

FDA UPDATE ON NTP PORTFOLIO

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FDA update on NTP portfolio



FDA Mission

The Food and Drug Administration (FDA) is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

FDA also has responsibility for regulating the manufacturing, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.

FDA is responsible for the oversight of more than \$2.5 trillion in consumption of food, medical products, and tobacco, corresponding to approximately 20 cents of every dollar spent by consumers in the USA.

FDA's NTP research portfolio reflects the broad mission of the agency as a core agency of the Program.

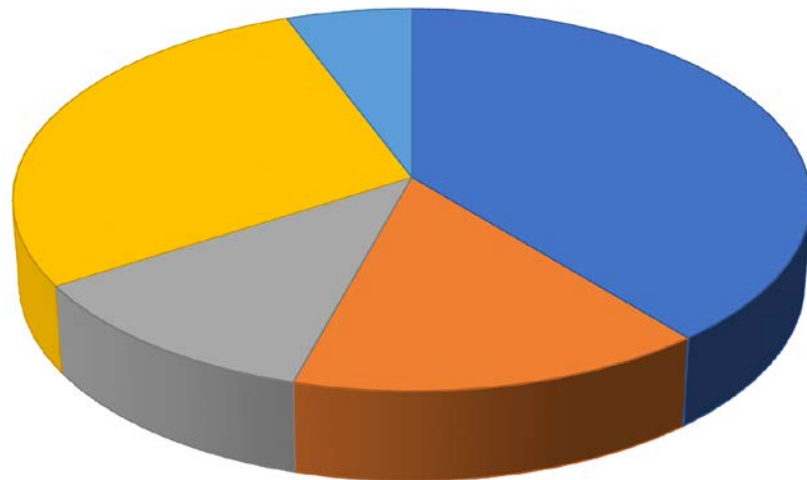







FDA update on NTP portfolio

- FDA-sponsored portfolio
- NIEHS-FDA Interagency Agreement (IAA)-sponsored portfolio

FDA-sponsored portfolio

Five Broad Areas of Research (FY18):

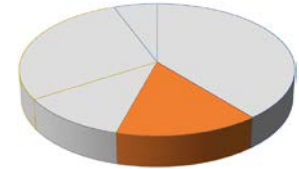


-  **Biochemical and Molecular Basis of Toxicology**
-  **Computational Toxicology**
-  **Nanotoxicology**
-  **Neurotoxicology**
-  **Bioassay and Biomarker Development and Evaluation**

FDA-sponsored portfolio

Biochemical and Molecular Basis of Toxicology

- 8 Protocols
- 15% of Investment Effort



Representative protocol: Tumor mutational signatures of acrylamide and glycidamide (PI: Fred Beland).

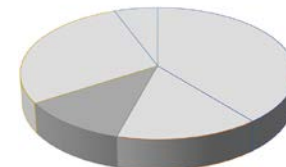
Main objectives:

To compare the mutational signatures obtained from acrylamide and glycidamide in experimental animals with mutational signatures of human tumors in published databases.

FDA-sponsored portfolio

Computational Toxicology

- 9 Protocols
- 12% of Investment Effort



Representative protocol: Improving methods and algorithms for enhancing 3D-QSDAR (PI: Svetoslav Slavov).

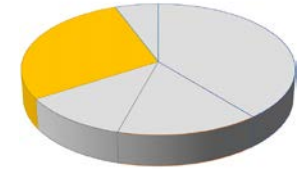
Main objectives:

To test the feasibility and implementation of software code for enhancements to the Three-Dimensional Quantitative Spectral Data-Activity Relationship (3D-QSDAR) technique and investigate the potential performance improvement of these models for various data sets and endpoints.

FDA-sponsored portfolio

Nanotoxicology

- 14 Protocols
- 28% of Investment Effort



Representative protocol: Evaluation of the migration and toxic potential of Ag nanoparticles in feminine hygiene products to vaginal tissue: *In vivo* rodent and *in vitro* 3D mucosal models (PI: Anil Patri).

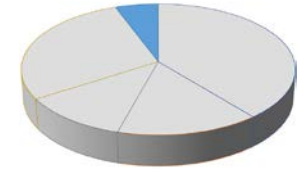
Main objectives:

To evaluate the migration, uptake, and toxicity of Ag nanoparticles and ions used in feminine hygiene products using a human cell-based *in vitro* three-dimensional culture model that has many of the structural and functional features of the human vaginal mucosal layer.

FDA-sponsored portfolio

Neurotoxicology

- 5 Protocols
- 6% of Investment Effort



Representative protocol: Effects of developmental sevoflurane exposure and pretreatment with acetyl-L-carnitine on complex brain function in rats (PI: John Talpos).

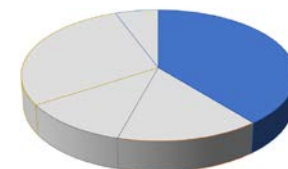
Main objectives:

To examine the effects of early developmental exposure to sevoflurane (pediatric anesthetic) on neurodegeneration and complex operant learning. To determine whether impairments in learning can be attenuated by pretreatment with acetyl-L-carnitine.

FDA-sponsored portfolio

Bioassay and Biomarker Development and Evaluation

- 19 Protocols
- 39% of Investment Effort



Representative protocol: Using metabolically competent human cell lines to perform high-throughput genotoxicity testing (PI: Nan Mei).

Main objectives:

To develop HepG2- and TK6-derived cell lines capable of stably expressing multiple Phase I CYPs and Phase II UDP-glucuronosyltransferase (UGT) or sulfotransferase (SULT) enzymes. To assess the utility of these newly developed cell lines for toxicity studies using a small set of chemicals with known or postulated metabolism-related toxicity.

IAA-sponsored portfolio



NIEHS-FDA Interagency Agreement (IAA)

- Established in 1992, supported by the NIEHS.
- Enables the conduction of toxicology and mechanistic studies at the FDA National Center for Toxicological Research (NCTR) on FDA-regulated agents nominated to the NTP.
- Oversight of the studies provided by the *Toxicology Study Selection and Review Committee* (TSSRC; convenes twice per year at FDA headquarters). NIEHS Project Officer – Nigel J. Walker; FDA Project Officer – Gonçalo Gamboa da Costa.
- IAA research resulted in 18 published NTP Technical and Research Reports and over 250 peer-reviewed journal publications.

IAA-sponsored portfolio

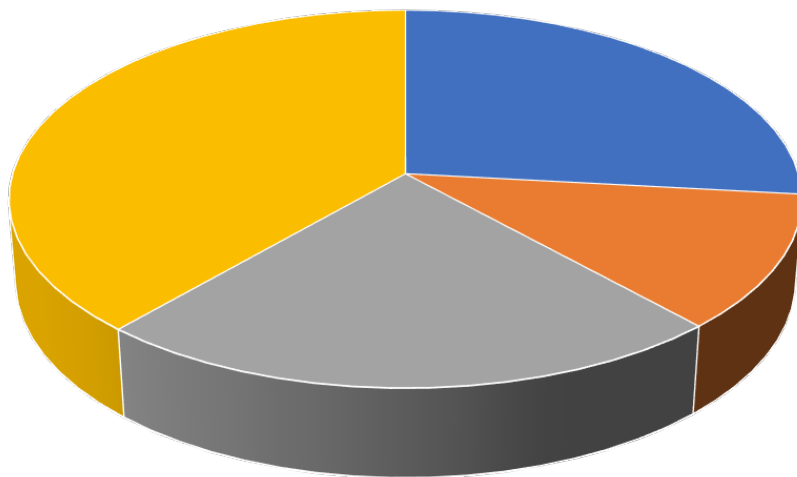
Examples of past NIEHS-FDA IAA research with clear translational impact





- Fumonisin B₁
- Acrylamide
- Melamine and Cyanuric acid
- Ketamine
- Antiretroviral AIDS therapeutics
- Furan

IAA-sponsored portfolio



Current Portfolio (FY19)



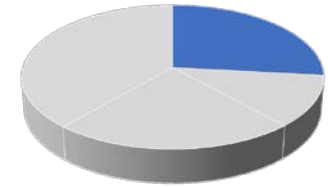
-  Food Additives and Contaminants
-  Dietary Supplements
-  Drugs
-  Enhancing Toxicology Program

IAA-sponsored portfolio



Food Additives and Contaminants

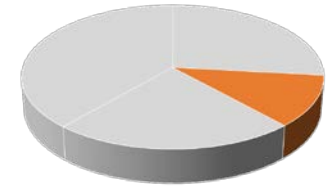
- **3 Protocols**
- **27% of Investment Effort**
- Role of perinatal development on toxicokinetics of inorganic arsenic (PI: Daniel Doerge).
- Long-term evaluation of cognitive, neurochemical, histopathology, and microbiome-related effects of developmental inorganic arsenic (iAs) exposure in Sprague-Dawley rats (PI: Sherry Ferguson).
- Evaluation of brominated vegetable oil in Sprague-Dawley rats (PI: Gonçalo Gamboa da Costa).



IAA-sponsored portfolio

Dietary Supplements

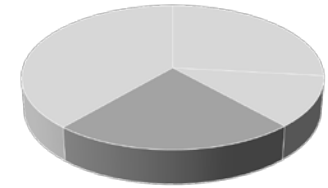
- **1 Protocol**
- **12% of Investment Effort**
- Effects of the fibrinolytic enzymes nattokinase and lumbrokinase alone or in combination with aspirin in blood parameters (PI: Luísa Camacho).



IAA-sponsored portfolio


Drugs

- **1 Protocol**
- **23% of Investment Effort**
- Toxicokinetic profile and toxicity of high-molecular-weight polyethylene glycols in Sprague Dawley rats (PI: Jia-Long Fang).



IAA-sponsored portfolio

Enhancing Toxicology Program

- **3 Protocols**
 - **39% of Investment Effort**
- 
- Developing an *in vitro* system to evaluate the disease-related toxic effects of inhaled test agents in human airway tissue models (PI: Xuefei Cao).
 - NTP capability building for microbiome assessment on toxicology studies: Assessment of the role that the microbiome may play in the toxicity of xenobiotics (PI: Sangeeta Kare).
 - Development of nanotoxicology standards (PI: Anil Patri).

FDA update on NTP portfolio

Coordination and Oversight of the Research Programs

