Update from the NIH

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Current Landscape for Drug Development

Risky Enterprise—Long Time Frame, High Attrition, Expensive, and Inefficient.
Need for More Predictive Pre-clinical Models for Drug Development

- Low efficacy and high toxicity account for approximately 70% of Phase II and 87% of Phase III clinical attrition. Improving the predictiveness of pre-clinical models is a high priority.

- NIH, DARPA, and FDA have recently made large investments in the development of exciting, innovative, and hopefully more predictive pre-clinical in vitro models. Should reduce or perhaps eventually eliminate the need for animal models.
Microphysiological Systems Program (Human-on-a-Chip)

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

- All ten human physiological systems will be functionally represented by human tissue constructs:
  - Circulatory
  - Endocrine
  - Gastrointestinal
  - Immune
  - Integumentary
  - 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.
Hand-in-hand with the Development of New In Vitro Models is the Need for **Validation**

Validation (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 specific assay will consistently produce a result that meets its predetermined specifications.
The NIH and the American Institute for Medical and Biological Engineering (AIMBE) have held a series of workshops on Validation and Qualification of New *in vitro* Tools and Models for the Pre-clinical Drug Discovery Process.

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

Steering Committee—NIST, FDA, NIH, Industry, Academia
Through the workshop series we are beginning to address some of the requirements for validating new human-on-a-chip technologies which include:

- Context of use
- Endpoints
- Limitations
- Accuracy
- Reproducibility
- Specificity
- Robustness and transferability
- Dynamic range
- Gold standard against which the technology will be compared
- Standardization
- Cost effectiveness
- Justification for the technology vs. existing technologies.
- All of the above will vary with the purpose, nature and proposed use of the technology.