FDA Perspectives on Organs and Tissues on a Chip

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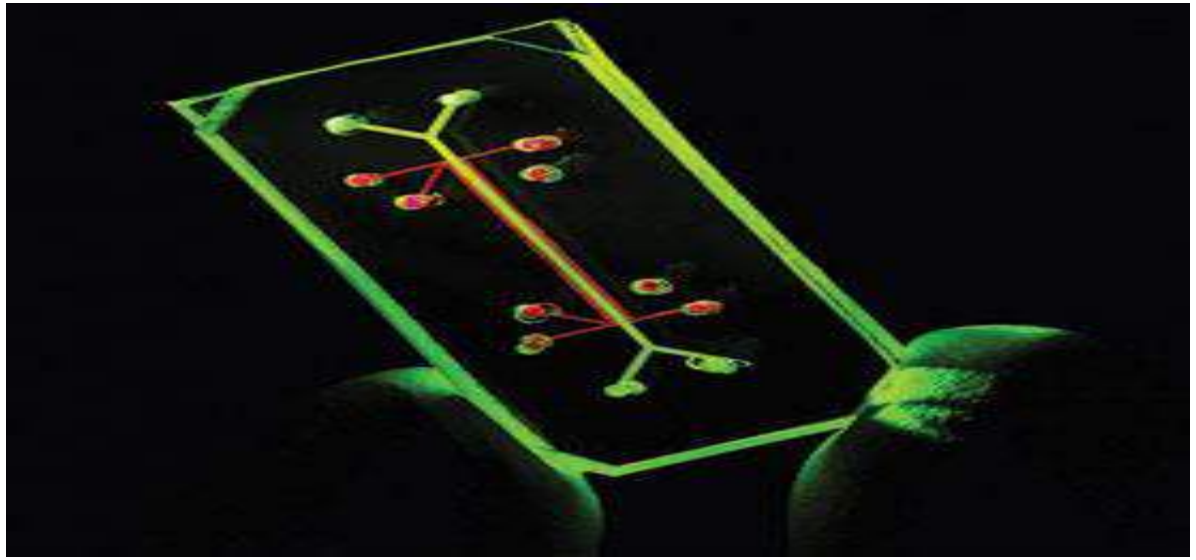


FDA Priorities for Advancing Regulatory Science

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**.

Challenges

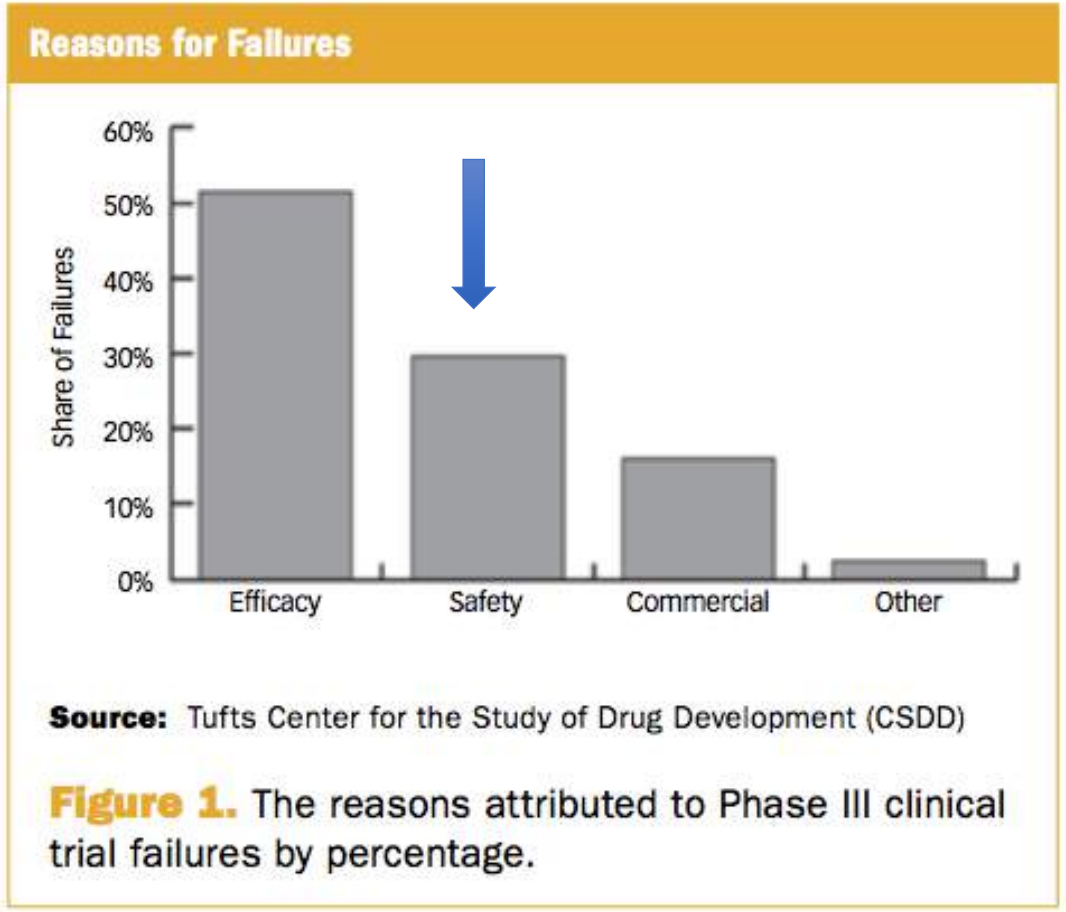
In Vitro

- 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



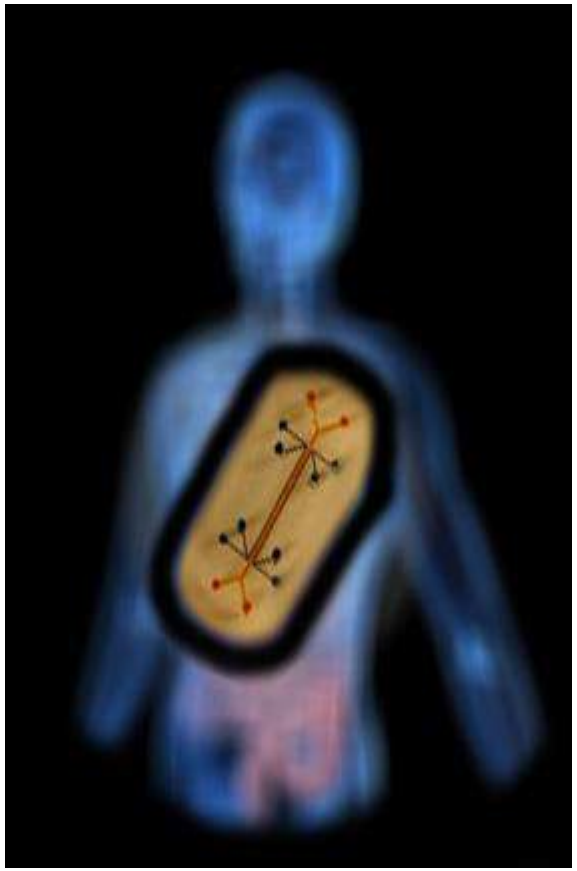
Grignolo and Pretorius, Phase III Trial Failures: Costly, But Preventable. Applied Clinical Trials **25**, 2016

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

- 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)

- ***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

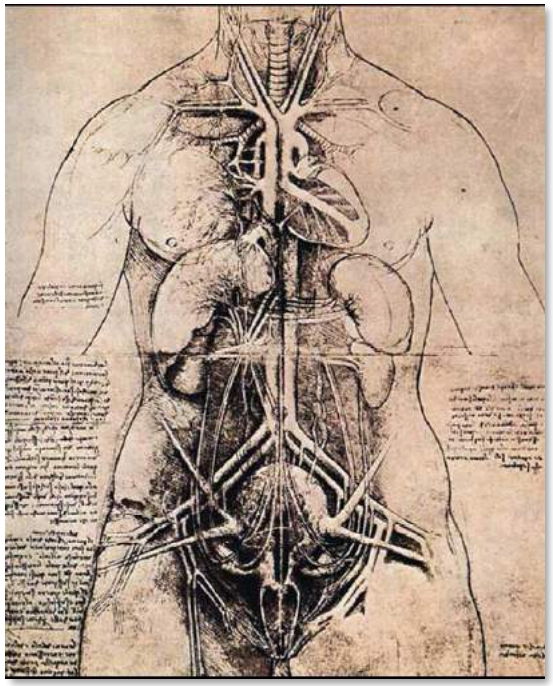
Integrated Microphysiological Systems for Drug Efficacy and Toxicity Testing (UH2/UH3)

- ***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 <u>human</u> 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 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

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3D TISSUE MODELS
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