikati Foundation Professor of Biomedical Engineering, Professor of Medical Sciences (in Medicine), Columbia University* (confirmed)

1:45-2:15 PM *William Murphy, Ph.D., Professor, Department of Biomedical Engineering, University of Wisconsin* (invited)

2:15-2:30 PM ***Break***

2:30-3:00 PM *George Truskey, Ph.D., R. Eugene and Susie E. Goodson Professor of Biomedical Engineering, Duke University* (confirmed)

3:00-3:30 PM *William Proctor, Ph.D., Senior Scientist, Head of Investigative Toxicology, Safety Assessment, Genentech, Inc.* (confirmed)

3:30-4:00 PM *TBD*

4:00-5:00 PM **Panel Discussion on Paths for Rare Disease Validation and Qualification**
Moderator: Šeila Selimović, Ph.D., Program Director, Tissue Chips/Tissue Preservation Technologies/Sensors, NIBIB/NIH
Dr. Chris Penland, Cystic Fibrosis Foundation

Federico Goodsaid, PhD, Senior VP Clinical and Regulatory Affairs, TOMA Biosciences

Anne R. Pariser, M.D., Deputy Director, Office of Rare Diseases Research, National Center for Advancing Translational Sciences, NIH–

Dr. Daria Julkowska, Coordinator, Agence Nationale de la Recherche - ANR
Health & Biology Department

Jonathan Goldsmith , Director of the Rare Disease Program in the Office of New Drugs (Confirmed)

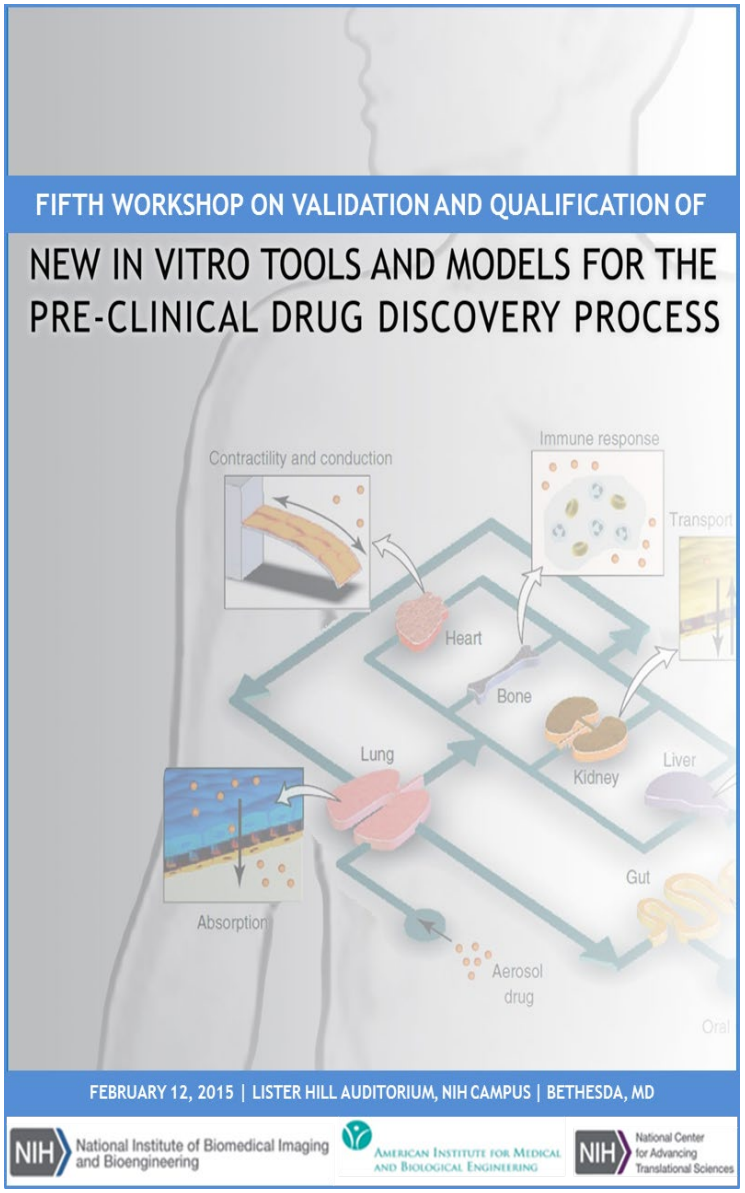
Workshops on Validation and Qualification

- The American Institute for Medical and Biological Engineering (AIMBE) and the National Institutes of Health have held a series of workshops on Validation and Qualification of New *in vitro* Tools and Models for the Pre-clinical Drug Development Process.

- Our goal is to help develop practical guidelines for technology developers on principles and practices for the validation and qualification of in vitro systems for drug development.

- The sixth workshop is addressing the application to rare diseases.

- NCATS is now an additional sponsor



Goals of Summit

- Obtain definition of validation from across the spectrum of the drug discovery enterprise for preclinical platforms and systems.
- Define qualification from the perspective of the FDA for these systems.
- Gather as much data/input on this topic as possible.
- Use to define concrete goals for a workshop to be held in September, 2012.