UNITED STATES ICCVAM Advancing Alternatives to Animal Testing

Interagency Coordinating Committee on the Validation of Alternative Methods

A Strategy for Implementing the Vision for Toxicity Testing in the 21st Century

Warren Casey, PhD, DABT

Director, NICEATM

Agency for Toxic Substances and Disease Registry • Consumer Product Safety Commission • Department of Agriculture
Department of Defense • Department of Energy • Department of the Interior • Department of Transportation
Environmental Protection Agency • Food and Drug Administration • National Institute for Occupational Safety and Health
National Institutes of Health • National Cancer Institute • National Institute of Environmental Health Sciences
National Library of Medicine • Occupational Safety and Health Administration

PUBLIC LAW 106–545 : ICCVAM Authorization Act of 2000

- To establish guidelines, recommendations, and regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness.
- Convened by the Director of the NIEHS as a permanent interagency coordinating committee under the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).
- Establish a Scientific Advisory Committee (SACATM). to advise ICCVAM and the NICEATM.

PUBLIC LAW 106–545 : ICCVAM Authorization Act of 2000

- **Composed of the heads of the following Federal agencies (or their designees):**

- Consumer Product Safety Commission
- Department of Agriculture
- Department of the Interior
- Department of Transportation
- Environmental Protection Agency
- Food and Drug Administration
- Occupational Safety and Health Administration
- National Institute for Occupational Safety and Health
- National Inst. of Environmental Health Sciences
- Agency for Toxic Substances and Disease Registry
- National Cancer Institute
- National Library of Medicine
- National Institutes of Health
- Department of Defense
- Department of Energy

- Other participants include: NIST, NCATS , Tox21 Representatives

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ICCVAM
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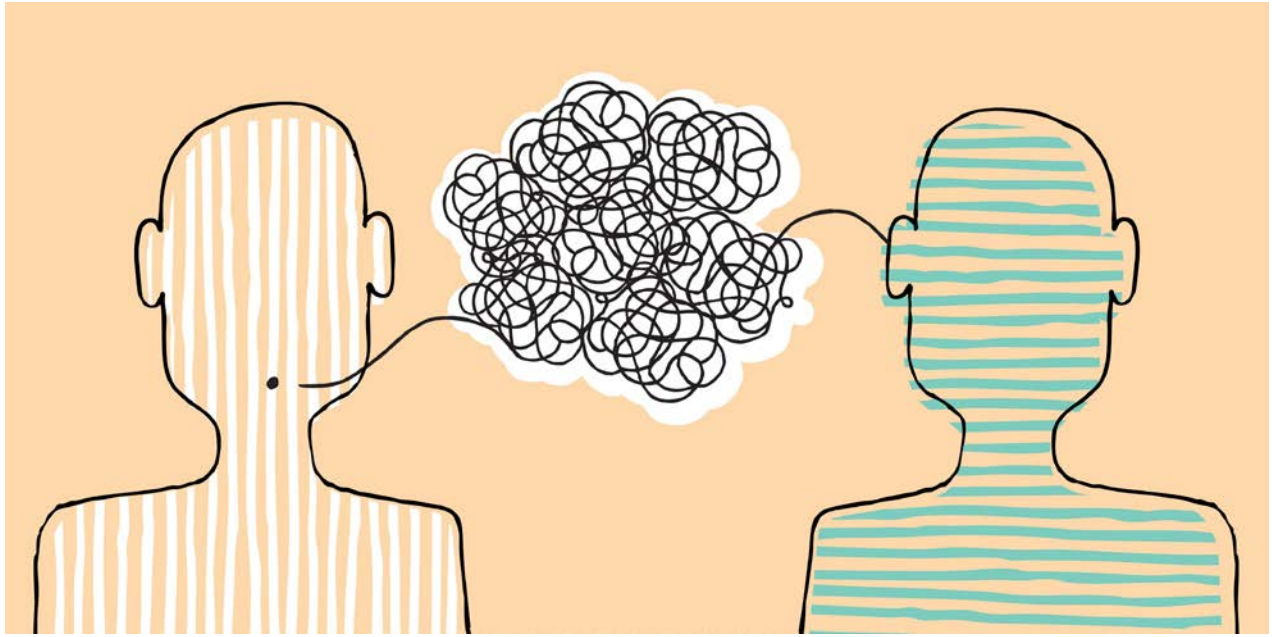
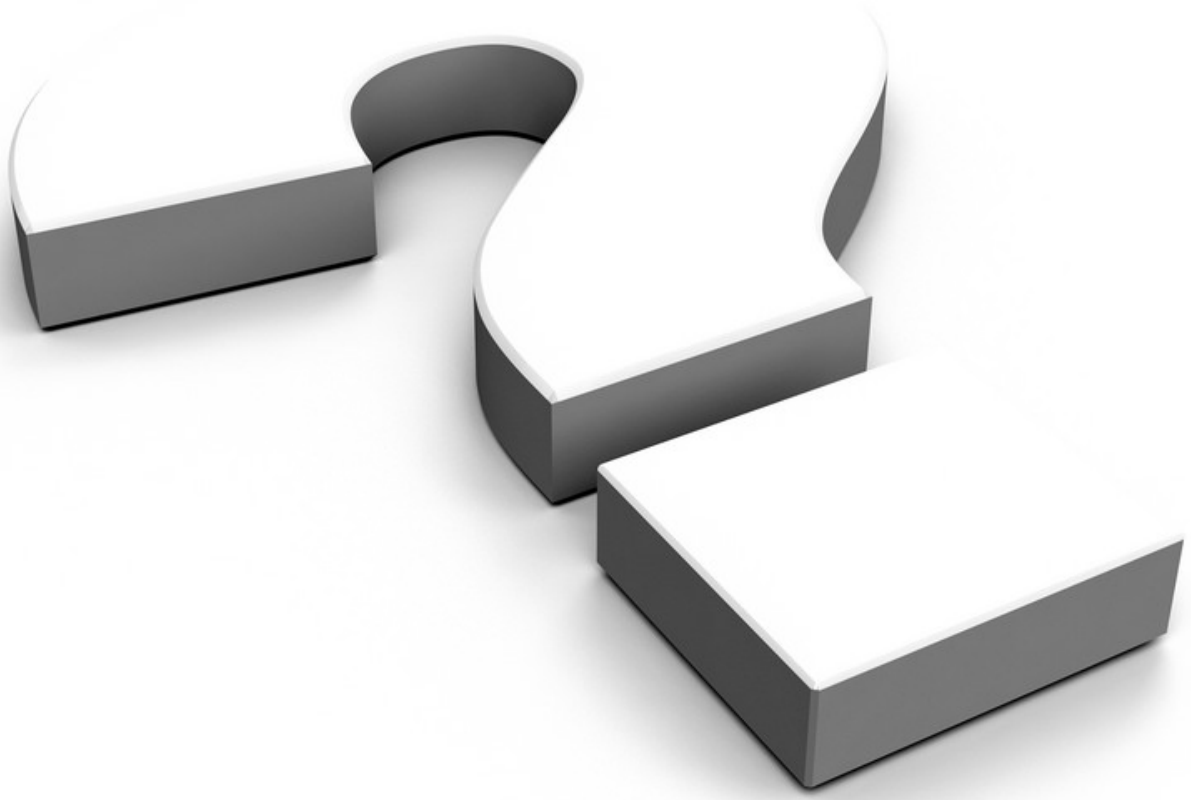
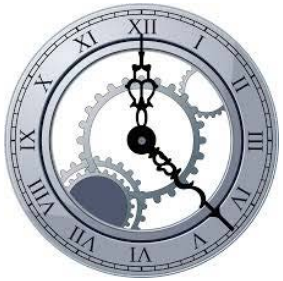
Modernizing Safety Assessment of Drugs and Chemicals in the US





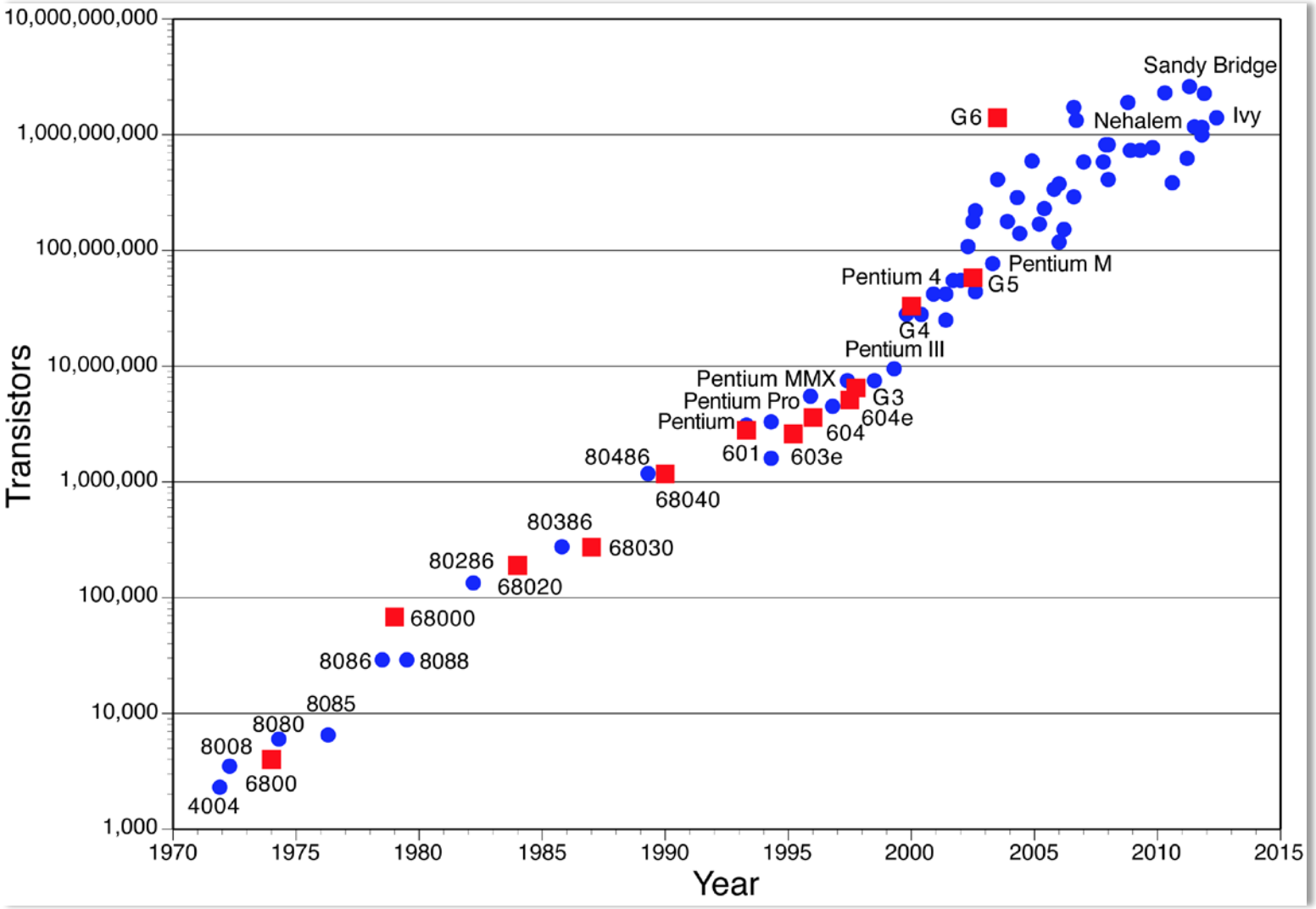
- **Ethics**

- **Efficiency**



- **Public Health (Human Relevance)**

Moore's Law



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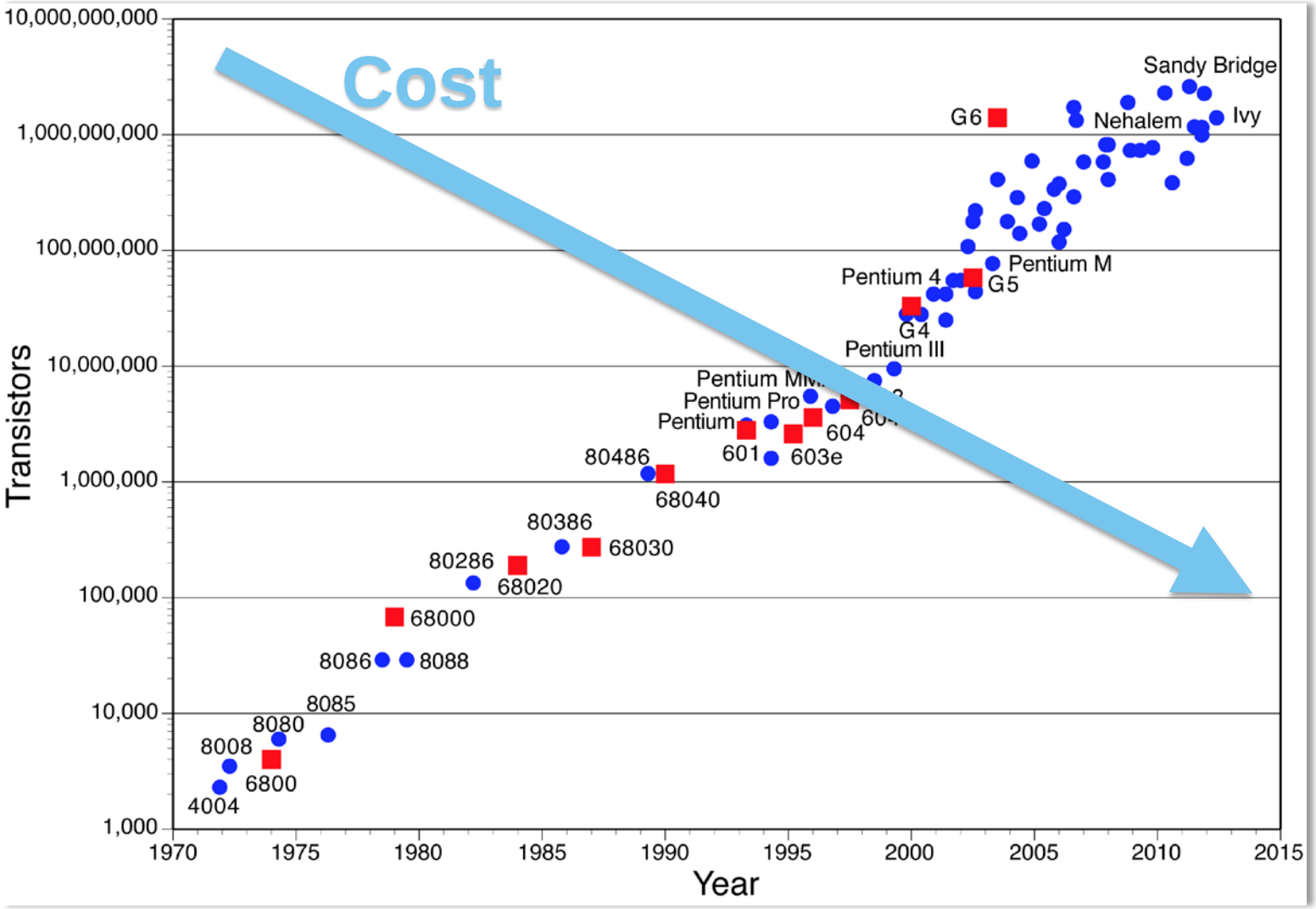
Moore's Law



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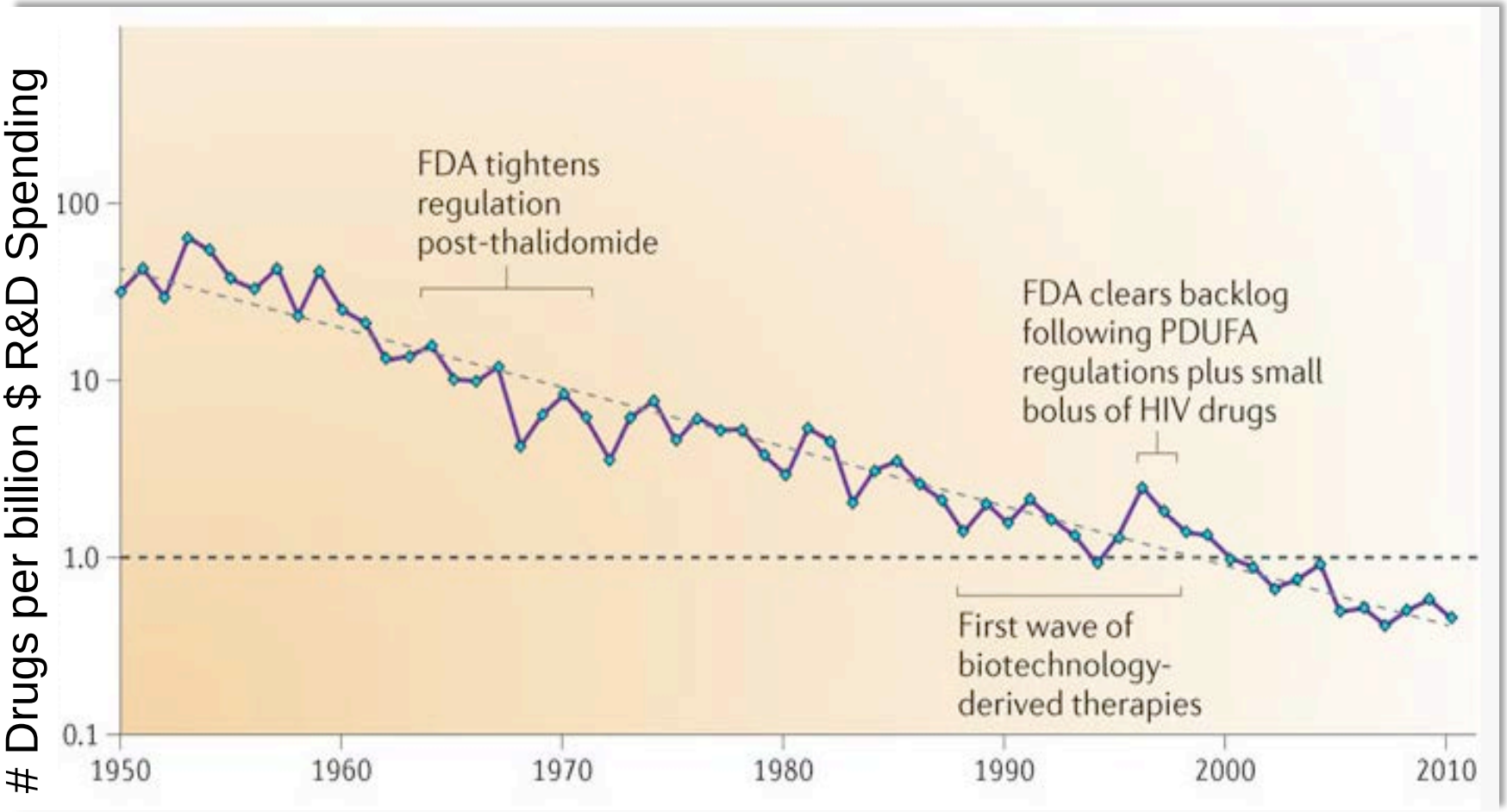
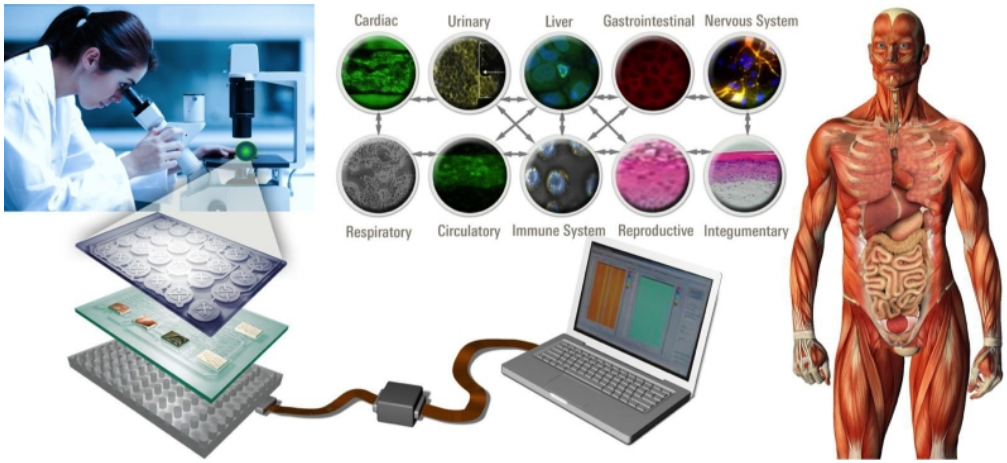
Moore's Law

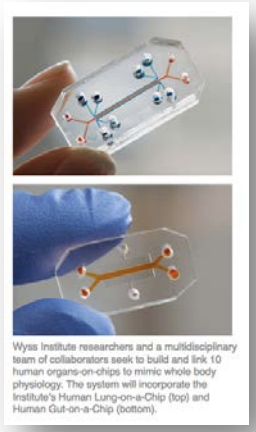
Eroom's Law



Diagnosing the decline in pharmaceutical R&D efficiency
Jack W. Scannell, Alex Blanckley, Helen Boldon & Brian Warrington
Nature Reviews Drug Discovery 11, 191-200 (March 2012)

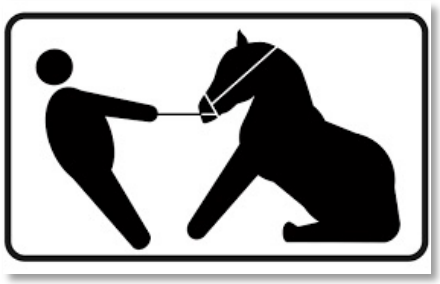
It is difficult for evolving institutional practices to keep pace with revolutionary advances in science and technology




Wyss Institute researchers and a multidisciplinary team of collaborators seek to build and link 10 human organs-on-chips to mimic whole body physiology. The system will incorporate the Institute's Human Lung-on-a-Chip (top) and Human Gut-on-a-Chip (bottom).

Barrangou & Doudna, Nat. Biotech 933–941 (2016)

- **Institutional Resistance**



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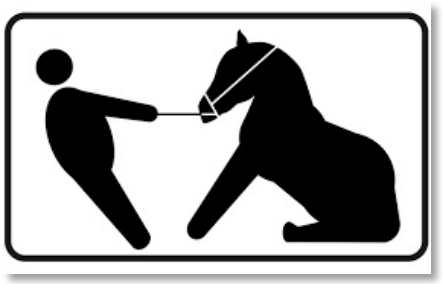
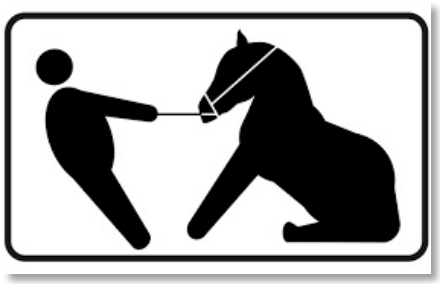


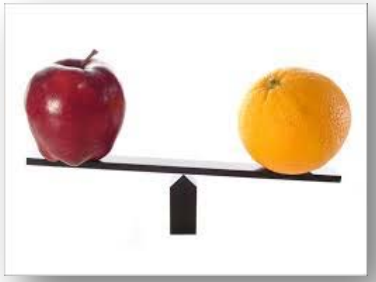
- **Harmonization**

- **Institutional Resistance**



- **Harmonization**

- **Animal Models as Reference Standard**

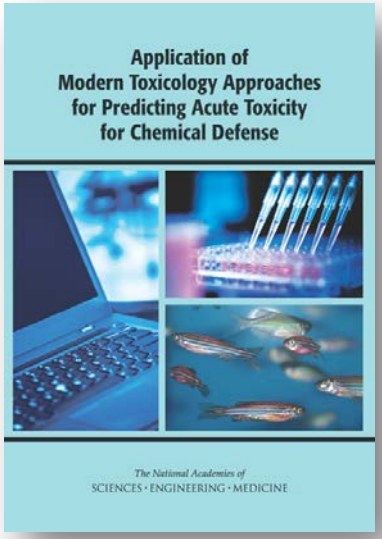


Important Aspects of the Strategy

- Process must be driven by regulators, with input from stakeholders
- Significant opportunities in new approaches, but we must have a collective willingness to accept managed risk
- There must be an incentive to change current practices

Modernizing Safety Assessment of Drugs and Chemicals in the US

- **Replacing Animals in Acute Toxicity Testing by 2020**
  - Significant reduction (>90%) in animals for “EPA 6-Pack”
  - Led by US EPA and US Dept. of Defense



Modernizing Safety Assessment of Drugs and Chemicals in the US

- **Document outlining the describing the rationale, operating principles, scope, critical objectives (4Q17)**
  - FR Notices
  - Public Meetings: SOT (March), ICCVAM Public Forum (May), SACATM (September)
  - At least one public workshop in 2017

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  - FR Notices
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  - At least one public workshop in 2017
- **Initiate key strategic projects (1Q17)**
  - Single Species Safety Initiative
  - Identify commonalities between sectors (i.e., Pharma and Ag Chem)
  - Systematic review of animal model relevance and variability

Pathophysiological