FDA Collaborations for Practical Applications

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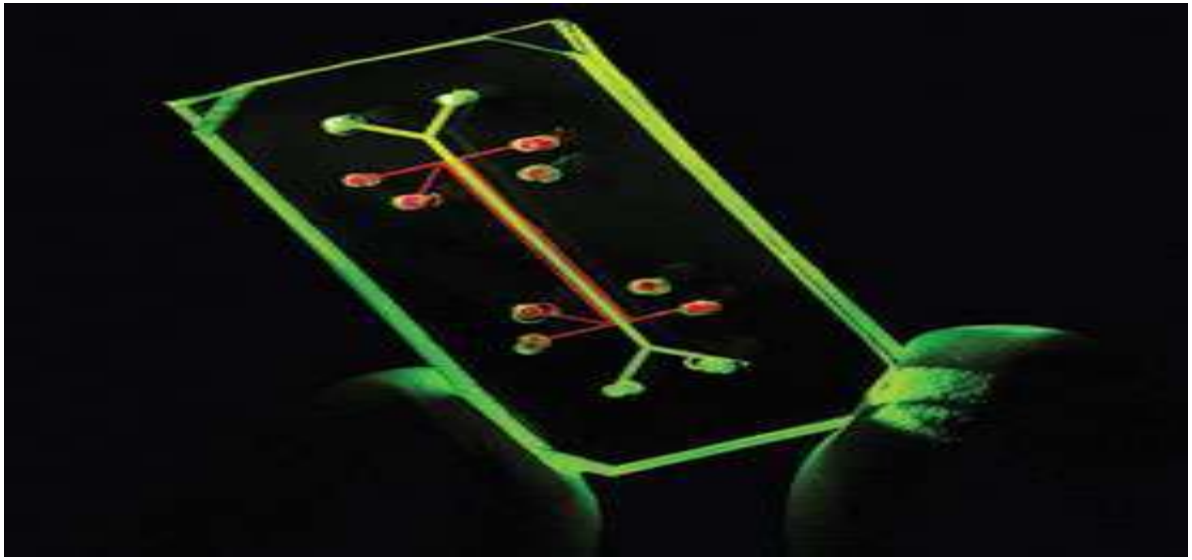
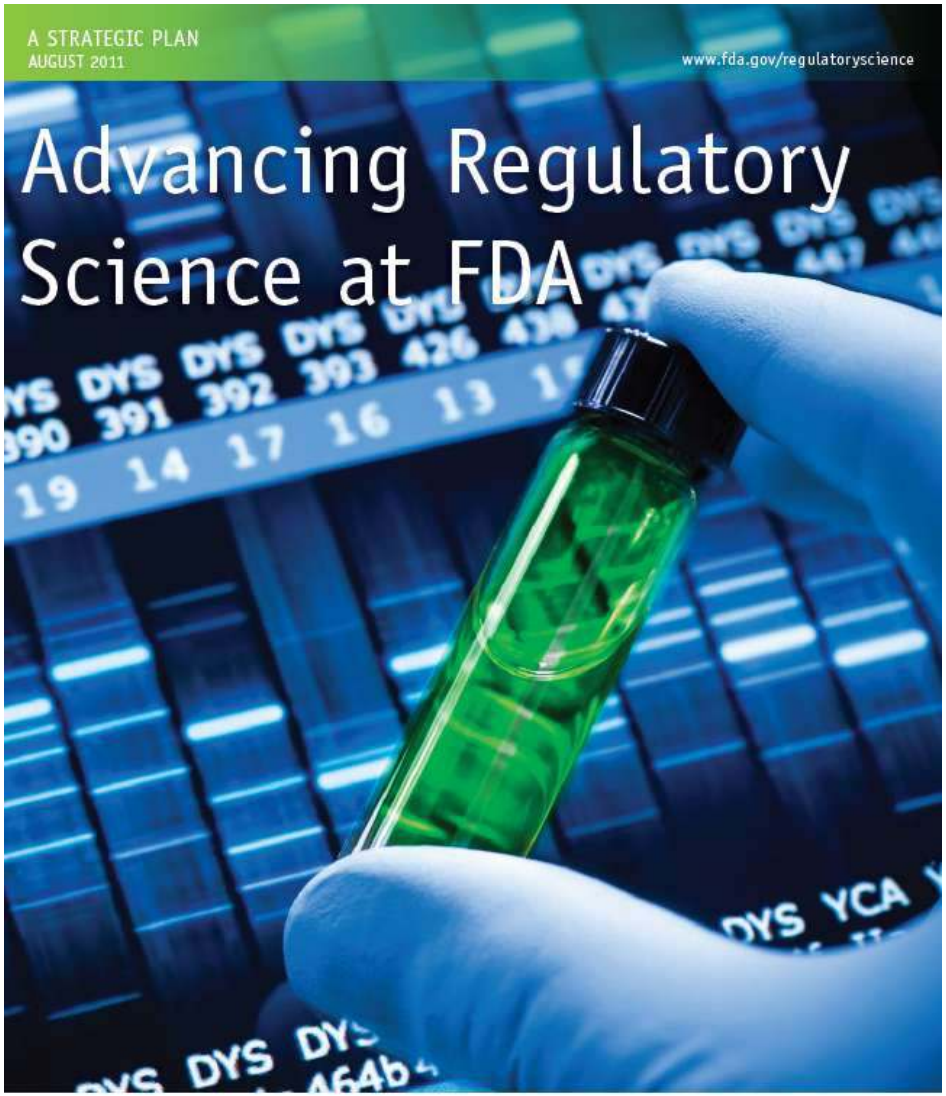




"FDA will advance regulatory science to speed innovation, improve regulatory decision-making, and get safe and effective products to people in need. 21st Century regulatory science will be a driving force as FDA works with diverse partners to protect and promote the health of our nation and the global community."

https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RegulatoryScience/UCM268225.pdf

Need for New More Predictive Models

- FDA recognizes that alternative test platforms that replace, reduce, or refine animal studies with both in vitro and *in silico* models can give regulators new tools that are more predictive.
- However. for new alternative methods to be acceptable for regulatory use to replace one or both animal species currently being used - confidence is needed that the questions can be answered at least as well by these new methods as with traditional testing

Acceptance of New Models

- Regulatory acceptance has, historically, been considered a challenge for developing alternative approaches
- Route to validation can be complex and lengthy
- International and even national differences in statutory requirements complicate regulatory acceptance
- Early engagement with regulators is the key to ultimately ensuring NATs can be used in regulatory risk assessments

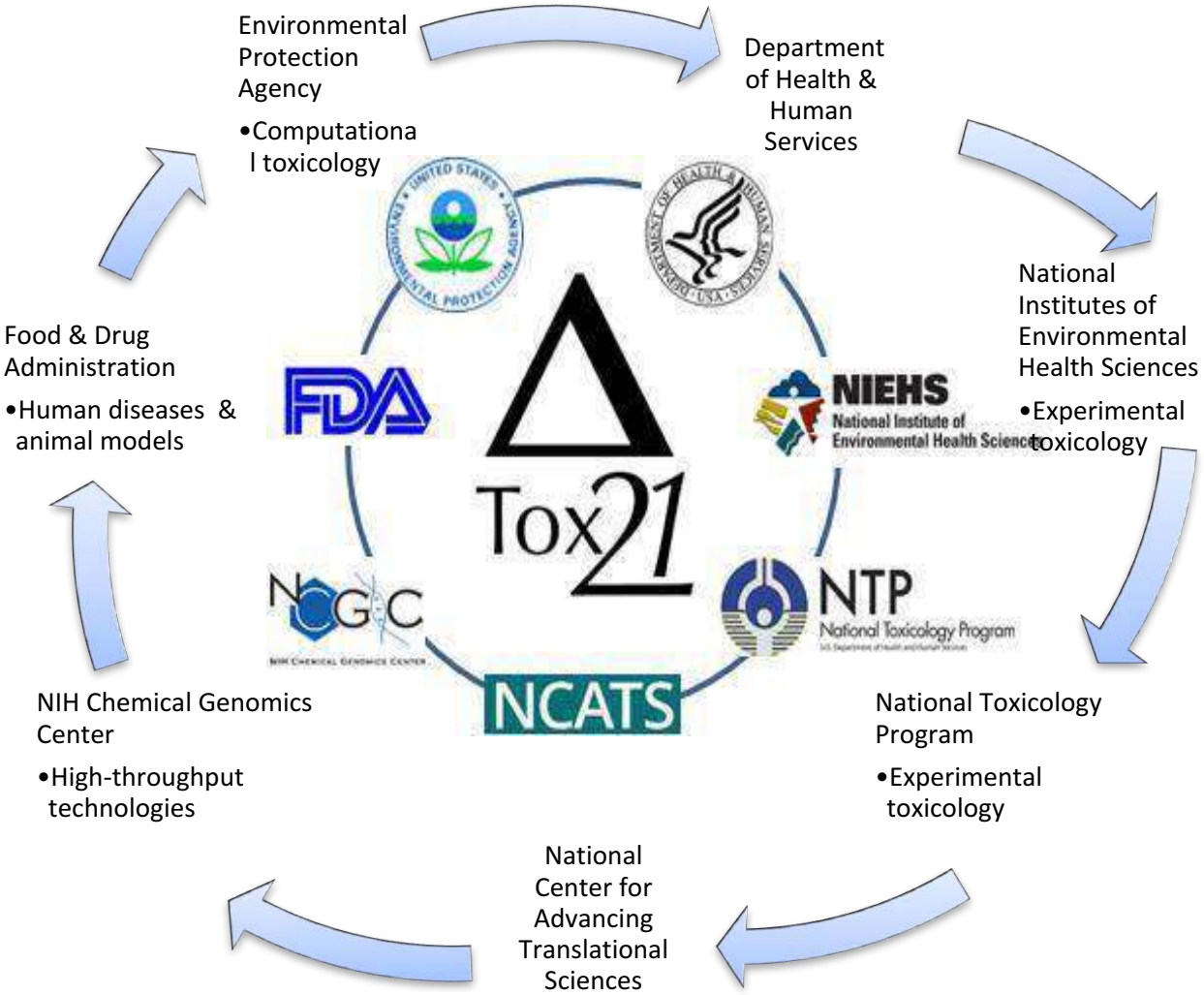
What is FDA Doing To Advance Regulatory Science?

- FDA has formed a FDA Senior Toxicologist Working Group to share information on new toxicology methods and to familiarize FDA Regulatory and Research Scientists on emerging toxicology tests and their usefulness in risk assessment.
- This work group charged with developing a Predictive Toxicology Framework for the agency. This framework emphasizes a “context of use” approach for determining confidence in emerging technologies.

Partnerships are Important for Accepting New Technologies

- Fostering collaborations between government researchers and regulators is important to ensure the most promising technologies are identified, developed, validated and integrated.

Toxicity Testing in the 21st Century (Tox21)



ICCVAM Read-Across Work Group

- Read-across is when the already available data of a data-rich substance (the source) is used for a data-poor substance (the target), which is considered *similar enough* to the source substance to use the same data as a basis for the safety assessment
- FDA has partnered with CAAT to give two read-across workshops
- FDA nominated Read Across for an ICCVAM Work Group

ICCVAM DART Working Group

- FDA/CFSAN chairs an ICCVAM working group to draft an ICCVAM strategy and roadmap for evaluating new methods for reproductive and developmental toxicity testing.
- Work Group will provide expertise in developing and evaluating alternative approaches to classify chemicals for reproductive and developmental toxicity hazards using in vitro and/or in silico methods.
- In addition to representatives from ICCVAM member agencies, ICATM partners (EURL ECVAM, JaCVAM, KoCVAM, and Health Canada) will be offered the opportunity to participate in the workgroup.

Partnerships are Important for Accepting New Technologies

- Foster collaborations between government regulators, industry , stakeholders and academia to ensure the most promising technologies are identified, developed validated and integrated into regulatory risk assessment.

SOT- FDA MOU Signed will Extend Colloquium Series

December 5, 2016 – Signing Ceremony with representatives from SOT and USFDA to renew the SOT-FDA Memorandum of Understanding that facilitates collaborative efforts in training, education, professional development, and innovative toxicology methods and regulatory science.

Colloquium Series

- Partnership SOT and US FDA Center for Food Safety and Applied Nutrition (CFSAN)
- High-quality, cutting-edge, future-oriented toxicological science
- Information for FDA employees and the public
- Not a public forum for discussion of toxicology regulatory issues

SOT Contemporary Concepts in Toxicology Conference

Predictive Toxicology and Preventive Medicine for Healthy Children

November 14–16, 2018 | Washington,

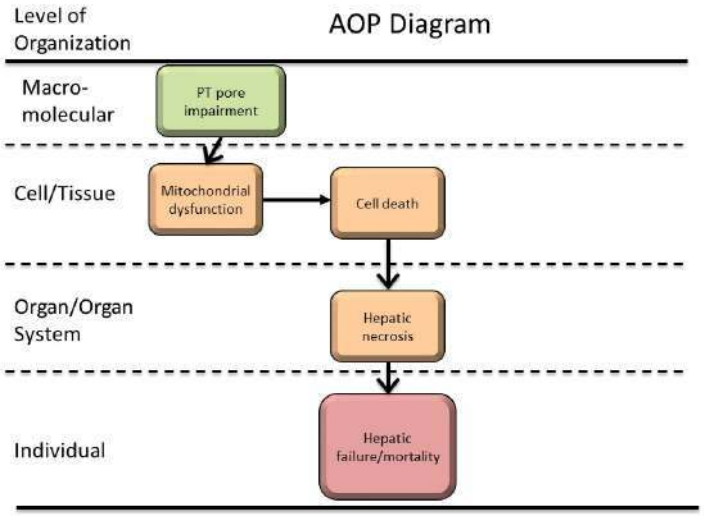
Establishing fitness-for-purpose of methods- ILSI HESI partnership

- Establishing criteria applicable to the intended decision to be addressed (e.g. screening, safety assessment, regulatory approval) would be instrumental in determining whether a method is fit-for-purpose for decision-making
- ILSI HESI proposed approach
  1. Method performance characterization

     e.g. *In vitro* assay for mitochondrial PT pore impairment
  2. Model predictive performance

     e.g. Prediction of hepatic cell death *in vivo*
  3. Utilization performance (utility in decision-making)

     e.g. Health-based guidance value based on POD for hepatic toxicity



FDA-DARPA-NIH 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- was able to address identified gaps in knowledge need to regulate FDA products

NATURE | NEWS

Miniature liver on a chip could boost US food safety

- CFSAN Researchers will be evaluating the effectiveness of this technology to better understand the effects of medicines, disease-causing bacteria in foods, chemicals, and other potentially harmful materials on the human body

Recommendations to facilitate regulatory decision-making and acceptance

- Networking and communication- talk to FDA about new approaches
- Involvement from regulatory agencies during all stages of test method development
- Cross-sector collaboration
- International collaboration and harmonization of approaches
- Joint stakeholder development of specific criteria promoting acceptance
- Continuing education for regulators

U.S. FOOD & DRUG ADMINISTRATION

Questions?

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