Overview of the National Center for Toxicological Research (NCTR)

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NCTR – A Unique FDA Resource

Established in January 1971 by Executive Order as a non-regulatory national resource owned and managed within HHS by FDA to conduct integrated, toxicological research and foster interagency, academic, and industrial collaboration in support of risk-assessment needs related to public health.

NCTR Vision and Mission

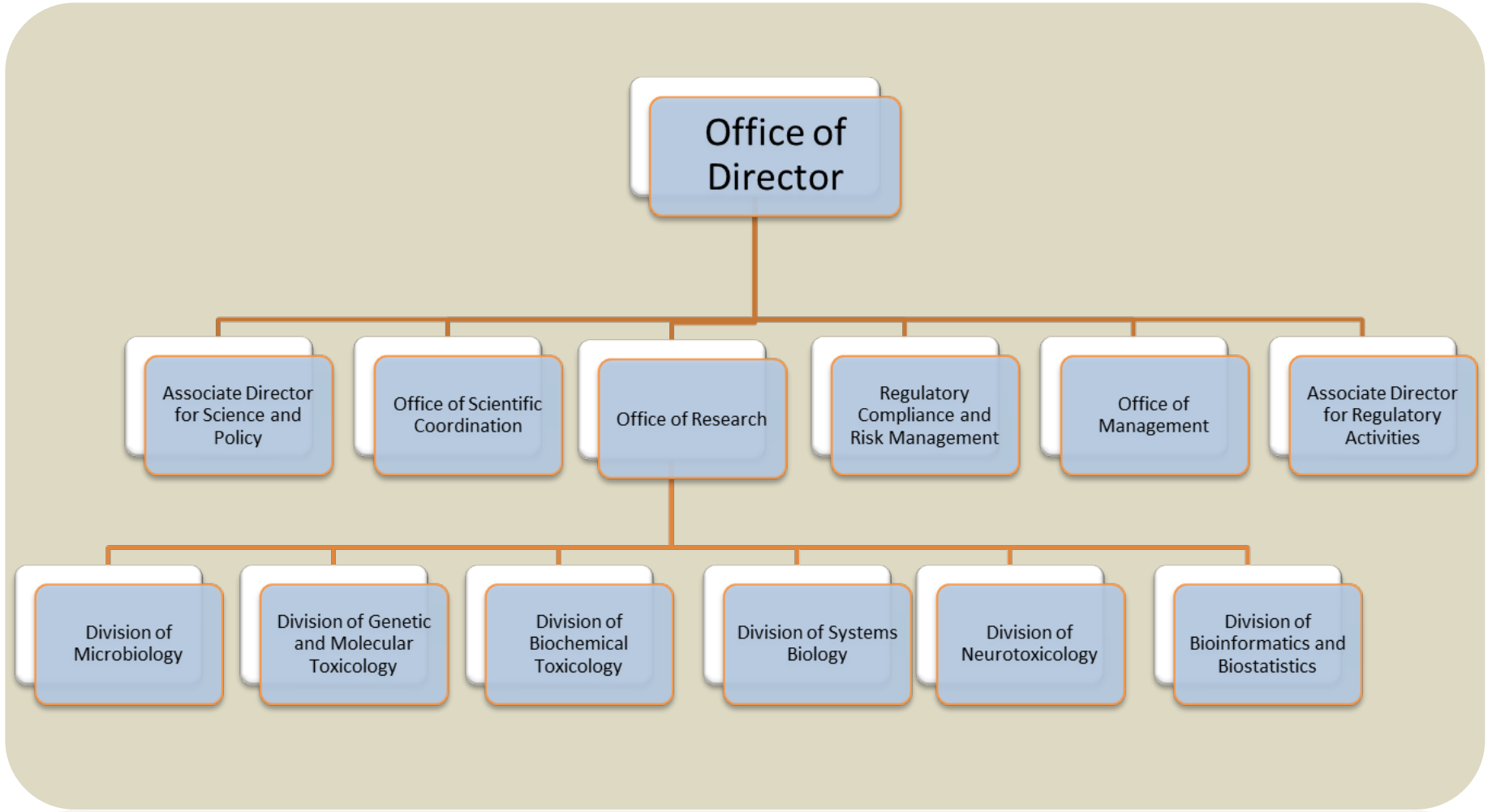
VISION

The U.S. Food and Drug Administration National Center for Toxicological Research (NCTR) is a global resource for collaboration providing consultation, training, and innovative scientific solutions in support of FDA's mission to improve public health.

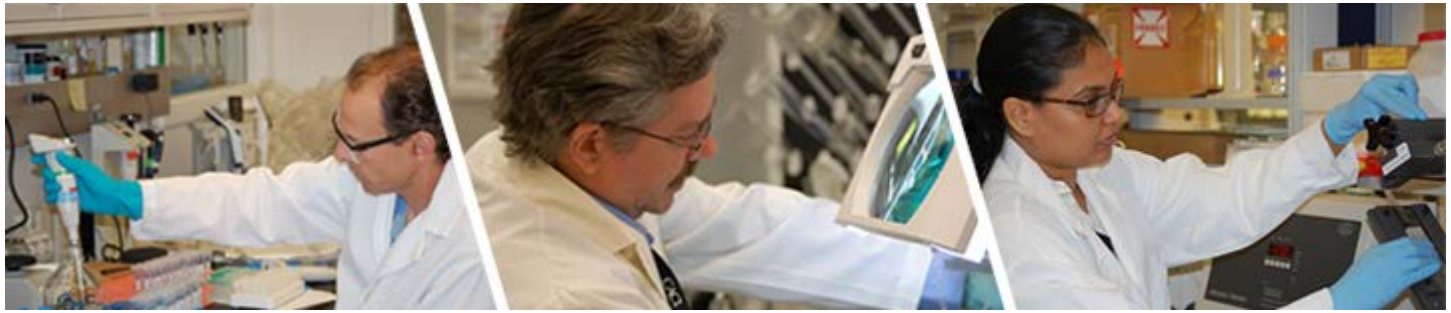
MISSION

NCTR conducts scientific research to generate data for FDA decision making, and develops and supports innovative tools and approaches that FDA uses to protect and promote individual and public health.

NCTR Organizational Structure



NCTR Staff



Government (FTEs) = 290

Research Scientists = 143

Support Scientists = 65

Administrative = 82

Onsite Contractors = 166

ORISE = 53

Current as of 11/8/2019

NCTR Research Goals

Advance scientific knowledge and tools required to support personal, animal, and public health

Enhance collaborations with other FDA Centers

Promote global interactions in regulatory science

Top Three Accomplishments in 2018/2019

#1 Improved scientific partnerships within FDA and with external collaborators that provided data for FDA decision making and identified new approaches for assessing safety.

#2 Advanced FDA regulatory science.

#3 Advanced regulatory science research globally.

Accomplishment #1 – Scientific Partnerships

CDER/NCTR

- **Opioids** – Completed method-development study on neural stem-cell growth and differentiation. A larger study to assess prenatal opioid exposure has begun.
- **Pediatric Anesthetics** – CDER and NCTR conducted exposure assessments on desflurane.
- **MOU Continues** – Data for monographs on sunscreen ingredients and other non-prescription drugs.
- **Developed methods** for the detection of Burkholderia cepacia in pharmaceutical products.

CVM/NCTR

- **Antimicrobial Resistance and the Human Microbiome** – Studied organism diversity and the presence of plasmids that can contribute to antimicrobial resistance.
- **Evaluating the impact** of veterinary drug residues in food on the intestinal microbiome

Accomplishment #1 – Scientific Partnerships continued

CFSAN/NCTR

- **Detection of microbial contaminants** – including pathogenic mycobacteria in tattoo inks—this research has led to product recalls

OWH/NCTR

- **Precision Medicine** – Studied triple-negative cancers in African-American women.

Public Workshop

- **Sequencing Quality Control-Phase 2 Next Generation Sequencing** in support of the Precision Medicine Initiative.

Accomplishment #1 – Scientific Partnerships continued

CTP/NCTR

Partnered with CTP to conduct toxicological research in support of tobacco product regulation.

- **Inhalation Toxicology**
  Conduct inhalation toxicology studies of select tobacco product constituents:
  - Nicotine: Ongoing pharmacokinetic (PK) study (inhalation, oral, and intravenous administration).
  - NNK: Finalizing reports on completed PK and subchronic toxicity studies.

- **Alternative Models/Toxicology/Adverse Health Consequences**
  Developed an *in vitro 3D* air-liquid-interface (ALI) human airway-cell culture model to evaluate the toxicity and inflammation produced by whole cigarette smoke.

- **Modeling/Predictive Toxicology**
  Developing computational tools (e.g., physiologically-based pharmacokinetic model, PBPK) to assess the internal dose metrics of nicotine in humans, and to inform the evaluation of the nicotine exposure-response relationship across different tobacco product types and user populations.

National Toxicology Program
U.S. Department of Health and Human Services

FDA

Accomplishment #1: Scientific Partnerships…continued

FDA/NCTR and NIEHS/NTP Interagency Agreement

- Evaluation of arsenic toxicity - behavior, metabolism and toxicokinetic studies in developing animals – CFSAN
- Assessment of the toxicity of high-molecular-weight polyethylene glycols (PEGs) – CDER and CBER
- Evaluation of brominated vegetable oil in SD rats – CFSAN
- Effects of the fibrinolytic enzymes nattokinase and lumbrokinase alone or in combination with aspirin in blood parameters – CFSAN
- In vitro system to evaluate the disease-related toxic effects of inhaled test agents in human airway tissue models – CDRH and NTP
- Role the microbiome may play in the toxicity of xenobiotics – NTP

Accomplishment #2:
Advancing FDA Regulatory Science

Scientific Focus Areas for Expansion:

- Safety Assessment
- Biomarkers
- Bio-Imaging
- 3D Models & Stem cells
- Microbiome
- Precision/Personalized Medicine
- Nanotoxicology
- Inhalation Toxicology
- PK/PD Modeling
- Bioinformatics
- Regulatory Science Training

Accomplishment #2:
Advancing FDA Regulatory Science…continued

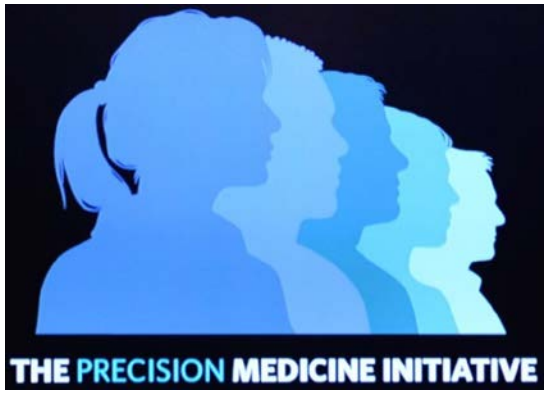
Review-to-Research and Return (R2R) Program

- As a result of NCTR SAB recommendations, created a new branch within the Division of Bioinformatics and Biostatistics (DBB) emphasizing the development of the R2R Program.

Example projects:

- Collaborating with CDER/OTS on the DASH system (Data Analysis Host System) to track progression from INDs to NDAs or BLAs and approval of NDAs and BLAs
- Start with upgrading the system and end with text mining and analysis of its source documents

Accomplishment #2:
Advancing FDA Regulatory Science…continued



Precision Medicine

- Collaborative bioinformatic solutions for Precision Medicine

Artificial Intelligence (AI) – Deep Learning Methodologies

- AI is a broad concept of training machines to think and behave like humans. Currently, the DBB is developing deep-learning methodologies to deal with the FDA text documents, such as FDA-approved drug-labeling documents and data from FDA Adverse Events Reporting System (FAERS).

Progress on Maternal and Children's Health

Perinatal Health Center of Excellence (PHCE)

Why is it beneficial to have a virtual Center of Excellence focused on the perinatal period?

Maternal/fetal pairs represent a unique regulatory responsibility.

Preterm and term-birth neonates and infants represent a vulnerable population that is understudied.

Provides conduit for addressing unmet FDA needs across Centers by creating expert teams and support for needed research across FDA.

Progress of the Perinatal Health Center of Excellence

1

Initial authorization and **funding was secured** in the FY19 budget.

2

FDA Centers/ORA **identified liaisons** to review 22 proposals and **14 were funded.**

3

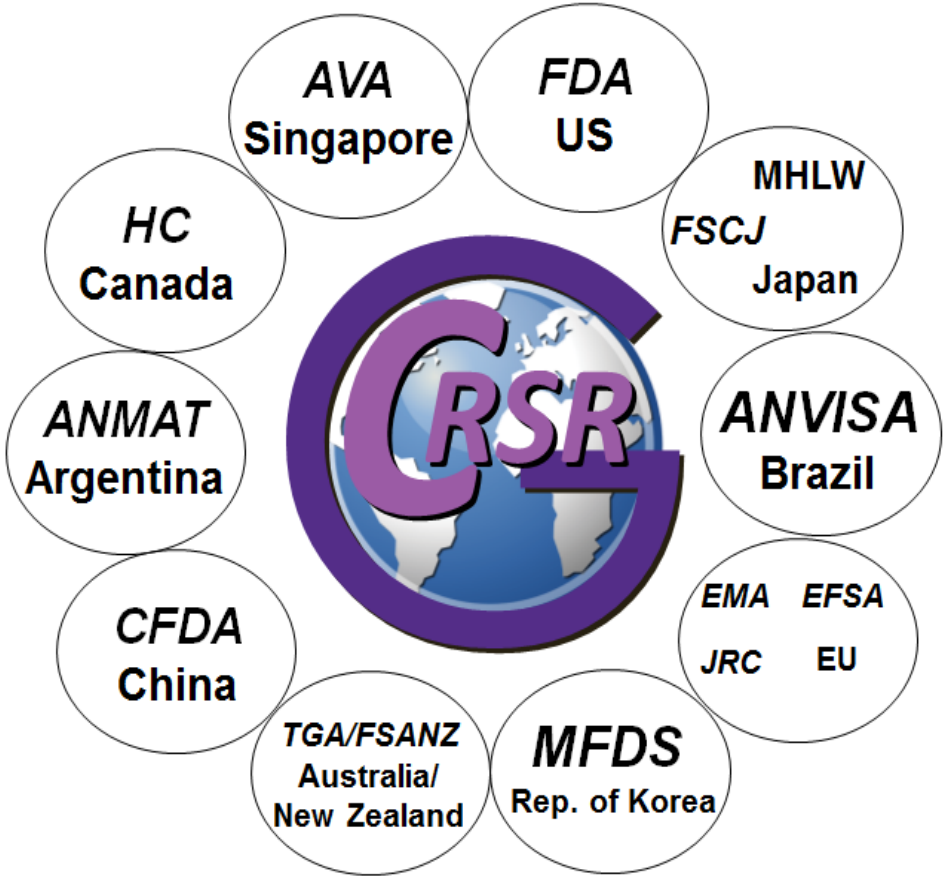
The first annual **PHCE Workshop** was held at WO to review research progress.

4

10 proposals were developed for review in FY20 and **3 were funded**.

Accomplishment #3:
Advancing regulatory science research globally

Global Coalition for Regulatory Science Research
(Member Countries/Agencies)



Advancing Regulatory Science Research Globally

GSRS 2018

The GCRSR and National Institutes for Food and Drug Control (NIFDC), China co-hosted the Global Summit of Regulatory Science (GSRS18) which focused on **"Risk/Benefit of Dietary Supplements and Herbal Medicine in the Era of Data Science"** on September 25-26, 2018, in Beijing, China with representatives from FDA and about 15 countries.

GSRS 2019

The **9th Global Summit** on Regulatory Science was held at Lake Maggiore, Italy and co-sponsored by the Joint Research Centre − European Commission from September 24-26, 2019. Representatives from FDA and 34 countries thoroughly discussed the topics focused on "**Nanotechnologies and Nano plastics**."

GLOBAL SUMMIT ON REGULATORY SCIENCE 2020

Theme – Emerging Technologies and Their Application to Regulatory Science
September 28-30, 2020 in Bethesda, Maryland

(Co-Hosted by the Global Coalition for Regulatory Science Research and the National Center for Advancing Translational Science)

Regulatory science research presentations from global regulatory, research, and standards communities on emerging technologies. Topics include:

- **Emerging technologies for the safety assessment of Food, Drugs, and Personal Care Products**
- **Approaches to Standardize and Validate Emerging Technologies for Regulatory Application**
- **Challenges and Opportunities of Emerging Technologies and Alternate Methods for Decision Making**

NOTE:** ***There is no registration fee; however, registration is required to attend the conference.

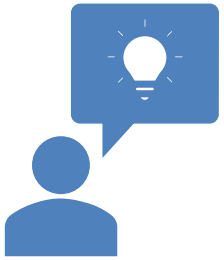
For more information and updates, please visit the Global Summit website

Scientific Program Committee Co-Chairs:
William Slikker Jr., U.S. Food and Drug Administration (William.Slikker@fda.hhs.gov)
Marta Hugas, European Food Safety Authority (Marta.Hugas@efsa.europa.eu)

Global Coalition for Regulatory Science Research

Approach to improve FDA collaborations

- Through coordinated efforts across Centers, prioritized action plans can be created to improve efficiency.
- Skills in areas such as those below are important and can be shared across Centers:
    - cell systems
    - emerging technologies
    - mathematical modeling
    - laboratory animal studies
    - bioanalytical chemistry
    - information sciences and AI
    - omics
- Collaborative research across Centers, quality science, and mission-focused outcomes are anticipated.



Questions for Discussion

- Can animal models be better utilized for preclinical decision making? What tools would help?
- What are some examples of current regulatory approaches that can be replaced with emerging technologies?
- What emerging technologies need further evaluation?
- What aspects of regulatory science can artificial intelligence (AI) and *in silico* research improve?
- Is there a need for additional *in vitro*-to-*in vivo* extrapolation?