National Institutes of Health
Turning Discovery Into Health

Update from the NIH

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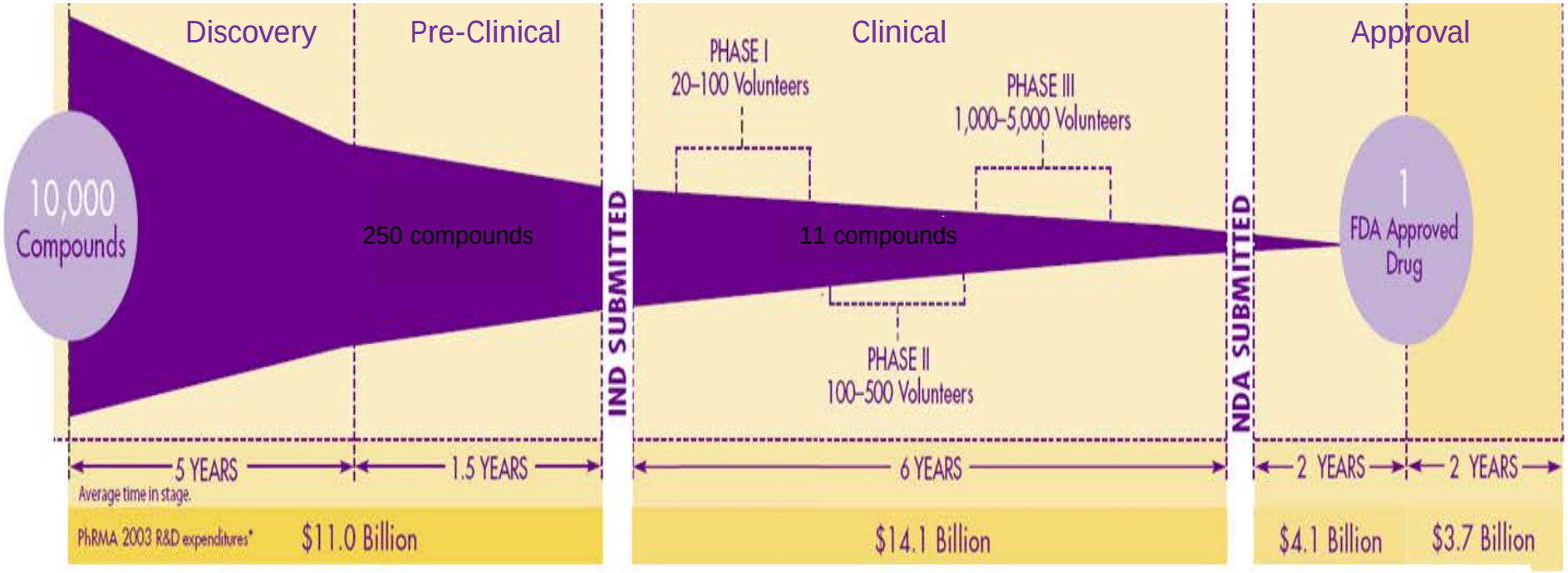
Current Landscape for Drug Development



Risky Enterprise—Long Time Frame, High Attrition, Expensive, and Inefficient.

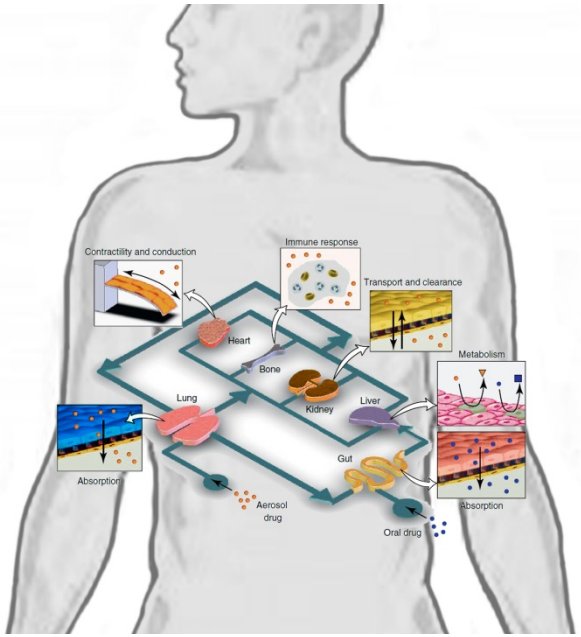
Need for More Predictive Pre-clinical Models for Drug Development

- 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 <u>human</u> 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.

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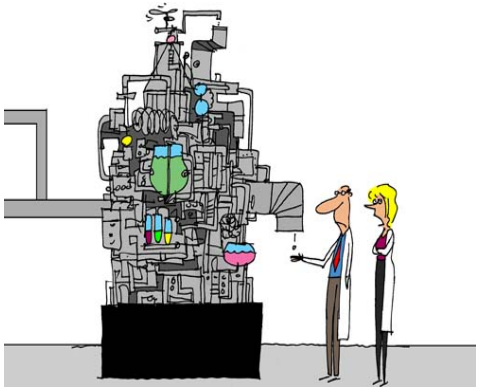
DARPA

FDA

Hand-in-hand with the Development of New In Vitro Models is the Need for Validation



Development of Technology

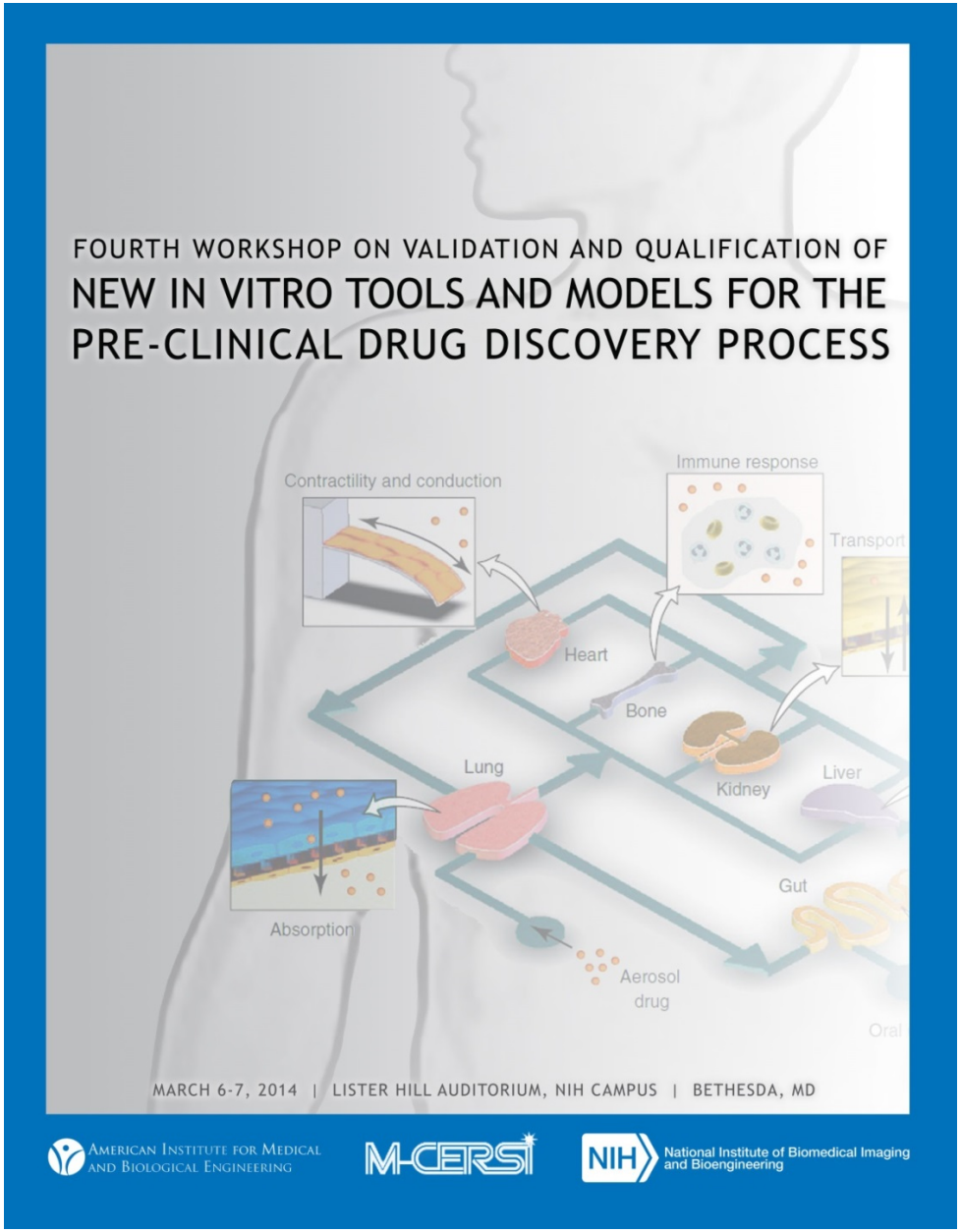
Validation

Regulatory Acceptance

Meaningful Use

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.