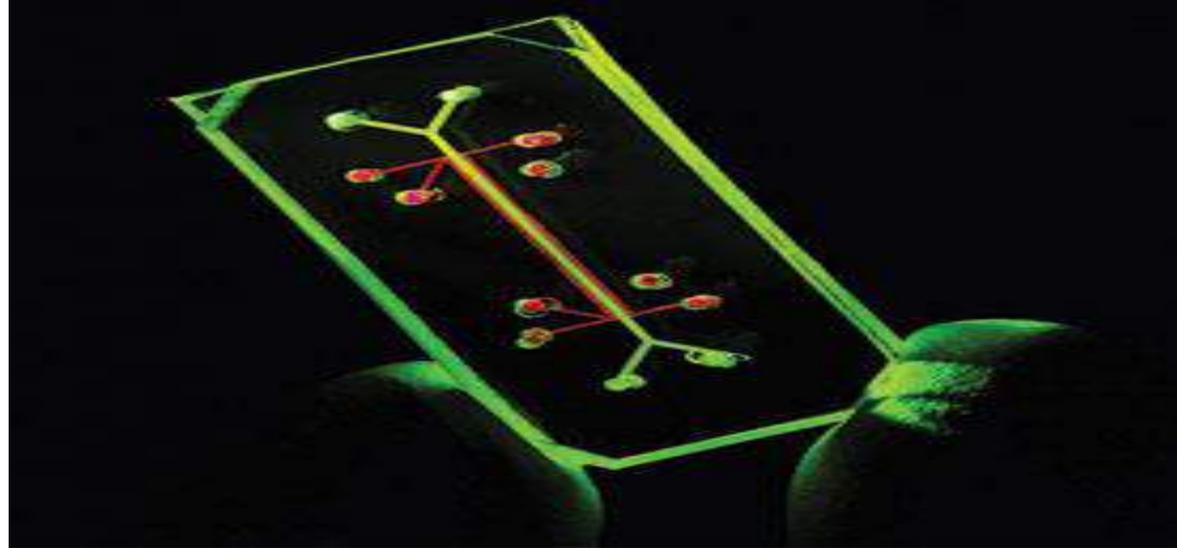


# FDA Perspectives on Organs and Tissues on a Chip

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US Food and Drug Administration  
Fall 2018 MASCOT Meeting  
October 24, 2018



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## Science & Research

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**About Science & Research at FDA**

- Scientific Integrity at FDA
- Scientific Professional Development at FDA
- 1. Transform Toxicology to Enhance Product Safety**
- 2. Stimulate Innovation in Clinical Trials and Personalized Medicine
- 3. Support New Ways to Improve Product Manufacturing and Quality
- 4. Ensure FDA Readiness to Evaluate Innovative Emerging Technologies
- 5. Harness Data through Information Sciences to Improve Health Outcomes
- 6. Implement a New Prevention-Based Food Safety System
- 7. Support Medical Countermeasures Development to Protect National Health and Security
- 8. Strengthen Social and Behavioral Science to Promote Informed Decision-Making About FDA-Regulated Products

### 1. Transform Toxicology to Enhance Product Safety



**In the News**

See Complete Web Cast of May 10, 2018 FDA-Cosponsored Workshop: [Microphysiological Systems for Use as Regulatory Tools!](#)

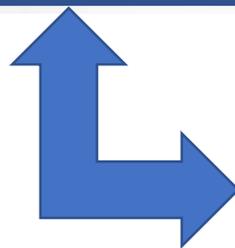
Preclinical testing plays a crucial role in identifying the potential risks associated with new FDA-regulated products. However, serious and unexpected negative side effects are sometimes discovered in clinical trials or once a product is on the market, suggesting that critical gaps exist in our understanding of the relationship between patient response and preclinical toxicology findings.

For example, non-clinical safety assessment is often conducted in normal healthy test systems and tends to be exposure-based; it does not attempt to evaluate the possible risk of rare or idiosyncratic responses that may arise from potential interactions with the presence or progression of disease or a patient's genetic background. New measurement technologies and increasing knowledge about toxicity mechanisms and pathways offer important opportunities for advanced computational analyses that can promote effectively translating non-clinical findings to the clinical setting.

FDA can close these gaps and improve preclinical safety predictions by further investing in three particular areas of regulatory science:

- evaluating and developing models and assays that better predict patient response
- identifying and evaluating more reliable biomarkers for monitoring toxicities, side effects, and abnormalities, and
- using computational tools to integrate and draw conclusions from a wide range of preclinical safety data types and sources.

# FDA Priorities for Advancing Regulatory Science



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- evaluating and developing models and assays that better predict patient response
- identifying and evaluating more reliable biomarkers for monitoring toxicities, side effects, and abnormalities, and
- **using computational tools to integrate and draw conclusions from a wide range of preclinical safety data types and sources.**

# Challenges

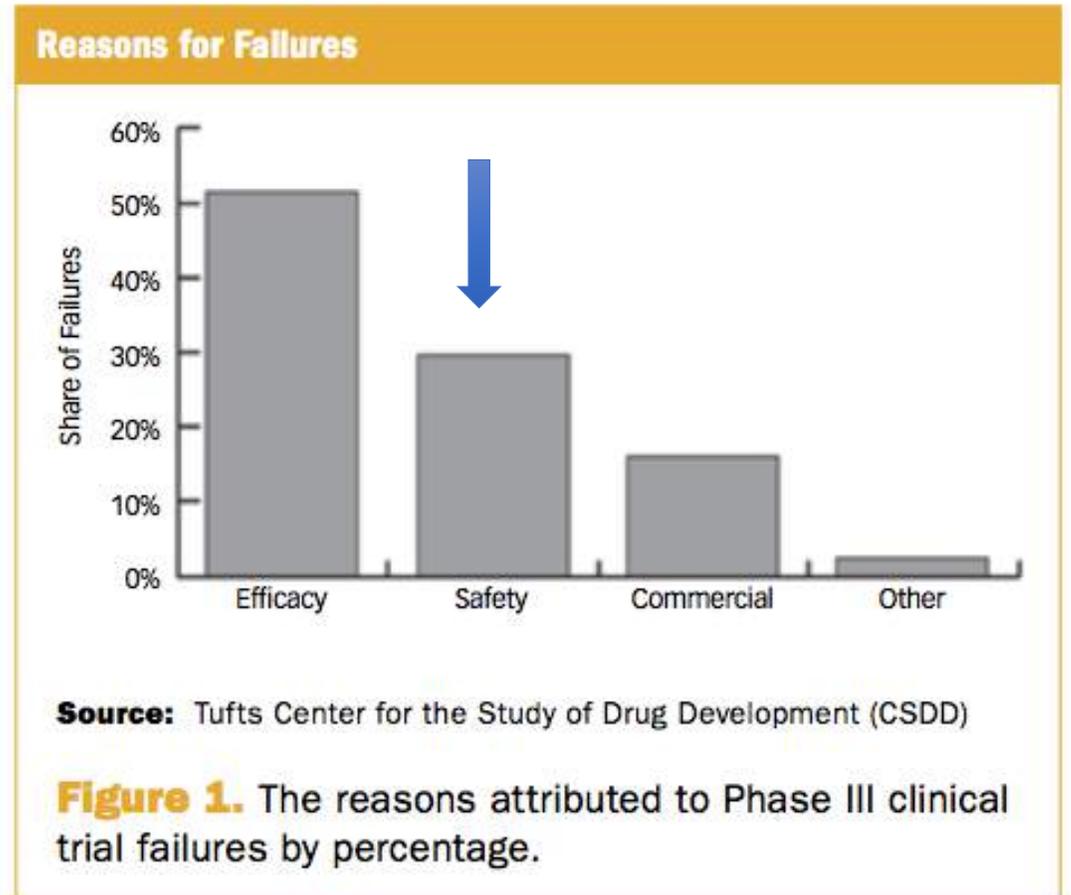
## *In Vitro*

- Usually not fully differentiated
- Immune systems, blood flow, etc. not fully represented
- Does not represent population, lacks genetic variability

## Animal Testing

- Some species better than others
- Two species better than one
- Not all toxicities identified in animals
- Using normal animals

## Humans Do Not Predict Humans



Grignolo and Pretorius, Phase III Trial Failures: Costly, But Preventable. *Applied Clinical Trials* **25**, 2016

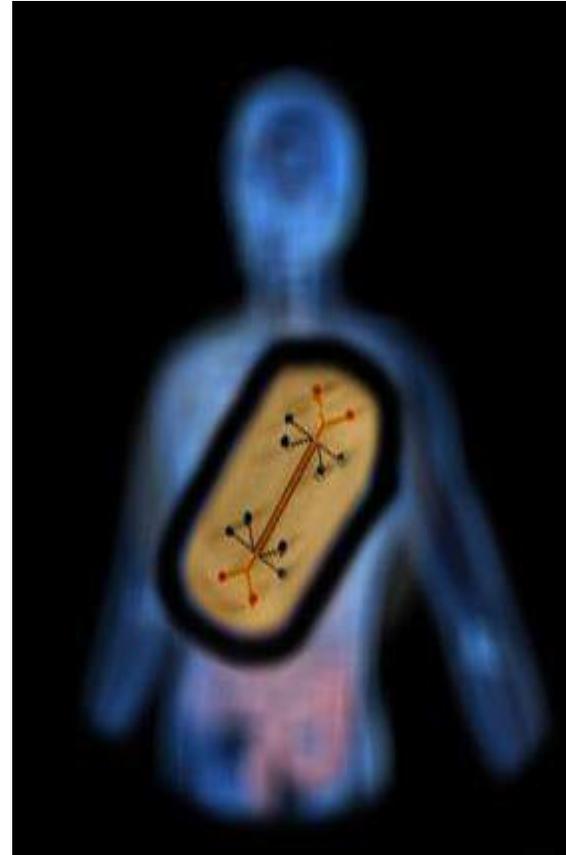
# Advancing Regulatory Science



- FDA-NIH Joint Leadership Council formed in 2010
- Issued RFA for Advancing Regulatory Science through Novel Research & Science-Based Technologies Program (\$7M, 4 awards):
  - Accelerating Drug & Device Evaluation through Innovative Clinical Trial Design
  - Replacement Ocular Battery
  - **Heart-Lung Micromachine for Safety and Efficacy Testing**
  - Characterization/Bioinformatics-modeling of Nanoparticle: Complement Interactions

# Heart-Lung Micromachine

- The microfluidic microdevice mimics the complex structural interfaces and functionalities of the alveolar-capillary interface of the living human lung.
- Using this model to look at medical counter-measures
- Compare to NIH whole animal studies



# DARPA-FDA-NCATS Microphysiological Systems Program

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- Started in 2011 to support the development of human microsystems, or organ “chips,” to screen for safe and effective drugs swiftly and efficiently (before human testing)
- Collaboration through coordination of independent programs



Engineering platforms and biological proof-of-concept (DARPA-BAA-11-73: Microphysiological Systems)



Underlying biology/pathology and mechanistic understanding (RFA-RM-12-001 and RFA RM-11-022)



Advise on regulatory requirements, validation and qualification

**This was a unique partnership because it involved regulatory scientists at the very beginning to address identified gaps in knowledge need to regulate FDA products.**

# Microphysiological Systems

## DARPA –BAA-11-73

- Reconfigurable platform
- Ten or more in vitro physiological systems
- Able to monitor resident tissues for up to 4weeks
- Uses human cells
- Commercial availability
- Includes plan for validating integrated platform performance
- 70 million over 5 years
- Applications jointly reviewed by DARPA, FDA, and NIH
- Contracts were awarded to Wyss and MIT

# Stem/Progenitor Cell-Derived Human Micro-organs and -tissues (U18)

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- **GOAL:** Develop stem- and progenitor-derived cell resources to seed circulatory, endocrine, gastrointestinal, immune, integumentary, musculoskeletal, nervous (including eye), reproductive, respiratory and urinary microsystems.
- **SCOPE/ACTIVITIES:**
  - Improvements in differentiation efficiencies towards cell-type diversity, genetic complexity, population diversity, and disease modeling
  - Development of 3D culturing approaches to enhance cellular microenvironments

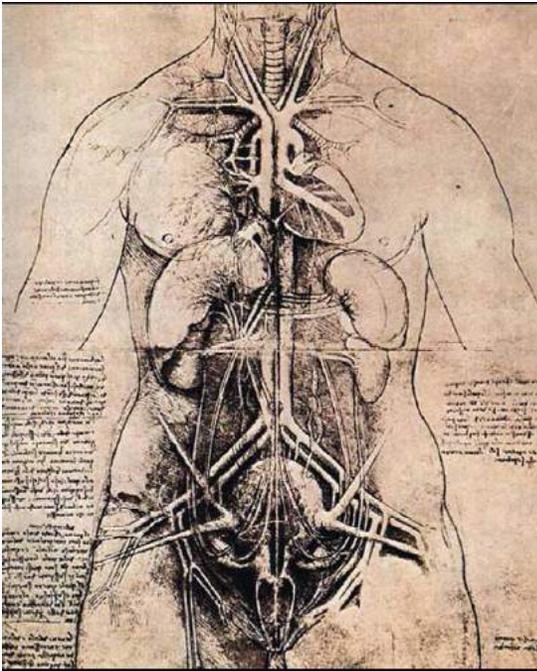
# Integrated Microphysiological Systems for Drug Efficacy and Toxicity Testing (UH2/UH3)

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- **GOAL:** Develop *in vitro* microphysiological systems representative of major organs/tissues in the human body, that will facilitate the assessment of biomarkers, bioavailability, efficacy, and toxicity of therapeutic agents prior to clinical trials.
- **SCOPE/ACTIVITIES:**
  - Multicellular architecture representative of the tissue of origin
  - Functional representation of normal human biology
  - Reproducible and viable operation under physiological conditions maintained up to 4 weeks in culture
  - Capacity for representation of normal and disease phenotypes,
  - Capacity for representation of population diversity
  - Amenable to high content screening for repeated dose efficacy testing, and for toxicology, and safety screening

# Microphysiological Systems Program “Tissue Chips”

**GOAL: Develop an *in vitro* platform that uses human tissues to evaluate the efficacy, safety and toxicity of promising therapies.**



- All ten human physiological systems will be functionally represented by human tissue constructs:
  - Circulatory
  - Endocrine
  - Gastrointestinal
  - Immune
  - Skin
  - Musculoskeletal
  - Nervous
  - Reproductive
  - Respiratory
  - Urinary
- Physiologically relevant, genetically diverse, and pathologically meaningful.
- Modular, reconfigurable platform.
- Tissue viability for at least 4 weeks.
- Community-wide access.

To receive the rest of the presentation, please get in touch at [info@hansonwade.com](mailto:info@hansonwade.com) regarding the 3D Tissue Models Summit. We'll be delighted to send you the full slide deck asap.

We look forward to hearing from you!

Kind regards,

The PREDiCT Team

