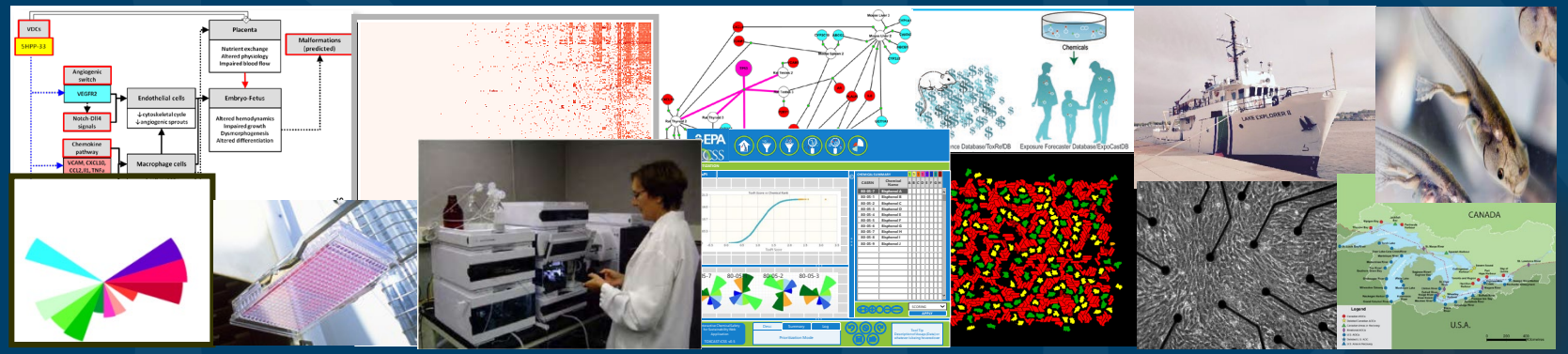
EPA's Path Towards More Rapid, Efficient, and Protective Chemical Testing with Fewer Animals

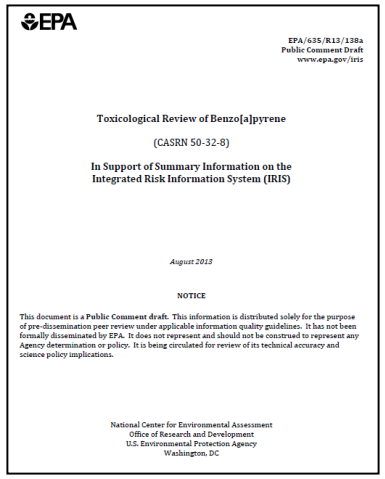


Superfund Research Program 2020 Annual Meeting

December 15, 2020

Rusty Thomas
Director
Center for Computational Toxicology and Exposure

The EPA Needs to Make A Range of Decisions on Chemicals



EPA

EPA/635/R13/138a
Public Comment Draft
www.epa.gov/iris

Toxicological Review of Benzo[a]pyrene

(CASRN 50-32-8)

In Support of Summary Information on the Integrated Risk Information System (IRIS)

August 2013

NOTICE

This document is a Public Comment draft. This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by EPA. It does not represent and should not be construed to represent any Agency determination or policy. It is being circulated for review of its technical accuracy and science policy implications.

National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC

Federal Register / Vol. 73, No. 215 / Wednesday, November 5, 2008 / Rules and Regulations 65743

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 721

[EPA–HQ–OPPT–2008–0251; FRL–8371–3]

RIN 2070–AB27

Significant New Use Rules on Certain Chemical Substances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Direct final rule.

SUMMARY: EPA is promulgating significant new use rules (SNURs) under section 5(a)(2) of the Toxic Substances Control Act (TSCA) for 56 chemical substances which were the subject of premanufacture notices (PMNs). Four of these chemical substances are subject to TSCA section 5(e) consent orders issued by EPA. This action requires persons who intend to manufacture, import, or process any of these 56 chemical substances for an activity that is designated as a significant new use by this rule to notify EPA at least 90 days before commencing that activity. The required notification will provide EPA with the opportunity to evaluate the intended use and, if necessary, to prohibit or limit that activity before it occurs.

DATES: The effective date of this rule is January 5, 2009 without further notice, unless EPA receives written adverse or critical comments, or notice of intent to submit adverse or critical comments before December 5, 2008. This rule shall be promulgated for purposes of judicial review at 1 p.m. (e.s.t.) on November 19, 2008. If EPA receives written adverse or critical comments, or notice of intent to submit adverse or critical comments, on one or more of these SNURs before December 5, 2008, EPA will withdraw the relevant sections of this direct final rule before its effective date. EPA will then issue a proposed SNUR for the chemical substance(s) on which adverse or critical comments were received, providing a 30-day period for public comment.

ADDRESSES: Submit your comments, identified by docket identification (ID) number EPA–HQ–OPPT–2008–0251, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the on-line instructions for submitting comments.
- *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:* OPPT Document Control Office (DCO), EPA East, Rm. 6428, 1201 Constitution Ave., NW., Washington, DC. Attention: Docket ID Number EPA–HQ–OPPT–2008–0251. The DCO is open from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number for the DCO is (202) 564–8930. Such deliveries are only accepted during the DCO's normal hours of operation, and special arrangements should be made for deliveries of boxed information.

Instructions: Direct your comments to docket ID number EPA–HQ–OPPT–2008–0251. EPA's policy is that all comments received will be included in the public docket without change and may be made available on-line at *http://www.regulations.gov*, including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through regulations.gov or e-mail. The regulations.gov website is an "anonymous access" system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through regulations.gov, your e-mail address will be automatically captured and included as part of the comment that is placed in the public docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD-ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses. For additional information about EPA's public docket, visit the EPA Docket Center homepage at *http://www.epa.gov/epahome/dockets.htm.*

Docket: All documents in the docket are listed in the docket index available at *http://www.regulations.gov.* Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, will be publicly available only in hard copy. Publicly available docket materials are available electronically at *http://www.regulations.gov*, or, if only available in hard copy, at the OPPT Docket. The OPPT Docket is located in the EPA Docket Center (EPA/DC) at Rm. 3334, EPA West Bldg., 1301 Constitution Ave., NW., Washington, DC. The EPA/DC Public Reading Room hours of operation are 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding Federal holidays. The telephone number of the EPA/DC Public Reading Room is (202) 566–1744, and the telephone number for the OPPT Docket is (202) 566–0280. Docket visitors are required to show photographic identification, pass through a metal detector, and sign the EPA visitor log. All visitor bags are processed through an X-ray machine and subject to search. Visitors will be provided an EPA/DC badge that must be visible at all times in the building and returned upon departure.

FOR FURTHER INFORMATION CONTACT: *For general information contact:* Colby Lintner, Regulatory Coordinator, Environmental Assistance Division (7408M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (202) 554–1404; e-mail address: *TSCA-Hotline@epa.gov.*

For technical information contact: Tracey Pennington, Chemical Control Division (7405M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (202) 564–2209; e-mail address: pennington.tracey@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you manufacture, import, process, or use the chemical substances contained in this rule. Potentially affected entities may include, but are not limited to:

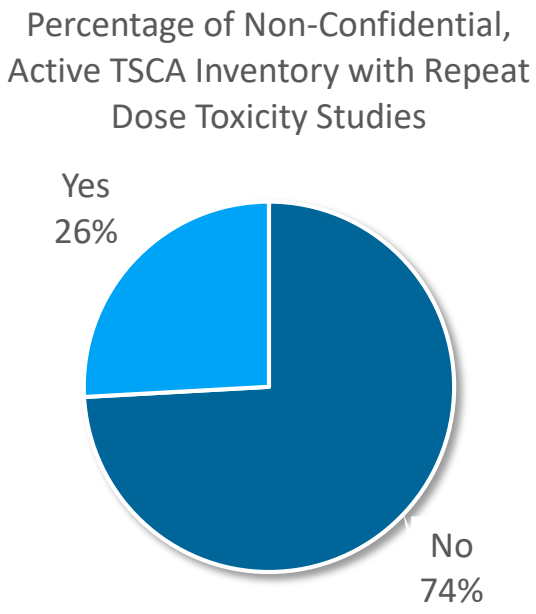
- Manufacturers, importers, or processors of one or more subject chemical substances (NAICS codes 325 and 324110), e.g., Chemical manufacturing and petroleum refineries.

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. To determine whether you or your business may be affected by this action, you should carefully examine the applicability provisions in

- Decisions on the manufacture, use, release, disposal, and clean-up of chemicals is governed by a range of statutes and associated amendments
  - e.g., Safe Drinking Water Act, Clean Air Act, Toxic Substances Control Act, Food Quality Protection Act
- The statutes provide the framework for the decisions while Agency rules and guidance outline the interpretation of the statutes and how decisions are implemented
- Different decision contexts exist within the statutes, which determine the type of data and level of certainty required
  - Prioritization (e.g., EDSP, TSCA)
  - Emergency response (e.g., AEGLs)
  - Screening-level assessments (e.g., CCL, PMN)
  - Provisional assessments (e.g., PPRTVs)
  - Toxicity assessments (e.g., IRIS)
  - Endangered species protection (e.g., pesticides)
  - Risk assessments (e.g., MCLs, pesticides, TSCA risk evaluations)

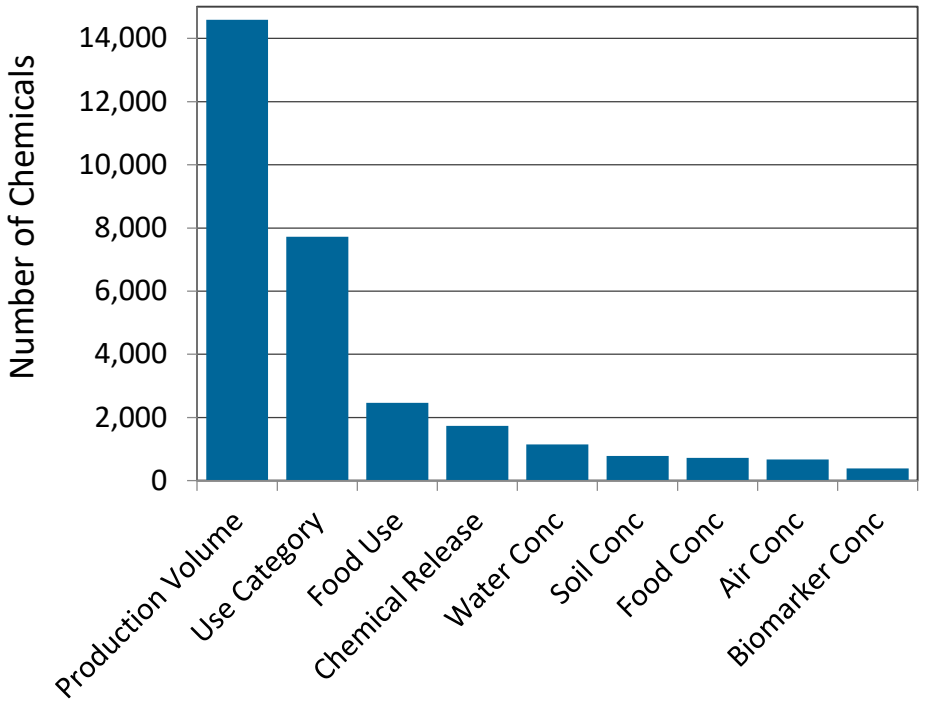
There is a Lack of Data on Hazard, Toxicokinetics, and Exposure for Most Chemicals

Hazard



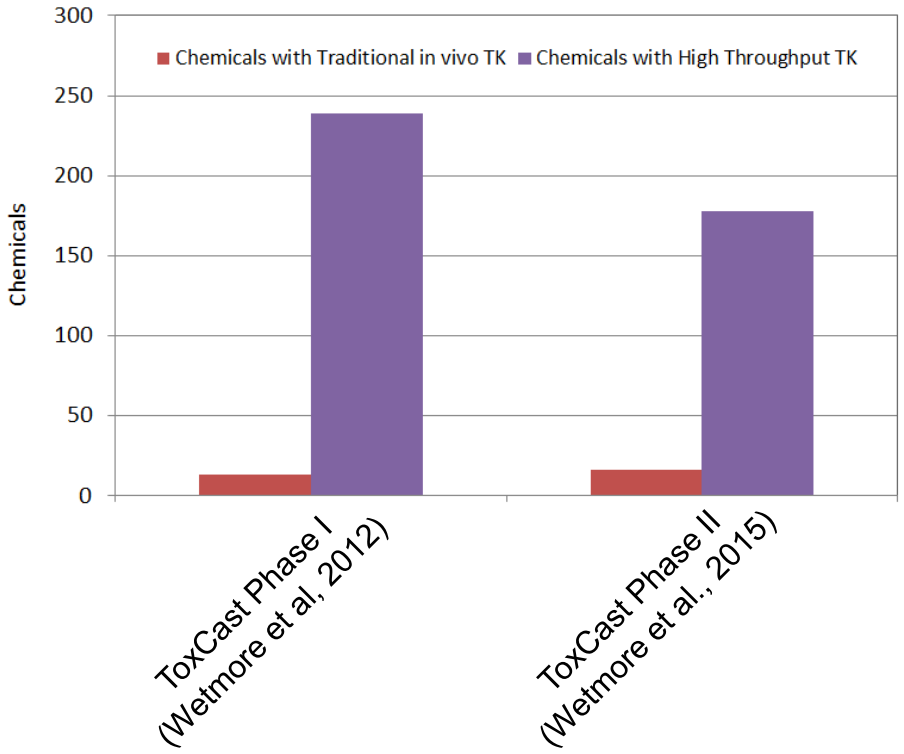
Data from ToxValDB (Dec 2019)

Exposure

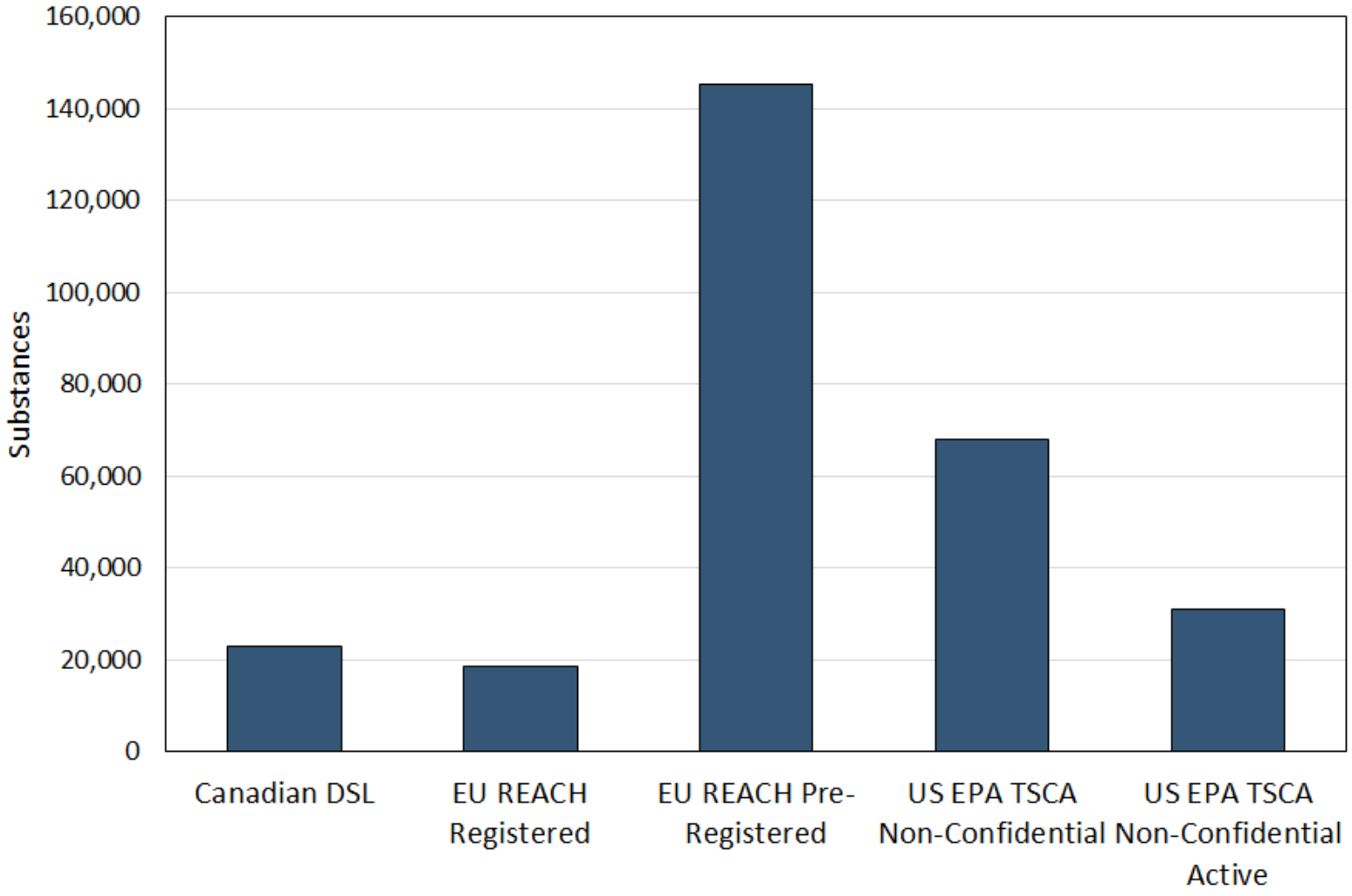


Egeghy et al., Science of the Total Environment, 2012

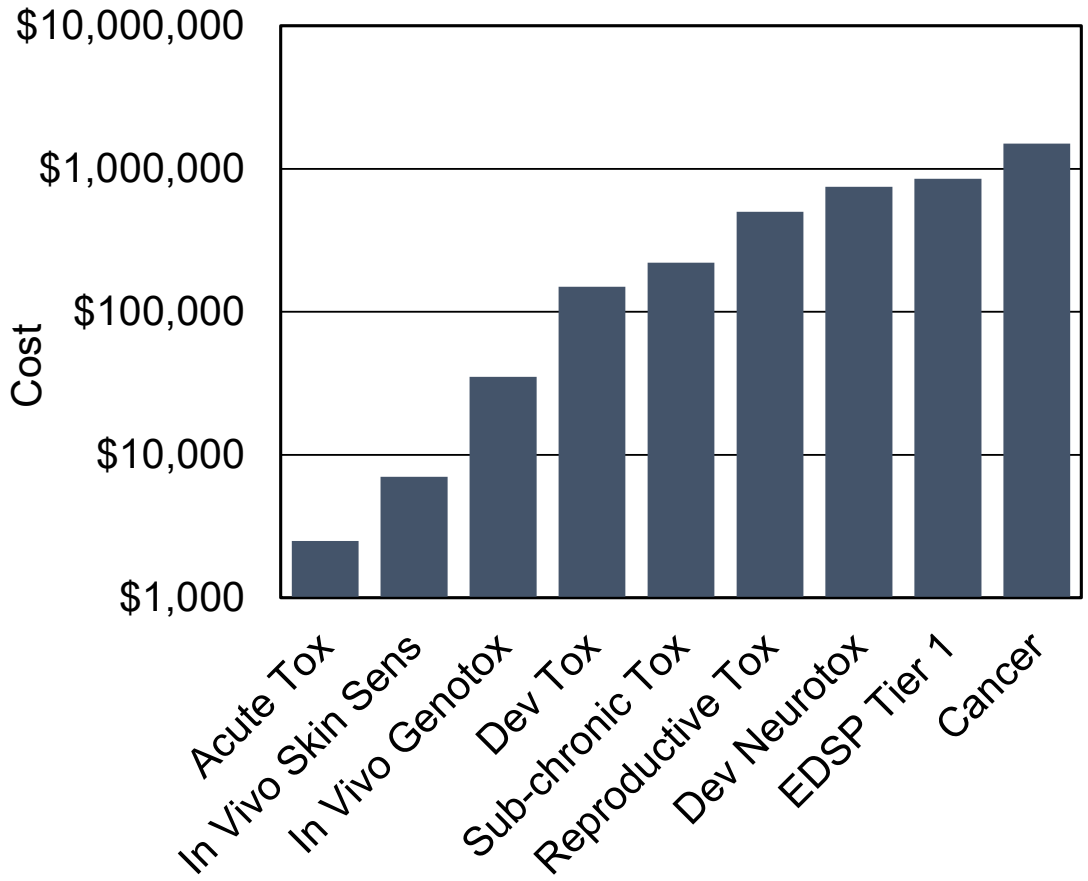
Toxicokinetics

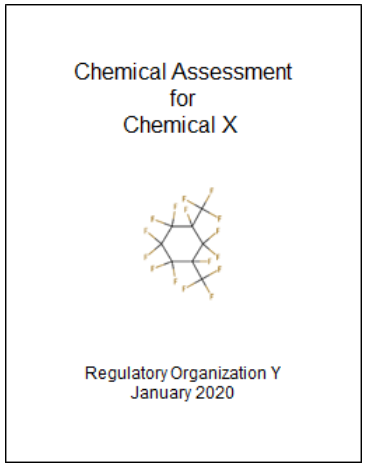


There are Large Numbers of Chemicals on Various National Inventories



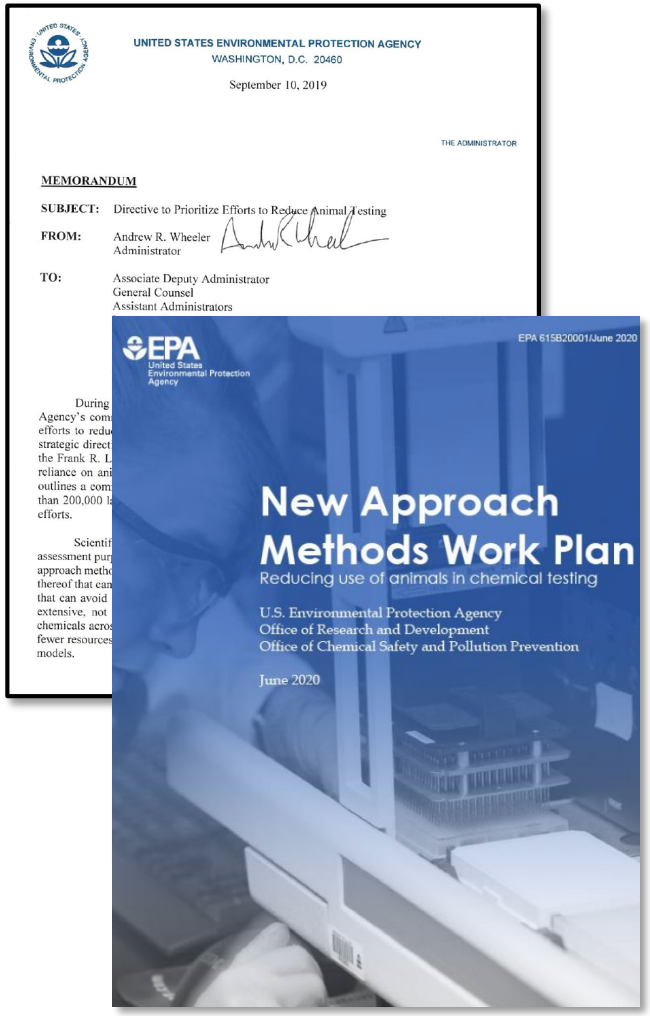
The Costs and Time Associated with Traditional Testing and Assessment are Extensive





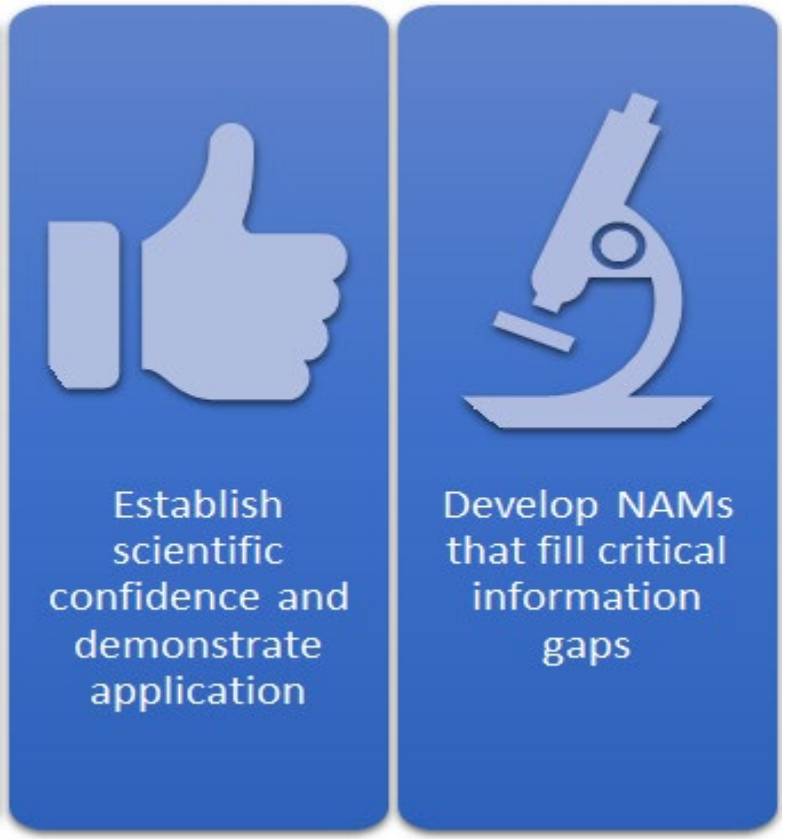
- Time from chemical selection to completion of subchronic and chronic tox studies requires 2+ years
- Time to perform a typical chemical assessment is 4+ years (Krewski et al., 2020)

EPA Intends to Overcome these Challenges while Reducing Animal Testing



- Aims to:
  - Reduce requests for, and funding of, mammalian studies by 30% by 2025
  - Eliminate all mammalian study requests and funding by 2035
  - Come as close as possible to excluding reliance on mammalian studies from its approval process (subject to applicable legal requirements).
  - Achieve reduction in animal use through the development and application of New Approach Methods (NAMs)
- Work Plan includes:
  - Evaluating regulatory flexibility for accommodating NAMs
  - Develop baselines and metrics for assessing progress
  - Establish scientific confidence in NAMs and demonstrate application to regulatory decisions
  - Develop NAMs to address scientific challenges and fill important information gaps
  - Engage and communicate with stakeholders

Multiple Opportunities Exist for Research in the SRP to Contribute



- The EPA NAM work plan explicitly encourages development and evaluation of NAMs by external parties
  - More rapidly closes important information gaps and accelerates movement toward achieving the overall goals.
  - Increase acceptance of new methods
- Superfund research program has a long history in developing methods that can help inform decisions on chemicals and demonstrating application

The Development and Integration of NAMs is a Key Component in Achieving the Goals

OXFORD | SOT Society of Toxicology
www.toxsci.oxfordjournals.org

TOXICOLOGICAL SCIENCES, 169(2), 2019, 317–332
doi: 10.1093/toxsci/kfz058
Advance Access Publication Date: March 5, 2019
Forum

FORUM

The Next Generation Blueprint of Computational Toxicology at the U.S. Environmental Protection Agency

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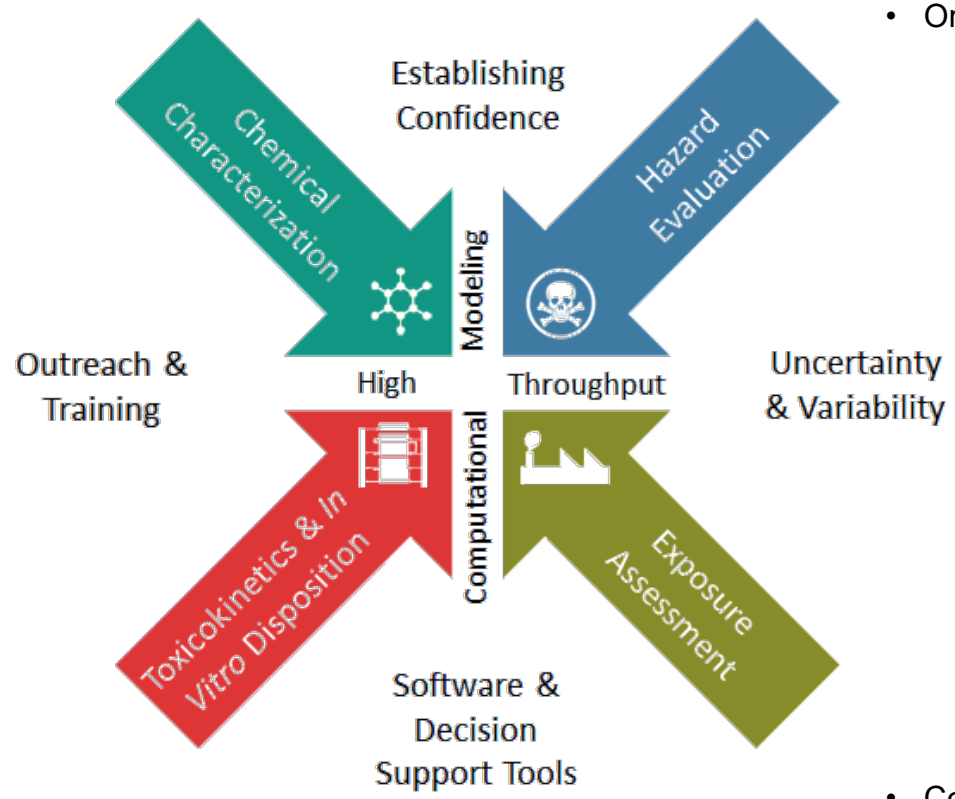
Disclaimer: The U.S. Environmental Protection Agency has provided administrative review and has approved this article for publication. The views expressed in this article are those of the authors and do not necessarily reflect the views of the U.S. Environmental Protection Agency.

ABSTRACT

The U.S. Environmental Protection Agency (EPA) is faced with the challenge of efficiently and credibly evaluating chemical safety often with limited or no available toxicity data. The expanding number of chemicals found in commerce and the environment, coupled with time and resource requirements for traditional toxicity testing and exposure characterization,

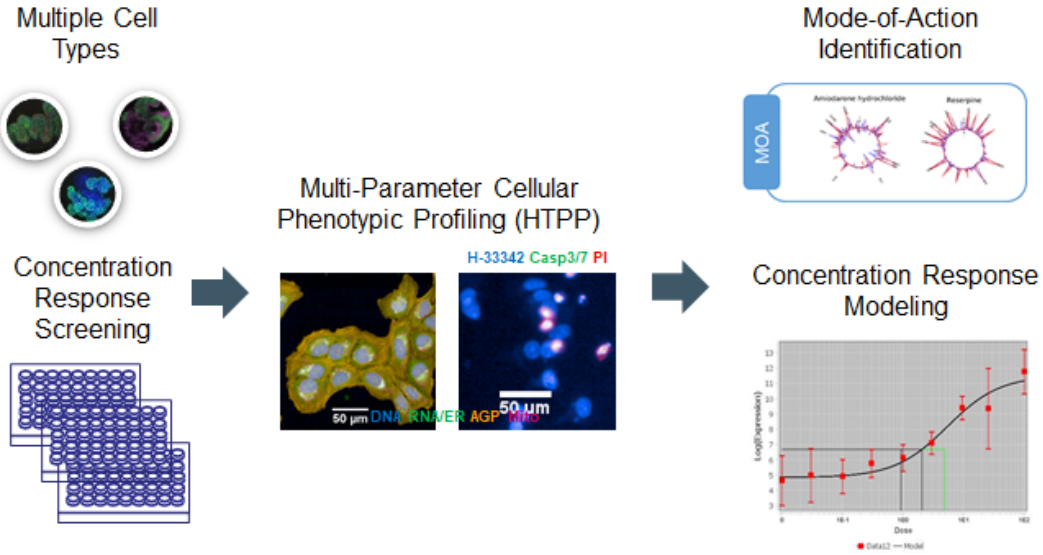
- High-throughput and high-content screening
- Tiered testing
- Organotypic models

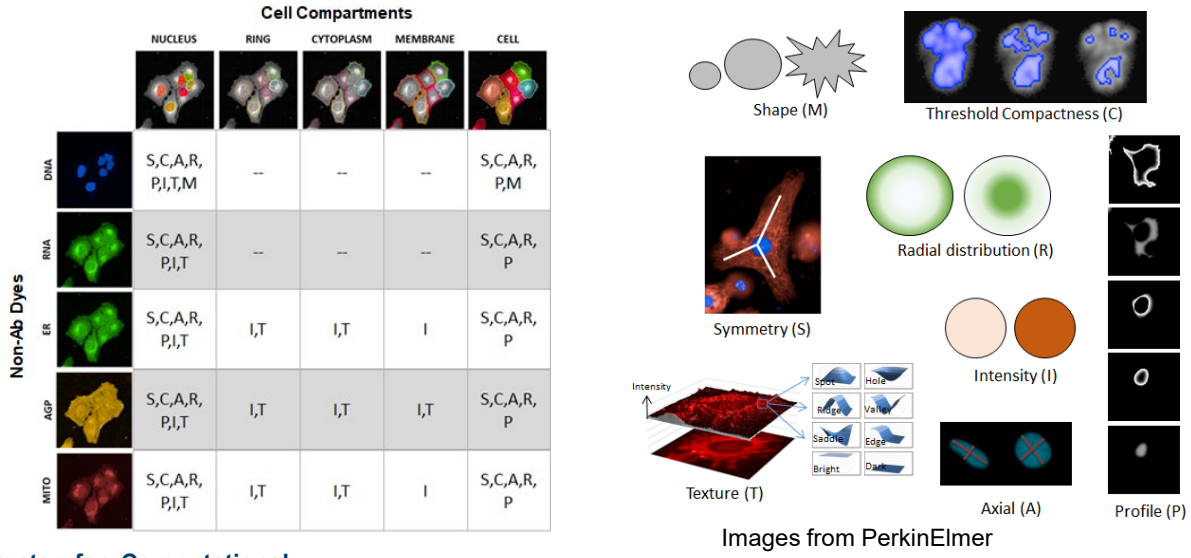


- HTTK assays
- IVIVE methods and models

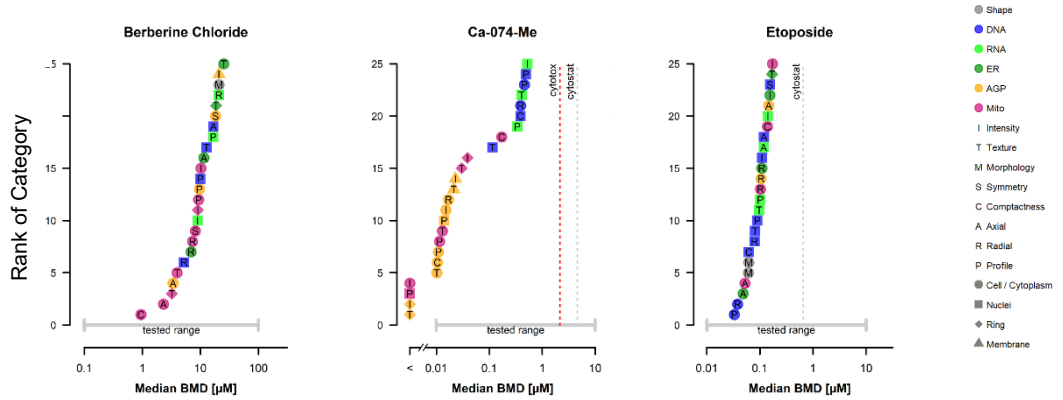
- Consensus exposure models
- NTA/SSA

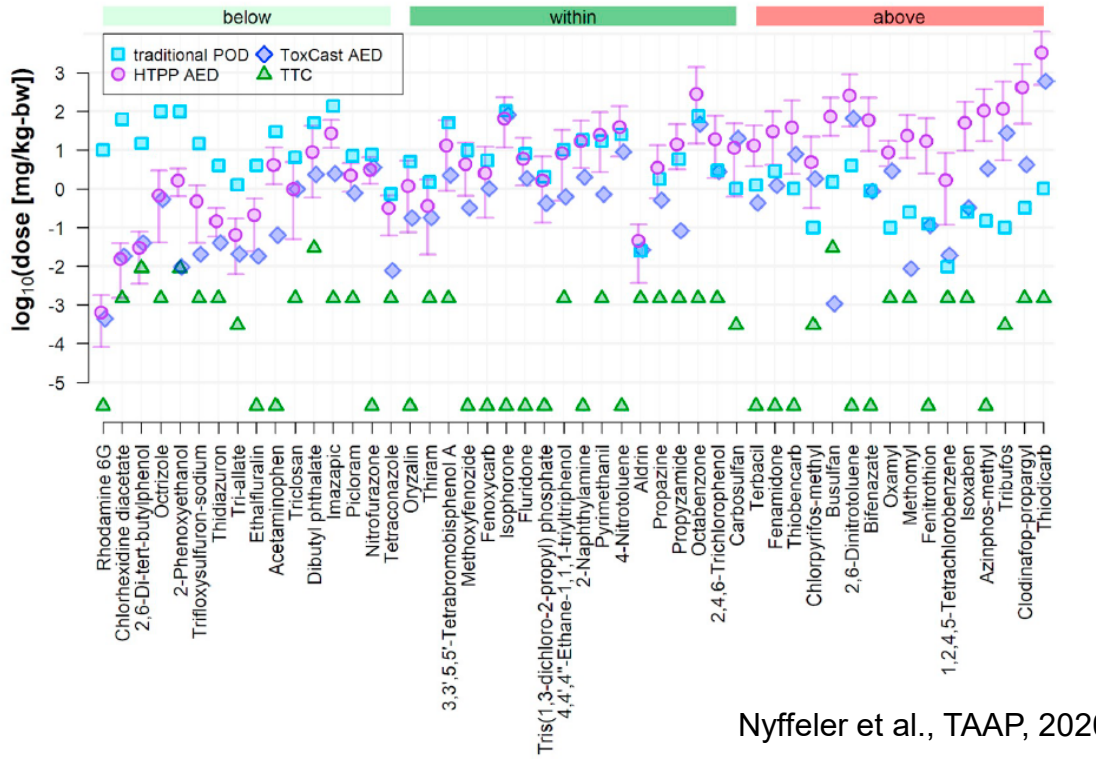
Developing High-Throughput Phenotypic Profiling Methods to Evaluate Effects in Multiple Human Cell Types





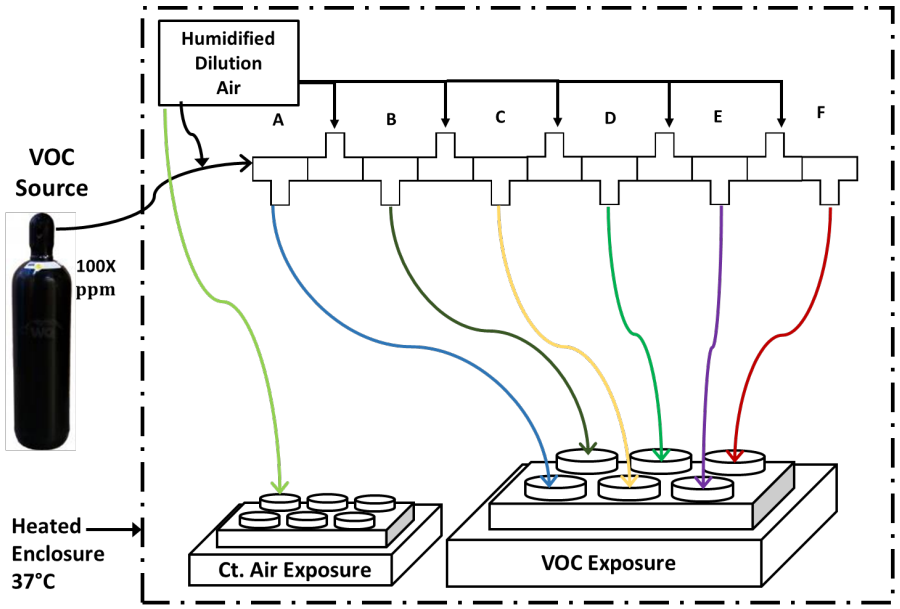
Images from PerkinElmer

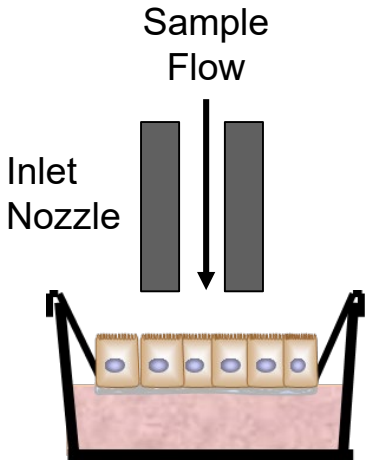




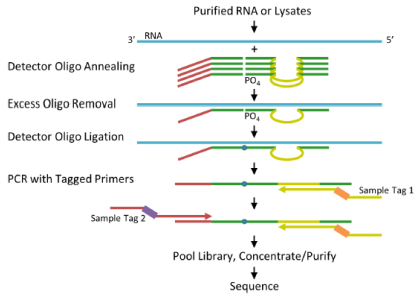
Nyffeler et al., TAAP, 2020

Expanding High-Throughput Transcriptomic Assays to Evaluate Volatile Chemicals

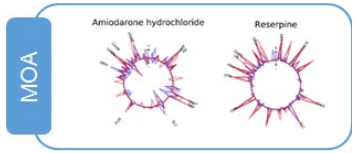




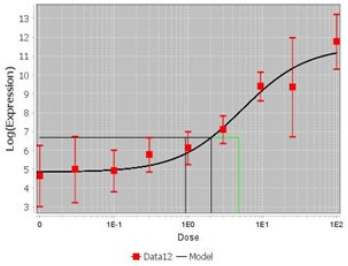
Whole Genome Transcriptomics (HTTr)



Mode-of-Action Identification



Concentration Response Modeling

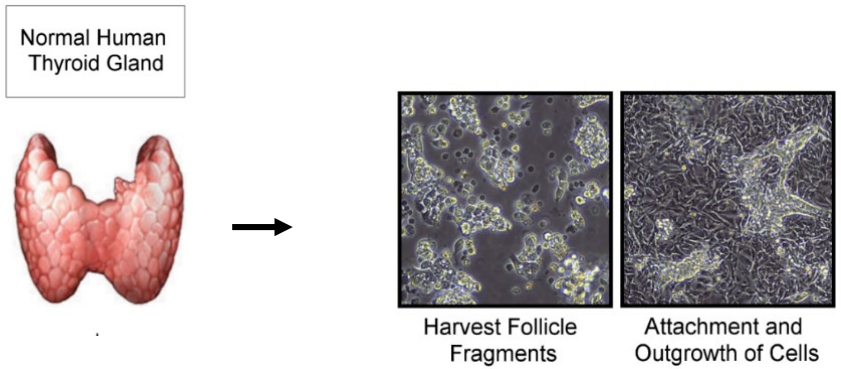


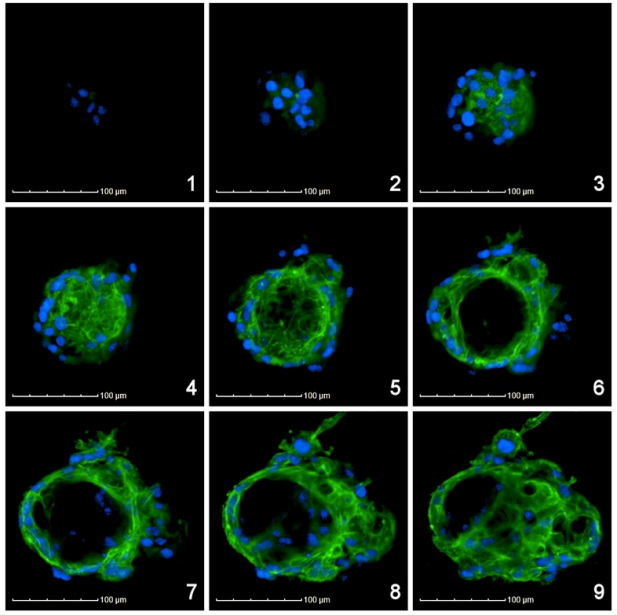
	ACGIH TLV-TWA (ppm)	BEAS-2B HTTr POD (ppm)	HBEC HTTr POD (ppm)
Acrolein	0.1	0.58	--
Formaldehyde	0.3	NA	--
1,3-Butadiene	10	13.98	--
Acetaldehyde	25	NA	--
1-Bromopropane	0.1 *	2.25	NA
Carbon Tetrachloride	10	9.56	NA
Trichloroethylene	50	44.8	28.1
Dichloromethane	100	142.13	266.7

* The ACGIH TLV TWA for 1-bromopropane was updated to 0.1 ppm in 2012. Prior to that the TLV-TWA for 1-bromopropane was 10 ppm.

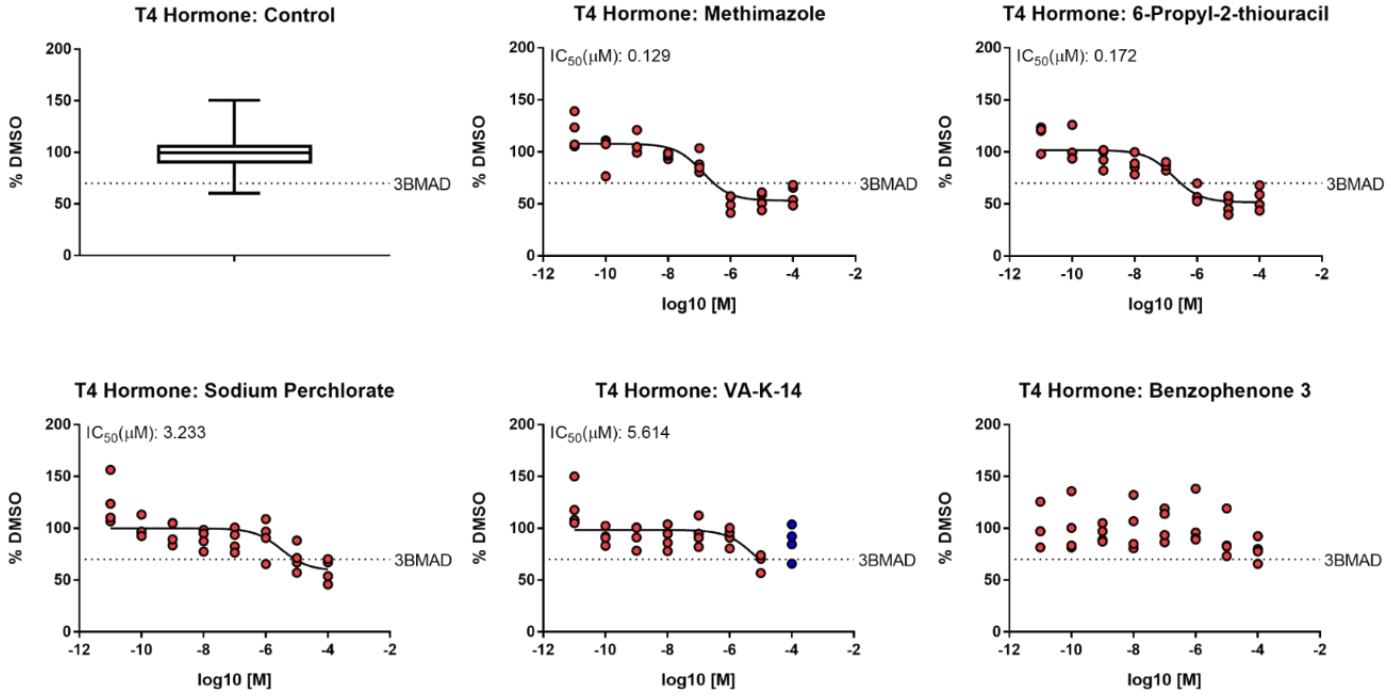
A.Speen (CPHEA), M. Higuchi (CPHEA), and J. Harrill, Unpublished

Developing Organotypic Culture Models to Identify Tissue/Organ Effects



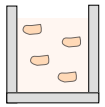


Blue, Hoechst 33342 /DNA
Green, Phalloidin/Actin



Deisenroth *et al.*, *Toxicol Sci*, 2020

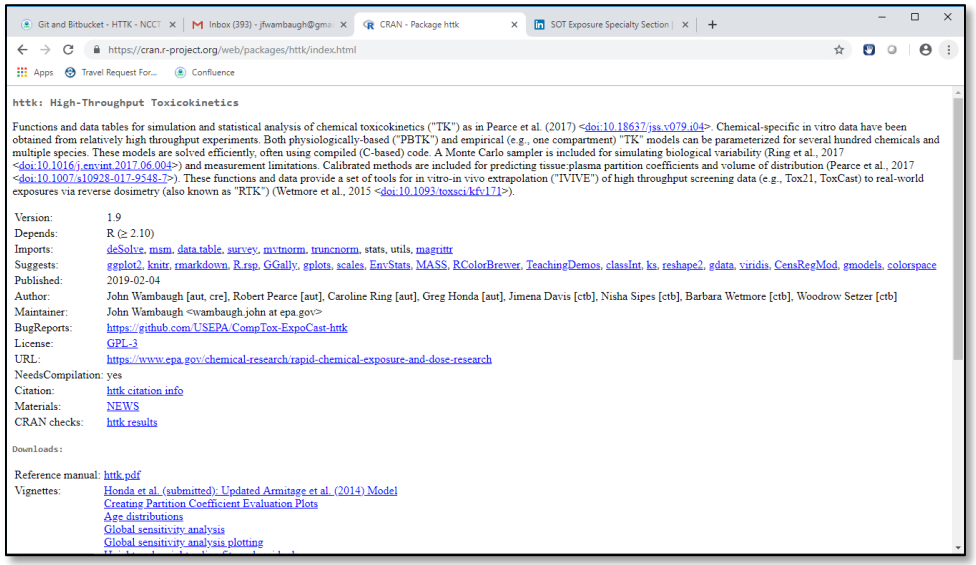
Developing and Improving High-Throughput Toxicokinetic Assays and Modeling Approaches



Liver Metabolism | Tissue Partitioning | Plasma Protein Binding

Population-Based IVIVE Model

Oral Dose Required to Achieve Concentrations Equivalent to *In Vitro* Bioactivity



httk: High-Throughput Toxicokinetics

Functions and data tables for simulation and statistical analysis of chemical toxicokinetics ("TK") as in Pearce et al. (2017) <doi:10.18637/jss.v079.i04>. Chemical-specific in vitro data have been obtained from relatively high throughput experiments. Both physiologically-based ("PBTK") and empirical (e.g., one compartment) "TK" models can be parameterized for several hundred chemicals and multiple species. These models are solved efficiently, often using compiled (C-based) code. A Monte Carlo sampler is included for simulating biological variability (Ring et al., 2017 <doi:10.1016/j.envint.2017.06.004>) and measurement limitations. Calibrated methods are included for predicting tissue:plasma partition coefficients and volume of distribution (Pearce et al., 2017 <doi:10.1007/s10928-017-9548-7>). These functions and data provide a set of tools for in vitro-in vivo extrapolation ("IVIVE") of high throughput screening data (e.g., Tox21, ToxCast) to real-world exposures via reverse dosimetry (also known as "RTK") (Wetmore et al., 2015 <doi:10.1093/toxsci/kfv171>).

Version:	1.9
Depends:	R (≥ 2.10)
Imports:	deSolve, msm, data.table, survey, mvtnorm, truncnorm, stats, utils, magrittr
Suggests:	ggplot2, knitr, rmarkdown, R.rsp, GGally, gplots, scales, EnvStats, MASS, RColorBrewer, TeachingDemos, classInt, ks, reshape2, gdata, viridis, CensRegMod, gmodels, colorspace
Published:	2019-02-04
Author:	John Wambaugh [aut, cre], Robert Pearce [aut], Caroline Ring [aut], Greg Honda [aut], Jimena Davis [ctb], Nisha Sipes [ctb], Barbara Wetmore [ctb], Woodrow Setzer [ctb]
Maintainer:	John Wambaugh <wambaugh.john at epa.gov>
BugReports:	https://github.com/USEPA/CompTox-ExpoCast-httk
License:	GPL-3
URL:	https://www.epa.gov/chemical-research/rapid-chemical-exposure-and-dose-research
NeedsCompilation:	yes
Citation:	httk citation info
Materials:	NEWS
CRAN checks:	httk results

Downloads:

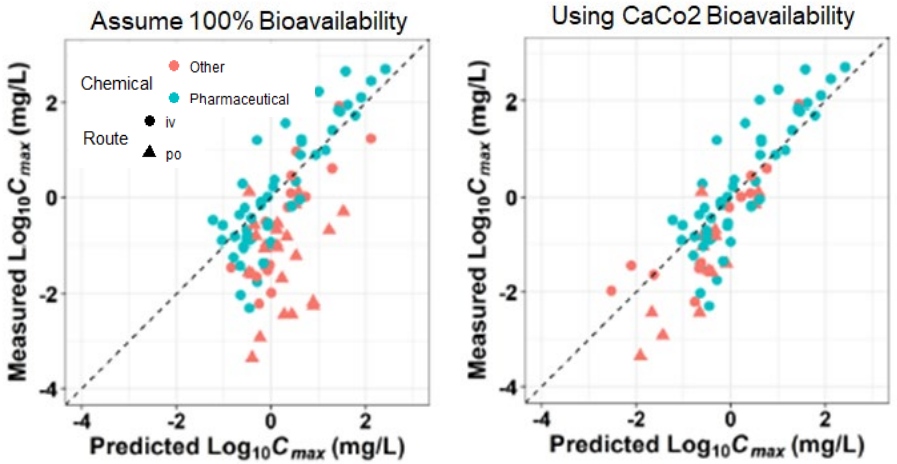
Reference manual: httk.pdf

Vignettes: Honda et al. (submitted): Updated Armitage et al. (2014) Model; Creating Partition Coefficient Evaluation Plots; Age distributions; Global sensitivity analysis; Global sensitivity analysis plotting

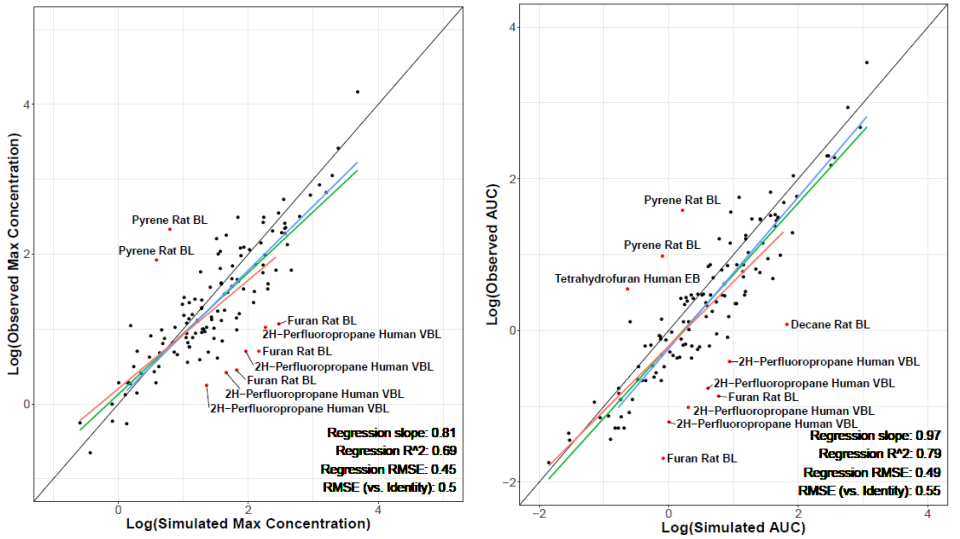
R package "httk"

- Open source, transparent, and peer-reviewed tools and data for **high throughput toxicokinetics (httk)**
- Allows *in vitro-in vivo* extrapolation (IVIVE) and physiologically-based toxicokinetics (PBTK)
- Human-specific data for 987 chemicals
- Allows propagation of uncertainty

Improving Oral PK Models



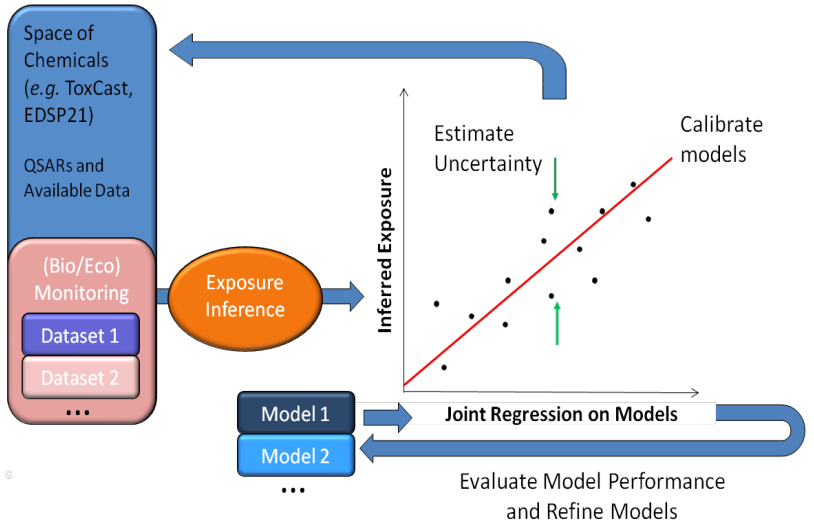
Incorporating Generic Inhalation PBPK Model

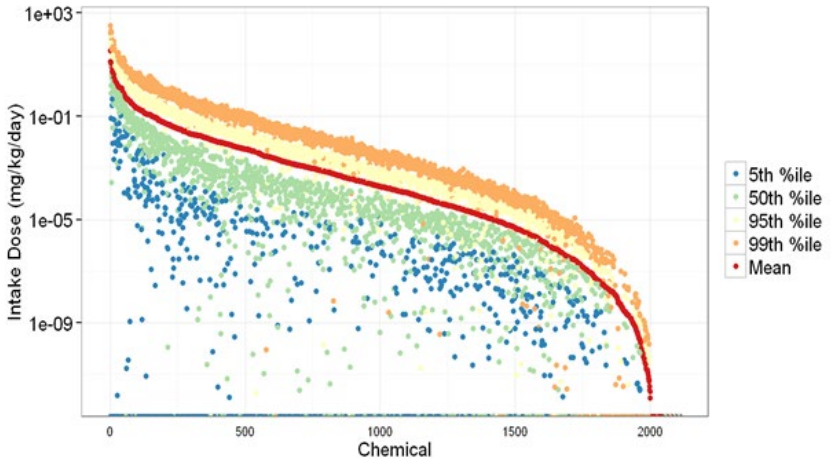


Rotroff *et al., Tox Sci.*, 2010
Wetmore *et al., Tox Sci.,* 2012
Wetmore *et al., Tox Sci.,* 2015
Wambaugh *et al.,Tox Sci.,* 2018
Wambaugh *et al.,Tox Sci.,* 2019
Linakis *et al., J Expo Sci Environ Epidemiol.* 2020
G. Honda and J. Wambaugh, Unpublished

Developing and Improving High-Throughput Exposure Modeling Approaches

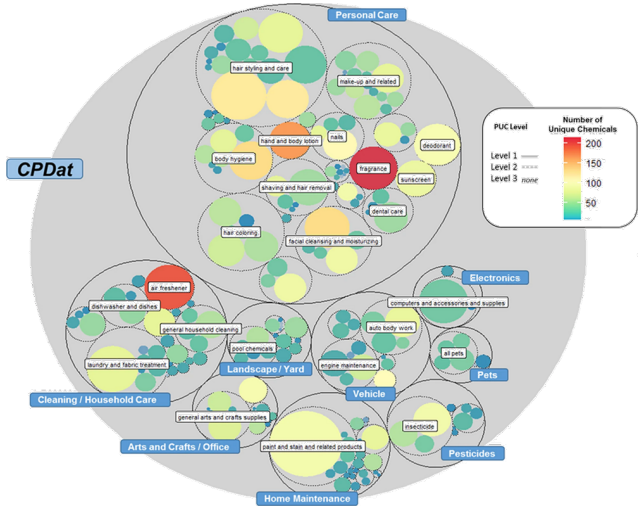
Predictor	Reference(s)	Chemicals Predicted	Pathways
EPA Inventory Update Reporting and Chemical Data Reporting (CDR) (2015)	US EPA (2018)	7856	All
Stockholm Convention of Banned Persistent Organic Pollutants (2017)	Lallas (2001)	248	Far-Field Industrial and Pesticide
EPA Pesticide Reregistration Eligibility Documents (REDs) Exposure Assessments (Through 2015)	Wetmore et al. (2012, 2015)	239	Far-Field Pesticide
United Nations Environment Program and Society for Environmental Toxicology and Chemistry toxicity model (USEtox) Industrial Scenario (2.0)	Rosenbaum et al. (2008)	8167	Far-Field Industrial
USEtox Pesticide Scenario (2.0)	Fantke et al. (2011, 2012, 2016)	940	Far-Field Pesticide
Risk Assessment IDentification And Ranking (RAIDAR) Far-Field (2.02)	Arnot et al. (2008)	8167	Far-Field Pesticide
EPA Stochastic Human Exposure Dose Simulator High Throughput (SHEDS-HT) Near-Field Direct (2017)	Isaacs (2017)	7511	Far-Field Industrial and Pesticide
SHEDS-HT Near-field Indirect (2017)	Isaacs (2017)	1119	Residential
Fugacity-based INdoor Exposure (FINE) (2017)	Bennett et al. (2004), Shin et al. (2012)	645	Residential
RAIDAR-ICE Near-Field (0.803)	Arnot et al., (2014), Zhang et al. (2014)	1221	Residential
USEtox Residential Scenario (2.0)	Jolliet et al. (2015), Huang et al. (2016,2017)	615	Residential
USEtox Dietary Scenario (2.0)	Jolliet et al. (2015), Huang et al. (2016), Ernstoff et al. (2017)	8167	Dietary





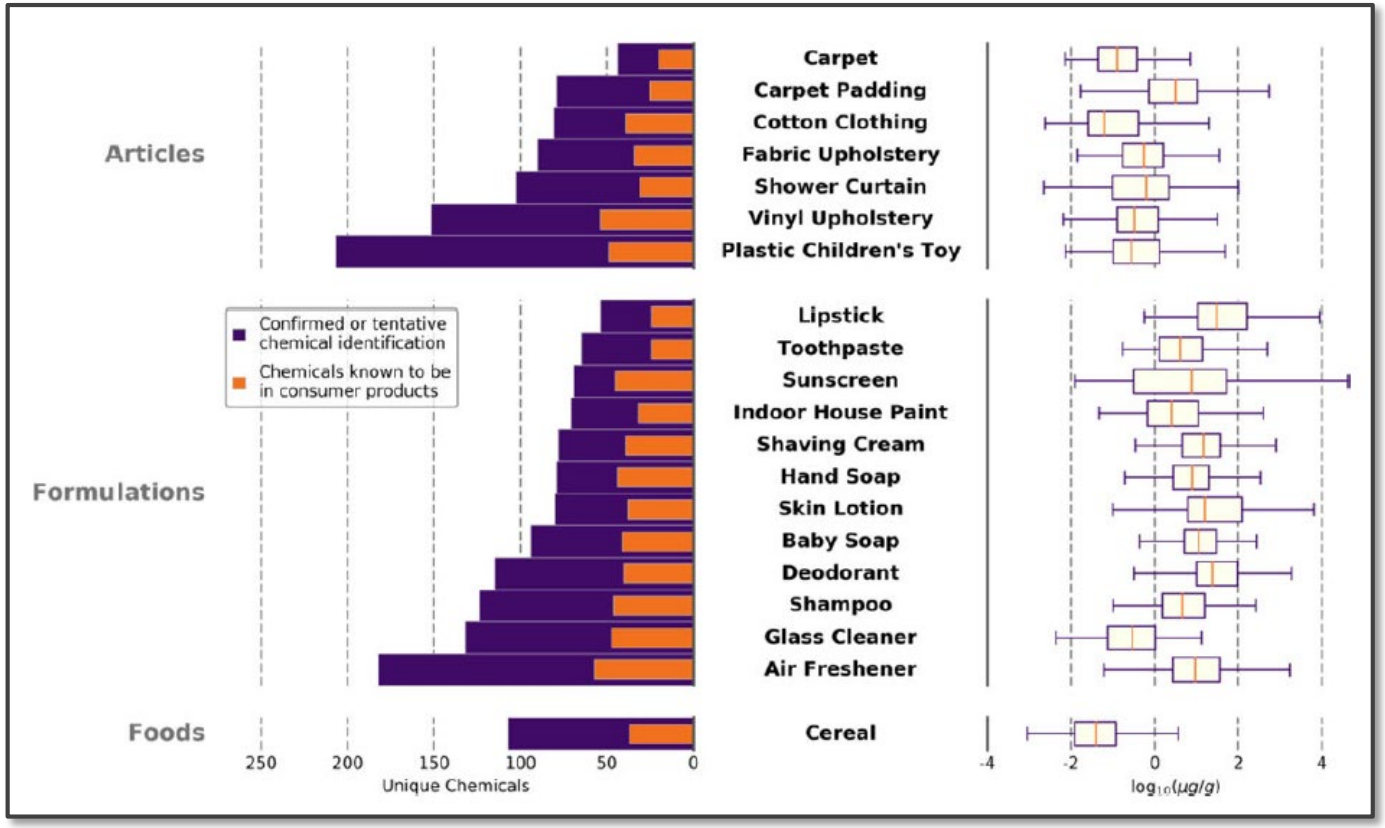
Ring et al., *Environ Sci Technol*. 2019

Data Curation and Non-Targeted Measurement Methods to Parameterize Exposure Models



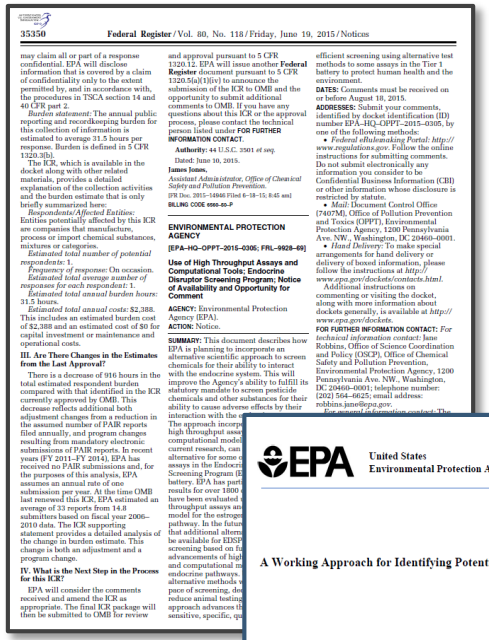
Group Type	Documents	Raw Chemical Records	Curated Chemical Records
Consumer Product Composition	473,271	3,738,350	1,791,250
Functional use	33,770	34,680	11,946
CPCat Categories (Public chemical lists)	2,088	117,231	68,133
Occupational exposure	1,304	4,825	1078
Literature monitoring	1,175	966	In process
Habits and practices (Consumer Product Use Patterns)	202	NA	NA

Dionisio et al., *Sci Data*. 2018



Phillips et al., *Env. Sci. Tech*. 2018

NAM-based Hazard, Toxicokinetic, and Exposure Methods are Beginning to Be Used for Prioritization and Screening-Level Assessments


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. 2015–14948 Filed 6–18–15; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPPT–2015–0305; FRL–9928–69]

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

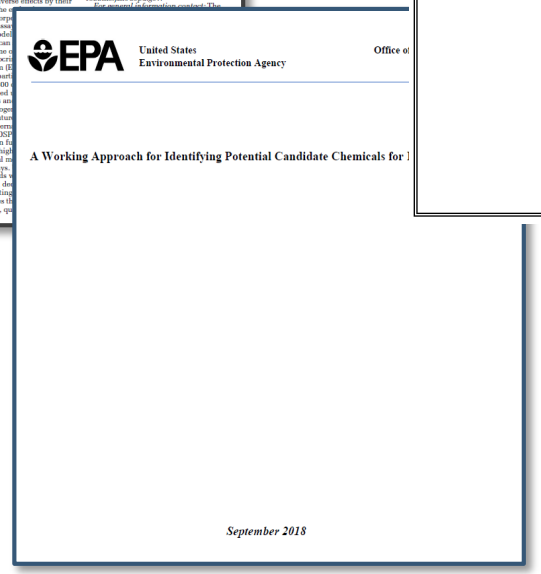
FOR FURTHER INFORMATION CONTACT: *For technical information contact:* Jane Robbins, Office of Science Coordination and Policy (OSCP), Office of Chemical Safety and Pollution Prevention, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001; telephone number: (202) 564–6625;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

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

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.*

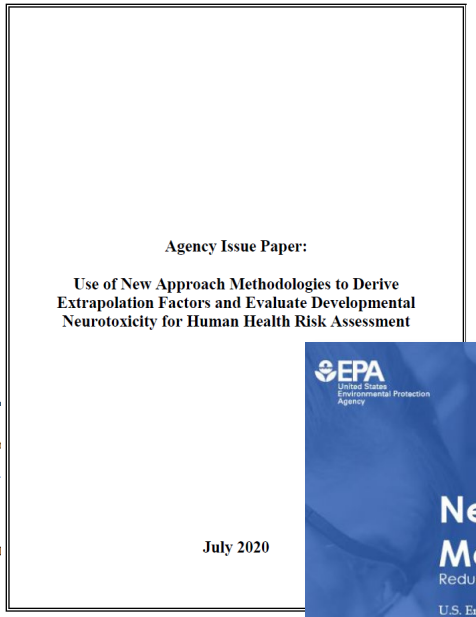
DATES: Comments must be received on or before August 18, 2015.


EPA United States Environmental Protection Agency

Office o

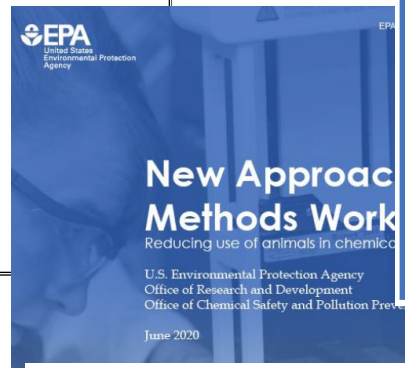
A Working Approach for Identifying Potential Candidate Chemicals for

September 2018


Agency Issue Paper:

Use of New Approach Methodologies to Derive Extrapolation Factors and Evaluate Developmental Neurotoxicity for Human Health Risk Assessment

July 2020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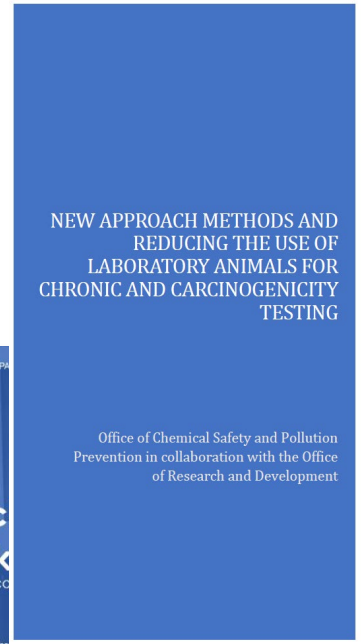
New Approac
Methods Work
Reducing use of animals in chemica

U.S. Environmental Protection Agency
Office of Research and Development
Office of Chemical Safety and Pollution Prev

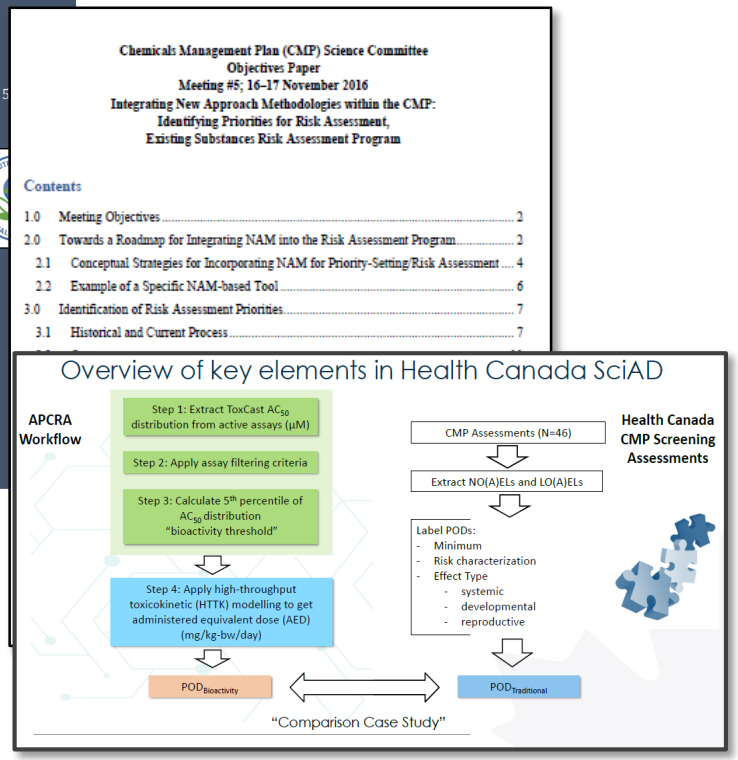
June 2020


NEW APPROACH METHODS AND REDUCING THE USE OF LABORATORY ANIMALS FOR CHRONIC AND CARCINOGENICITY TESTING

Office of Chemical Safety and Pollution Prevention in collaboration with the Office of Research and Development

Table 2. Initial Selection of On-Going EPA Case Studies for Potential Incorporation into Work Plan

Title	Description
Refining Inhalation Risk Assessment with NAMs	Refine inhalation risk assessment for point of contact toxicity using a three-dimensional *in vitro* test system of human respiratory tissues to derive a point of departure, in conjunction with computational fluid dynamic modeling.
Integrating *In Vitro* Assay and Toxicokinetic Data in Read Across	Use of *in vitro* toxicity and toxicokinetic testing to refine/support read across categories for per- and polyfluoroalkyl substances (PFAS).
Application of *In Vitro* Bioactivity for Screening-Level Risk Decisions	Use of bioactivity from *in vitro* assays and *in vitro* toxicokinetics to prioritize chemical contaminants in biosolids.
Application of NAMs for Chronic and Carcinogenicity Testing	Integration of NAMs to identify chronic toxicity and non-genotoxic carcinogenicity modes-of-action and quantitative points-of-departure for regulatory decisions


June 5

Chemicals Management Plan (CMP) Science Committee
Objectives Paper
Meeting #5; 16–17 November 2016
Integrating New Approach Methodologies within the CMP:
Identifying Priorities for Risk Assessment,
Existing Substances Risk Assessment Program

Contents

https://www.epa.gov/sites/production/files/2020-01/documents/6_508_tara_barton-maclaren_nams_2019.pdf

EPA United States Environmental Protection Agency

Take Home Messages…

- EPA makes a broad range of decisions on chemicals that require different data and levels of certainty
- Most chemicals EPA regulates have limited data on hazard, toxicokinetics, exposure
- EPA is committed to filling data gaps and evaluating chemicals for potential human health and environmental risks while reducing animal testing
- Research on NAMs by both EPA and external groups will play an important role in achieving the Agency's goals
- Use of NAMs in regulatory decisions has increased rapidly over the last 5 years

EPA United States Environmental Protection Agency

Questions?