Accelerating Medical Device Innovation with Regulatory Science Tools

FDA Small Business Regulatory Education for Industry (REdI)

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Learning Objectives

- Provide some background about the Office of Science and Engineering Labs (OSEL)
- Identify Regulatory Science Tools (RSTs) in the Precompetitive Space and how to use them in product development
- Identify and distinguish among Reg Science tools, MDDTs and Consensus Standards
- Discuss how CDRH uses Regulatory Science Tools

CDRH's Office of Science and Engineering Labs

165
FEDERAL EMPLOYEES
Up to 180 visiting scientists

140 Research Projects
In 20 Program Areas

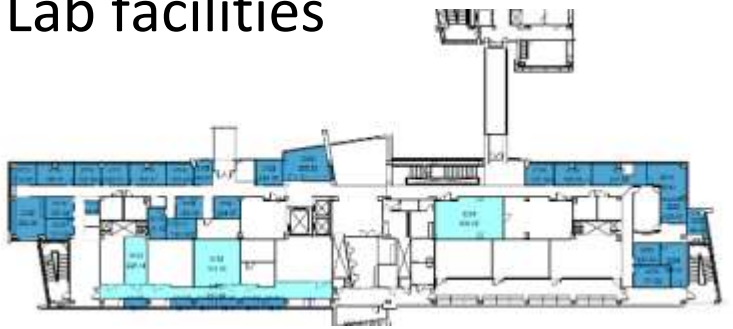
400/year
Peer-reviewed presentations, articles, and other public disclosures

> 3,000/year
Premarket regulatory reviews

75
Standards and conformity assessment committees

70%
Staff with a graduate degree

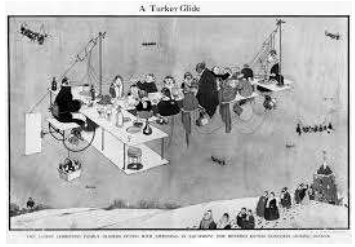
55,000 ft²
Lab facilities



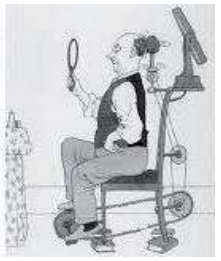
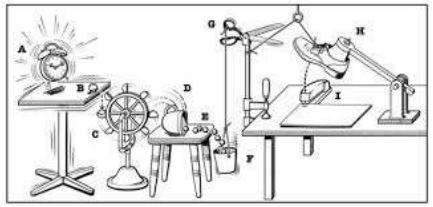
The Challenge of Product Development

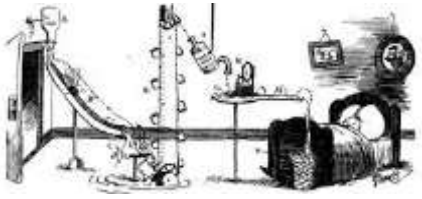


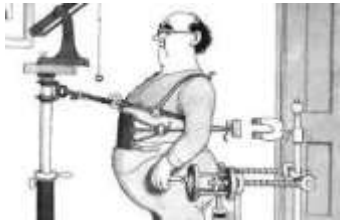
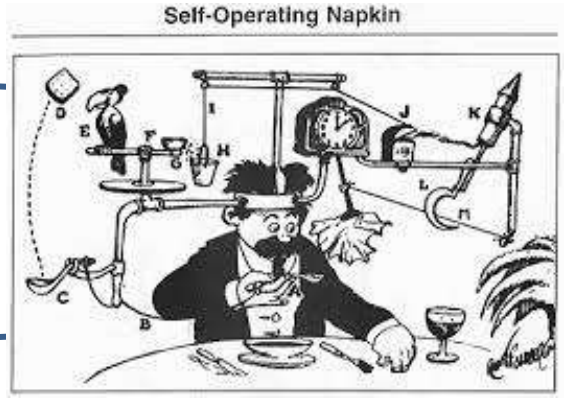






Regulatory Science Tools

- Innovative, peer reviewed approach or methodology to help assess the safety or effectiveness of a medical device or emerging technology
  - Brought into the public domain as early as possible before other standards may be available
- We have identified a number of types
  - Virtual and physical phantoms
  - CM&S and related datasets
  - Lab methodologies
  - Best practices

The Family of Evaluation Tools

- Reg Science Tools
  - May be developed in parallel with novel technology
- Medical Device Development Tools
  - Qualified for regulatory use within a specific and defined Context of Use (CoU)
  - Voluntary
  - If used within CoU, methodology prequalified for regulatory pathway use
- Recognized Consensus Standards
  - Quite burdensome to come to consensus
  - Heavy lifting often done by innovators

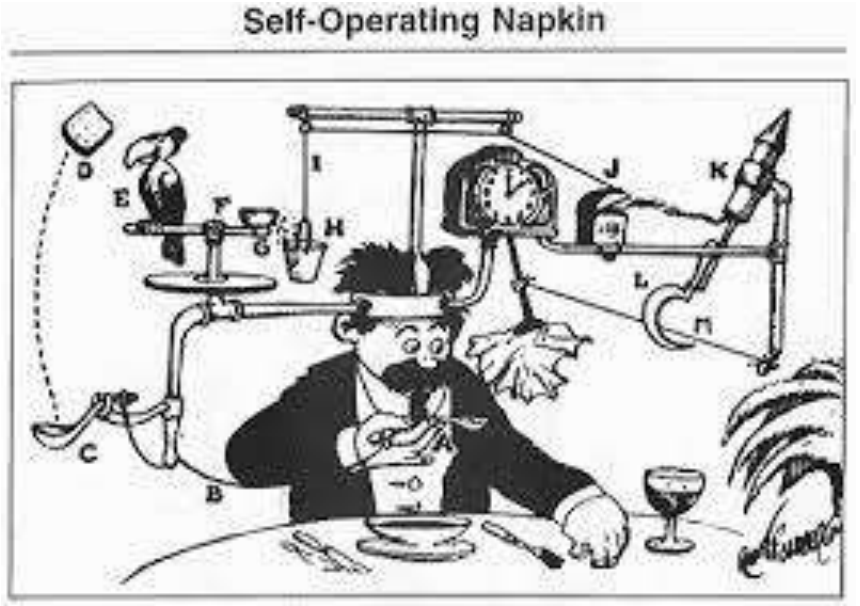
An Evaluation Tool for All Seasons

(with apologies to Robert Bolt and Sir Thomas More)

- Early de-risking of technology and product development
  - Focus on how good an innovation is and not just how well it is tested
  - More efficient use of scarce resources
- Breadth of technology increasing from other industries
  - E.g. Augmented/ virtual/ extended reality being adapted from gaming
  - Is it sufficiently robust for medical applications?
- Common methodologies drive predictability and premarket review

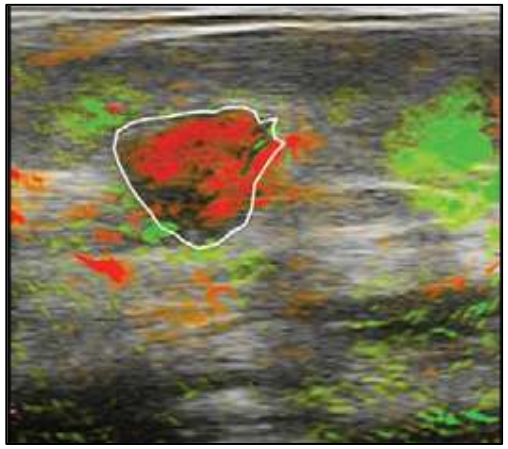
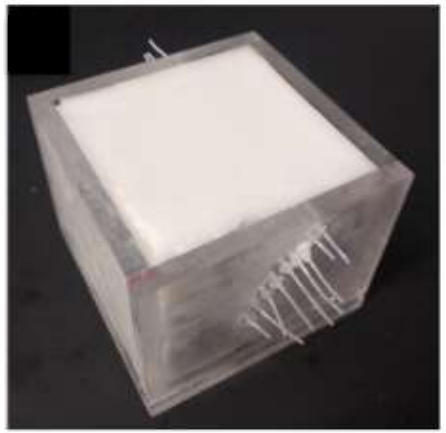
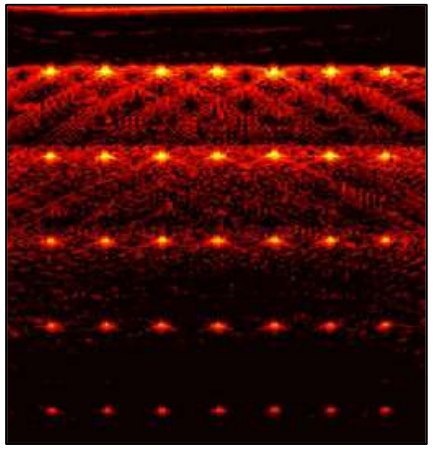
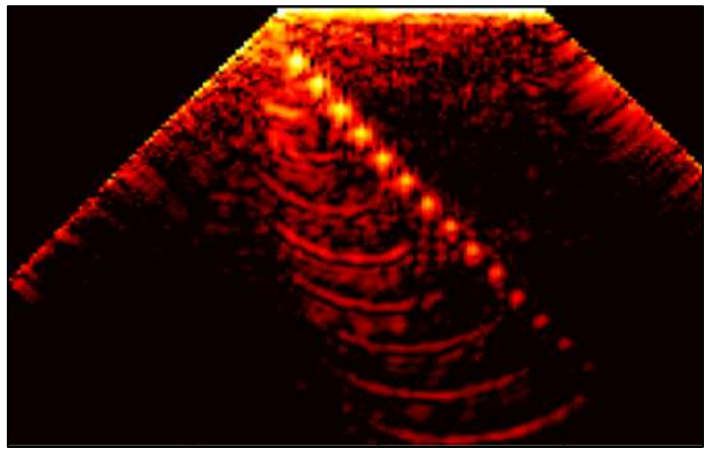
RST Examples

- Virtual and physical phantoms
  - Photoacoustic Imaging (PAI) physical phantom
- CM&S and related datasets
  - Virtual Family
- Lab methodologies
  - Color Hazard and Risk Calculator
  - Methods for extractables and leachables testing
- Best practices
  - Material selection for specific applications



Photoacoustic Imaging Phantom

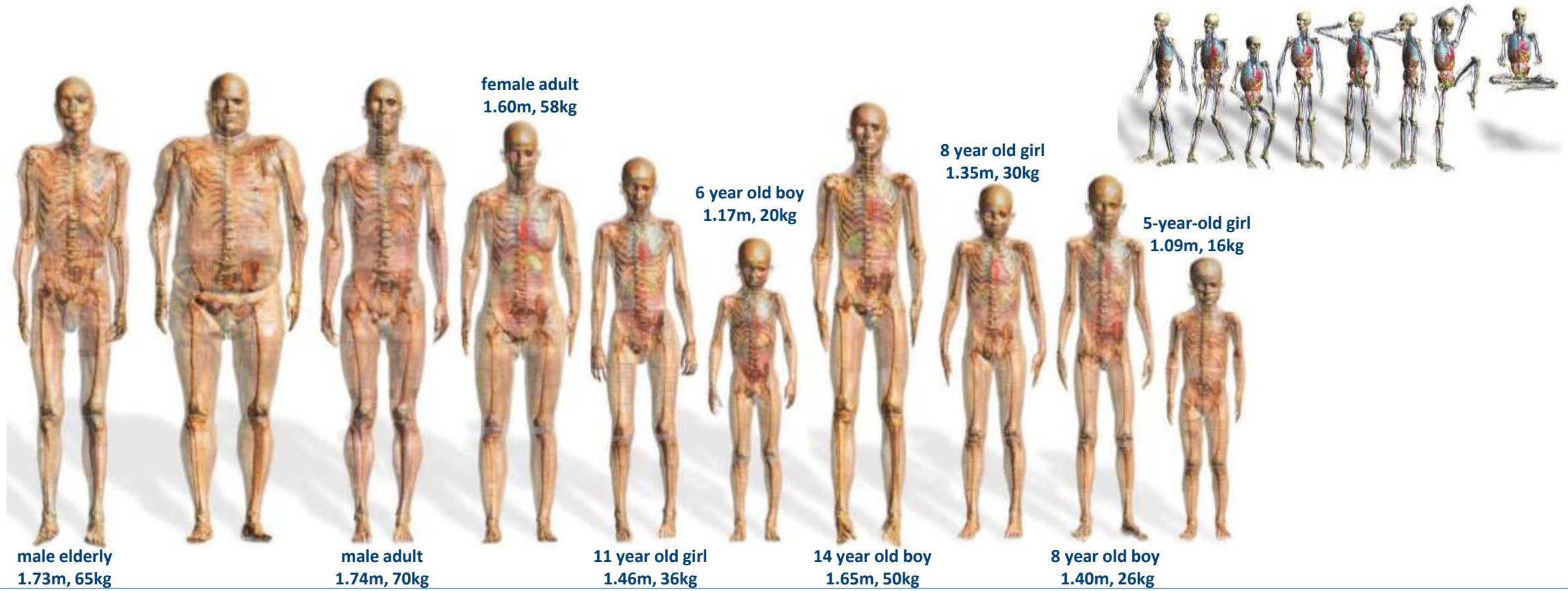
- PAI is used for deep imaging of blood vessels, for eg early cancer detection
  - We developed i) tissue mimics for testing of new devices and ii) performance methods
  - Already used in the first premarket submission from a small business

Hariri A, Palma-Chavez J, Wear KA, Pfefer TJ, Jokerst JV, **Vogt WC.** Photoacoustics. 2021 Feb 20;22:100245. doi: 10.1016/j.pacs.2021.100245. eCollection 2021 Jun.PMID: 33747787

The Virtual Family/Population

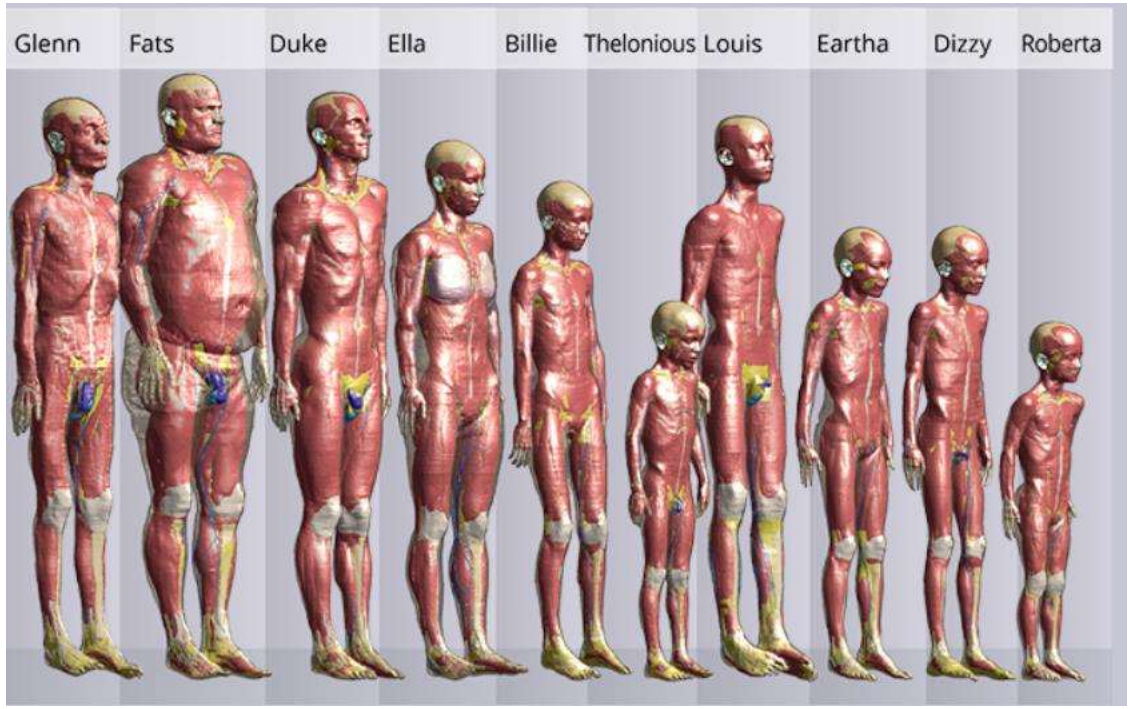
- The Virtual Population is a set of anatomically correct whole body models for thermal, electromagnetic and fluid dynamic simulations



The Virtual Family/Population

https://itis.swiss/virtual-population/virtual-population/overview/

- Developed between CDRH and the IT'IS Foundation, Zurich
  - Models have been downloaded 000s of times
  - The models have been used in over 200 premarket submissions…
  - Including the world's first 7T MRI without needing a clinical trial

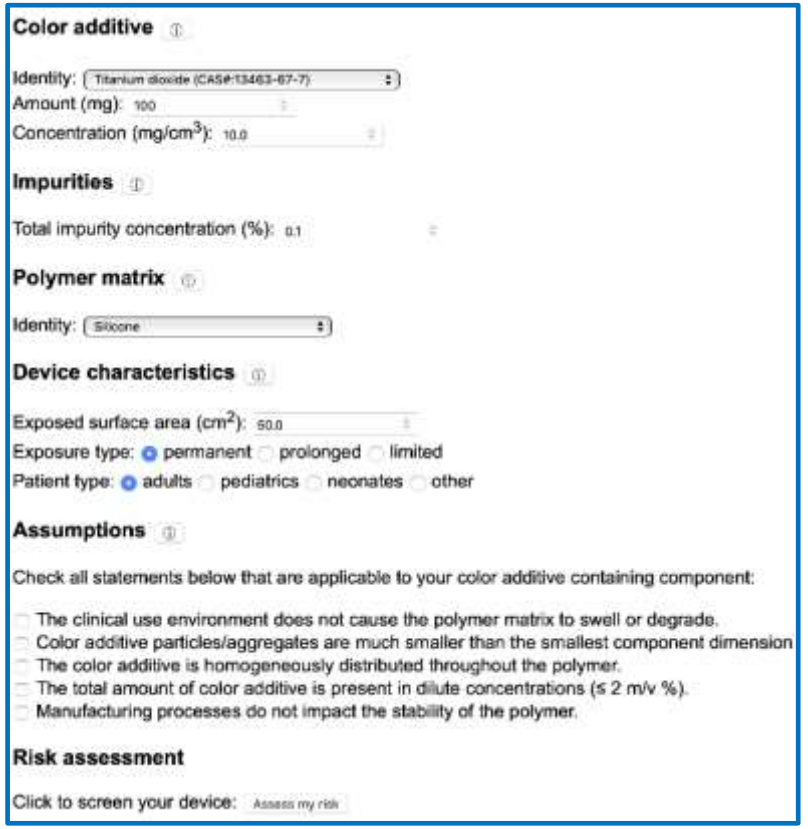


Christ et al, PhysMedBiol (2010), Gosselin et al, PhysMedBiol (2014) and Iacono et al, Plos One (2015)

CHRIS: Color Hazard and RISk Calculator

https://dsaylor.github.io/CHRIS/

- Is the level of a color additive likely to cause biocompatibility concerns?
- Define specific parameters including:
  - Polymer, color additive
  - Exposed surface area etc...
- Output used by both developers and reviewers
  - Design in safety early
  - Submit the OK as part of pre-market submission



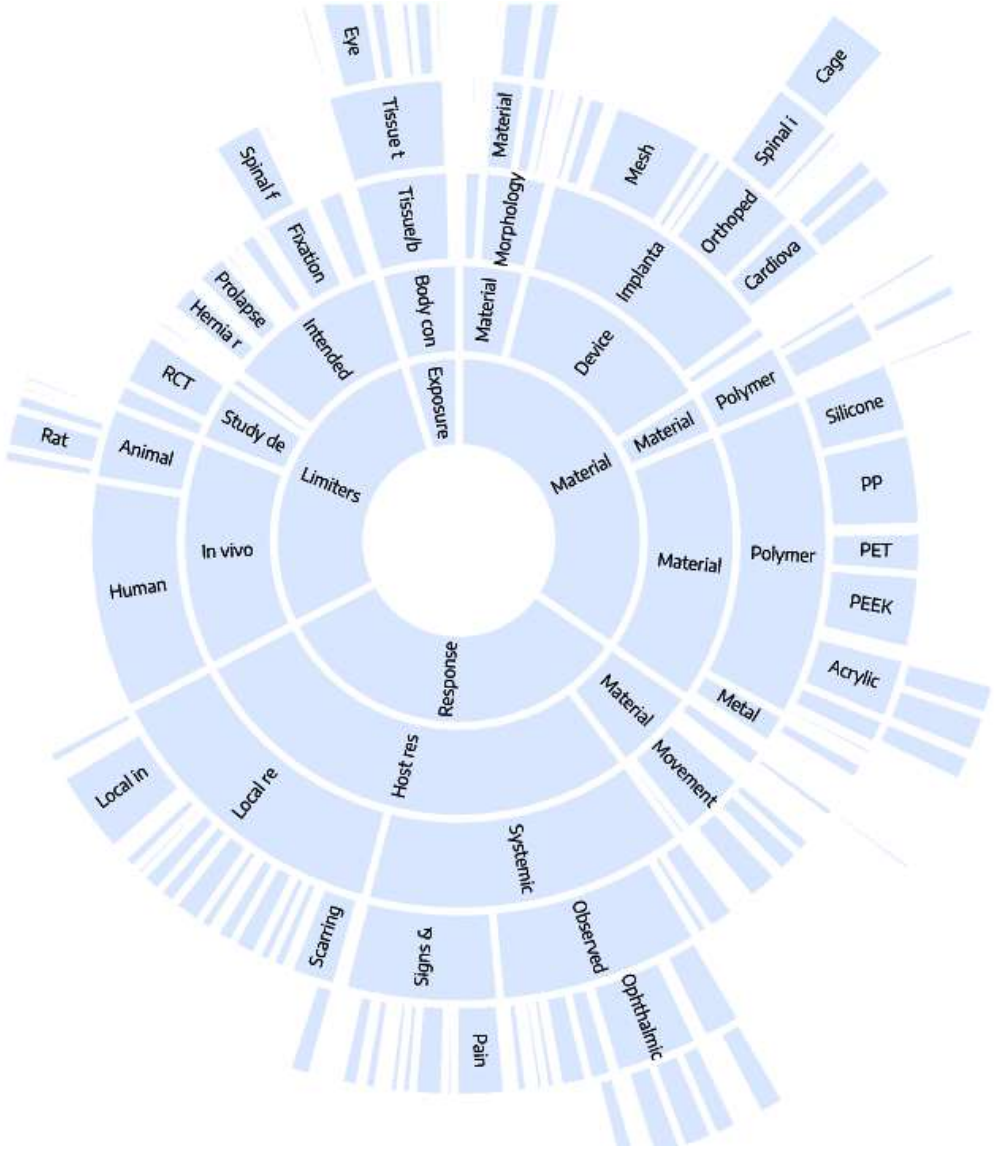
D.M. Saylor, et al., Strategies for rapid risk assessment of color additives used in medical devices, Toxicol. Sci. (2019).

CDRH/ ECRI Project Demo Output

- Correlation of:
  - Material Safety Publications from literature
  - Real World device performance

- Earlier material decision
  - What does the body do to the material?
  - What does the material do to the body?

  - Designing safety and effectiveness in early



Public Availability of RSTs

Phantom Name	Description	Type	Areas	Reference
3D printed phantom material and design with tissue-relevant Raman signature	A tool for performing Raman spectroscopy measurements on a well-characterized 3D printed sample that has tissue-simulating optical properties	Physical	Medical imaging and diagnostics	Article
Blood Mimicking Fluid for High Intensity Focused Ultrasound	A blood mimicking fluid (BMF) for the acoustic and thermal characterizations of high intensity focused ultrasound (HIFU) ablation devices	Physical	Therapeutic ultrasound	Article
Digital models of retinal vasculature based on a clinical fundus camera image	Digital model available on NIH's 3D Print Exchange site that can be used to fabricate tissue simulating phantoms with biomimetic vascular structures derived from a clinical image	Physical	Medical imaging and diagnostics	Article Article Assembly
Microcalcification templates	Templates containing clusters of microcalcifications that can be inserted into physical breast phantoms	Physical	Evaluation of 3D breast imaging systems	Article
Nanostructured Virus-simulating Phantoms for Evaluating Optical Biosensing Methods	A shelf-stable, biohazard-free viral particle phantom for evaluation of optical biosensing methods	Physical	Medical imaging and diagnostics	Article
Parchment breast phantom	A physical breast phantom fabricated from inkjet printing onto parchment paper that can be pendant, compressed, or contain masses	Physical	Evaluation of 3D breast imaging systems	Article
Phantom for assessing performance of near-infrared hematoma detectors	A modular, polymer phantom approach that enables evaluation of the performance of hematoma detectors using wavelengths close to the 805 nm isosbestic point of hemoglobin	Physical	Medical imaging and diagnostics	Article

www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

Future Plans

- Expand Reg Science Tools/ Product Catalogue
  - Towards a RST library that is the go to place for evaluations
  - Expand “Owners’ Manuals”
- Acceleration in the precompetitive space is a team sport
  - Strengthens and is fed by Collaborative Communities eg PiCC
  - Useful methodologies have an intrinsic and tangible value
- The program is now in place
  - >120 RSTs in the product catalog

Knowledge Check

Is the use of regulatory science tools mandatory in FDA submissions?

1. **True**
2. **False**

Knowledge Check

Which tool is useful in assessing the biocompatibility of color additives?

1. **Photoacoustic Imaging Phantoms**
2. **Virtual Family/Population**
3. **CHRIS**

Summary

- CDRH's Office of Science and Engineering Laboratories has an important role in the early-stage development of scientific tools
- Regulatory science tools (RSTs) may help to evaluate the safety and effectiveness of medical devices, and in emerging technology
- We have some examples of RSTs in place for use now, and plans for future expansion of the available catalog

Questions

U.S. FOOD & DRUG ADMINISTRATION (& Devices)