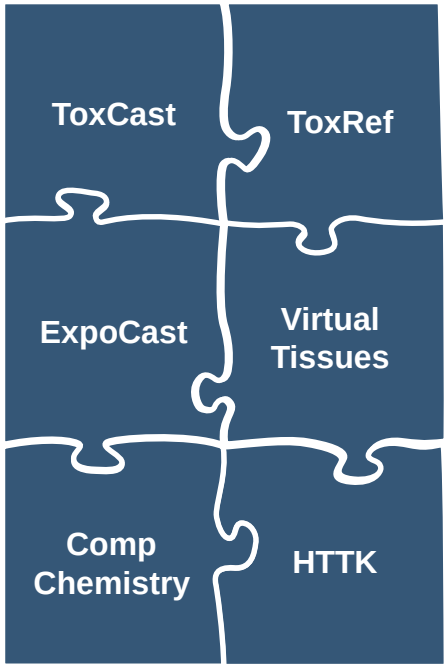
EPA United States Environmental Protection Agency

Development and Application of New Approach Methods for Regulatory Decisions: A Research Perspective

Helsinki Chemicals Forum
June 9, 2017

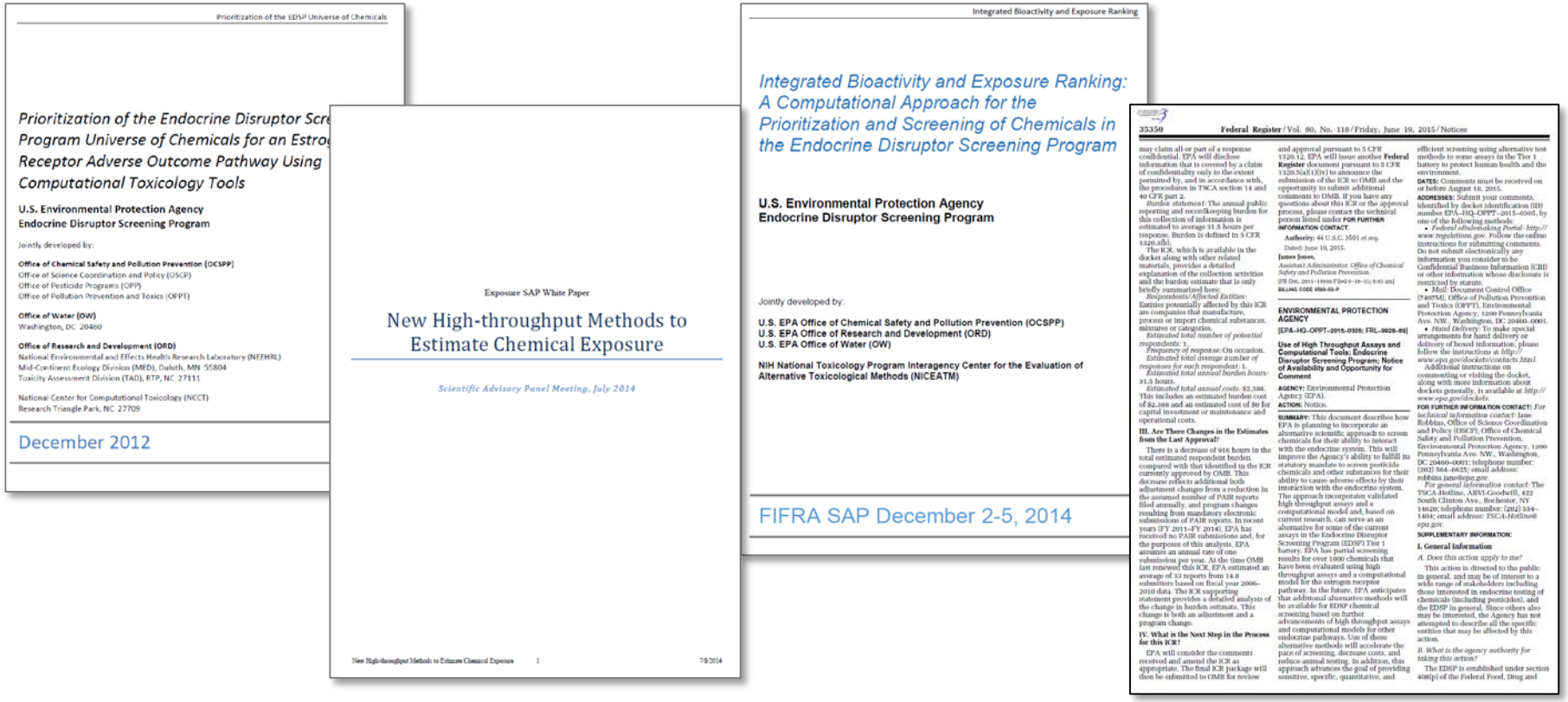
Russell Thomas
Director
National Center for Computational Toxicology

Progress in Developing New Approach Methods



- High-throughput *in vitro* screening of ~1,000 chemicals across ~700 assay endpoints (ToxCast) and ~8,000 chemicals in ~60 assay endpoints (Tox21)
- High quality, curated chemical structure and physical chemical properties database of >700,000 molecules
- Legacy *in vivo* data from 5,891 animal toxicology studies on ~1,110 unique chemicals
- High-throughput toxicokinetic models for ~700 chemicals based on *in vitro* measurements
- A database of chemical-product categories (CPCat) that maps over 45,000 chemicals to ~8,000 product uses or functions
- High-throughput exposure estimates with uncertainty for over 7,000 chemicals based on production volume and chemical use
- AOPs and virtual tissue models for broad range of developmental toxicities

Progress in Applying New Approach Methods



Prioritization of the EDSP Universe of Chemicals

Prioritization of the Endocrine Disruptor Scre
Program Universe of Chemicals for an Estro
Receptor Adverse Outcome Pathway Using
Computational Toxicology Tools

U.S. Environmental Protection Agency
Endocrine Disruptor Screening Program

Jointly developed by:

Office of Chemical Safety and Pollution Prevention (OCSPP)
Office of Science Coordination and Policy (OSCP)
Office of Pesticide Programs (OPP)
Office of Pollution Prevention and Toxics (OPPT)

Office of Water (OW)
Washington, DC 20460

Office of Research and Development (ORD)
National Environmental and Effects Health Research Laboratory (NEEHRL)
Mid-Continent Ecology Division (MED), Duluth, MN 55804
Toxicity Assessment Division (TAD), RTP, NC 27111

National Center for Computational Toxicology (NCCT)
Research Triangle Park, NC 27709

December 2012

Exposure SAP White Paper

New High-throughput Methods to Estimate Chemical Exposure

Scientific Advisory Panel Meeting, July 2014

New High-throughput Methods to Estimate Chemical Exposure 1 7/8/2014

Integrated Bioactivity and Exposure Ranking

Integrated Bioactivity and Exposure Ranking: A Computational Approach for the Prioritization and Screening of Chemicals in the Endocrine Disruptor Screening Program

U.S. Environmental Protection Agency
Endocrine Disruptor Screening Program

Jointly developed by:

U.S. EPA Office of Chemical Safety and Pollution Prevention (OCSPP)
U.S. EPA Office of Research and Development (ORD)
U.S. EPA Office of Water (OW)

NIH National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

FIFRA SAP December 2-5, 2014

35350 Federal Register / Vol. 80, No. 118 / Friday, June 19, 2015 / Notices

may claim all or part of a response confidential. EPA will disclose information that is covered by a claim of confidentiality only to the extent permitted by, and in accordance with, the procedures in TSCA section 14 and 40 CFR part 2.

Burden statement: The annual public reporting and recordkeeping burden for this collection of information is estimated to average 31.5 hours per response. Burden is defined in 5 CFR 1320.3(b).

The ICR, which is available in the docket along with other related materials, provides a detailed explanation of the collection activities and the burden estimate that is only briefly summarized here:

Respondents/Affected Entities: Entities potentially affected by this ICR are companies that manufacture, process or import chemical substances, mixtures or categories.

Estimated total number of potential respondents: 1.

Frequency of response: On occasion.

Estimated total average number of responses for each respondent: 1.

Estimated total annual burden hours: 31.5 hours.

Estimated total annual costs: $2,388. This includes an estimated burden cost of $2,388 and an estimated cost of $0 for capital investment or maintenance and operational costs.

III. Are There Changes in the Estimates from the Last Approval?

There is a decrease of 916 hours in the total estimated respondent burden compared with that identified in the ICR currently approved by OMB. This decrease reflects additional both adjustment changes from a reduction in the assumed number of PAIR reports filed annually, and program changes resulting from mandatory electronic submissions of PAIR reports. In recent years (FY 2011–FY 2014), EPA has received no PAIR submissions and, for the purposes of this analysis, EPA assumes an annual rate of one submission per year. At the time OMB last renewed this ICR, EPA estimated an average of 33 reports from 14.8 submitters based on fiscal year 2006–2010 data. The ICR supporting statement provides a detailed analysis of the change in burden estimate. This change is both an adjustment and a program change.

IV. What is the Next Step in the Process for this ICR?

EPA will consider the comments received and amend the ICR as appropriate. The final ICR package will then be submitted to OMB for review and approval pursuant to 5 CFR 1320.12. EPA will issue another **Federal Register** document pursuant to 5 CFR 1320.5(a)(1)(iv) to announce the submission of the ICR to OMB and the opportunity to submit additional comments to OMB. If you have any questions about this ICR or the approval process, please contact the technical person listed under **FOR FURTHER INFORMATION CONTACT**.

Authority: 44 U.S.C. 3501 *et seq.*

Dated: June 10, 2015.

James Jones,

Assistant Administrator, Office of Chemical Safety and Pollution Prevention.

[FR Doc. 2015–14993 Filed 6–18–15; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPPT–2015–0305; FRL–9926–89]

Use of High Throughput Assays and Computational Tools; Endocrine Disruptor Screening Program; Notice of Availability and Opportunity for Comment

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This document describes how EPA is planning to incorporate an alternative scientific approach to screen chemicals for their ability to interact with the endocrine system. This will improve the Agency's ability to fulfill its statutory mandate to screen pesticide chemicals and other substances for their ability to cause adverse effects by their interaction with the endocrine system. The approach incorporates validated high throughput assays and a computational model and, based on current research, can serve as an alternative for some of the current assays in the Endocrine Disruptor Screening Program (EDSP) Tier 1 battery. EPA has partial screening results for over 1000 chemicals that have been evaluated using high throughput assays and a computational model for the estrogen receptor pathway. In the future, EPA anticipates that additional alternative methods will be available for EDSP chemical screening based on further advancements of high throughput assays and computational models for other endocrine pathways. Use of these alternative methods will accelerate the pace of screening, decrease costs, and reduce animal testing. In addition, this approach advances the goal of providing sensitive, specific, quantitative, and efficient screening using alternative test methods to some assays in the Tier 1 battery to protect human health and the environment.

DATES: Comments must be received on or before August 18, 2015.

ADDRESSES: Submit your comments, identified by docket identification (ID) number EPA–HQ–OPPT–2015–0305, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.
- Mail: Document Control Office (7407M), Office of Pollution Prevention and Toxics (OPPT), Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.html.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: *For technical information contact:* Jane Robbins, Office of Science Coordination and Policy (OSCP), Office of Chemical Safety and Pollution Prevention, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001; telephone number: (202) 564–6625; email address: robbins.jane@epa.gov.

For general information contact: The TSCA-Hotline, ABVI-Goodwill, 422 South Clinton Ave., Rochester, NY 14620; telephone number: (202) 554–1404; email address: *TSCA-Hotline@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

This action is directed to the public in general, and may be of interest to a wide range of stakeholders including those interested in endocrine testing of chemicals (including pesticides), and the EDSP in general. Since others also may be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action.

B. What is the agency authority for taking this action?

The EDSP is established under section 408(p) of the Federal Food, Drug and

Scientific Challenges and Data Gaps

Hazard Characterization

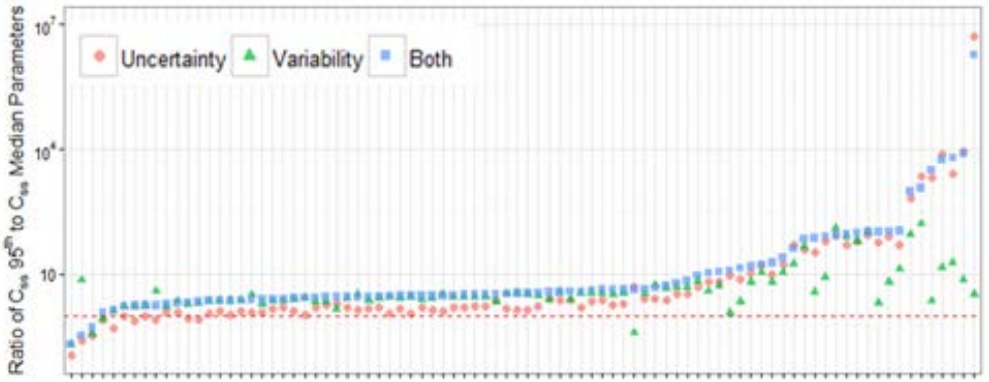
- Lack of metabolic competence of many current *in vitro* assays
- Biological coverage of assay portfolio
- Limited biological co
- Testing of volatile ar

nd Simmons, Unpublished

Dosimetry

- Predicting which che
- *In vitro* assays not a
- Reliance on nomina

tic modeling

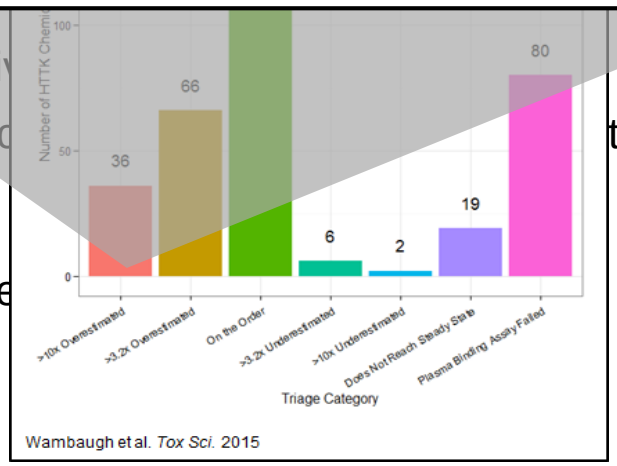


Wambaugh, Unpublished

Exposure

- Biomonitoring data for a greater di
- Quantitative data on chemicals in c

ty from household items



Wambaugh et al. *Tox Sci.* 2015

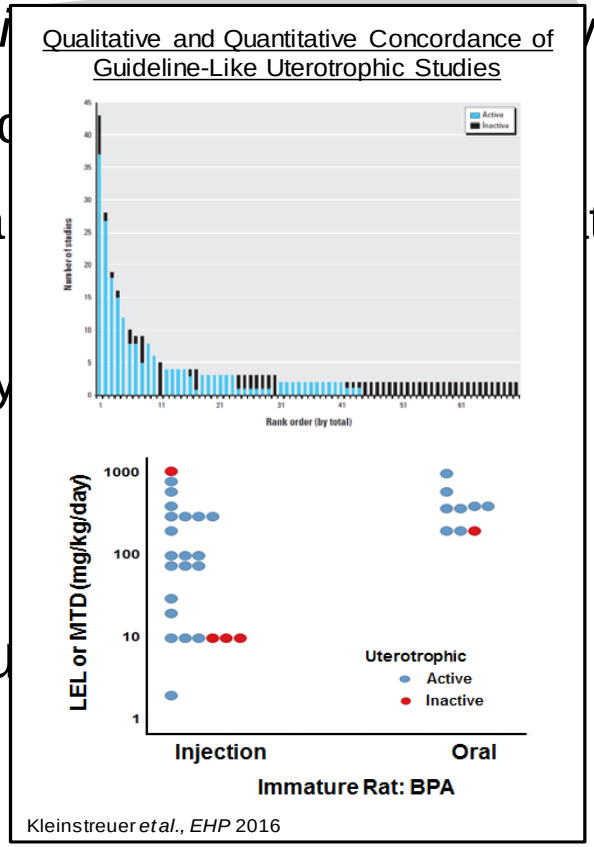
Other

- Quantifying and incorporating unce

Philosophical and Social Challenges

- Developing an acceptable and efficient validation approach
- Accepting and understanding qualitative and quantitative differences in uncertainty in the new approach methods and traditional *in vivo* studies
- Agreeing on the role of *i* validation
- Moving from an apical to
- Defining "adversity" in a t it was solved in an apical world)
- Predicting human safety

Cou



Kleinstreuer *et al.*, *EHP* 2016