United States Environmental Protection Agency

EPA Tools and Resources Webinar CompTox Dashboard:

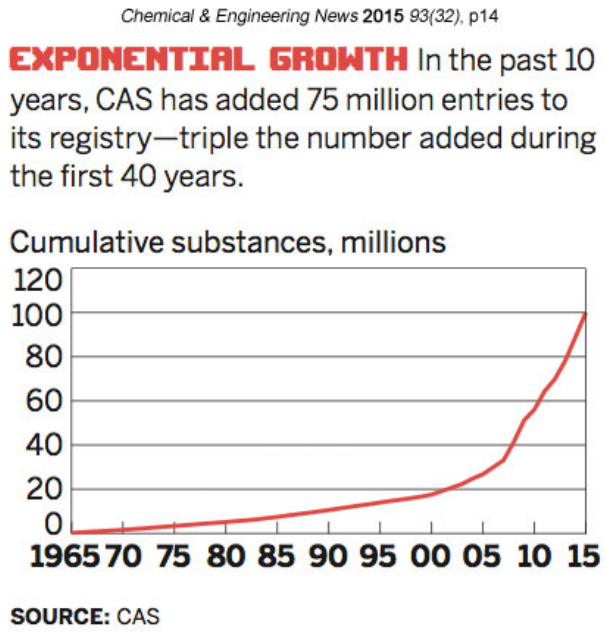
Data and Tools to Support Chemical and Environmental Risk Assessment

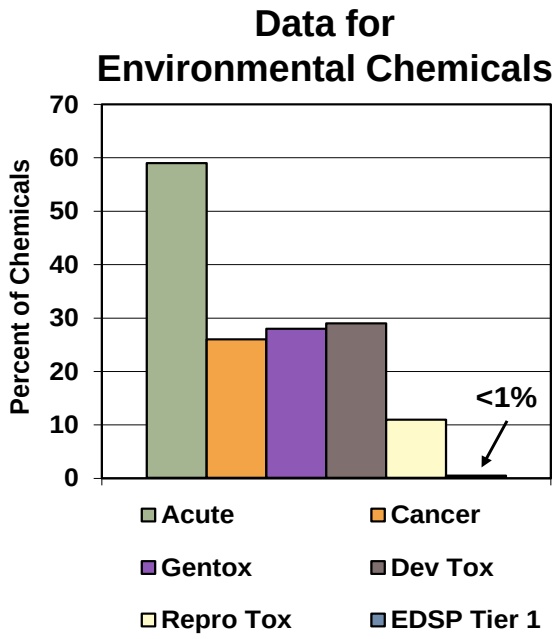
Reeder Sams, PhD
National Center for Computational Toxicology
US EPA Office of Research and Development

August 22, 2018

Problem: Too Many Chemicals, too Few Resources

- **Timely characterization of human and ecological risk posed by thousands of existing and emerging chemicals is a critical challenge to protect public health and the environment**
  - Significant growth in the number of substances and chemicals / and the associated data
  - Nearly 60% of chemicals on various EPA lists have acute toxicity data, 30% have data on other types of toxicity



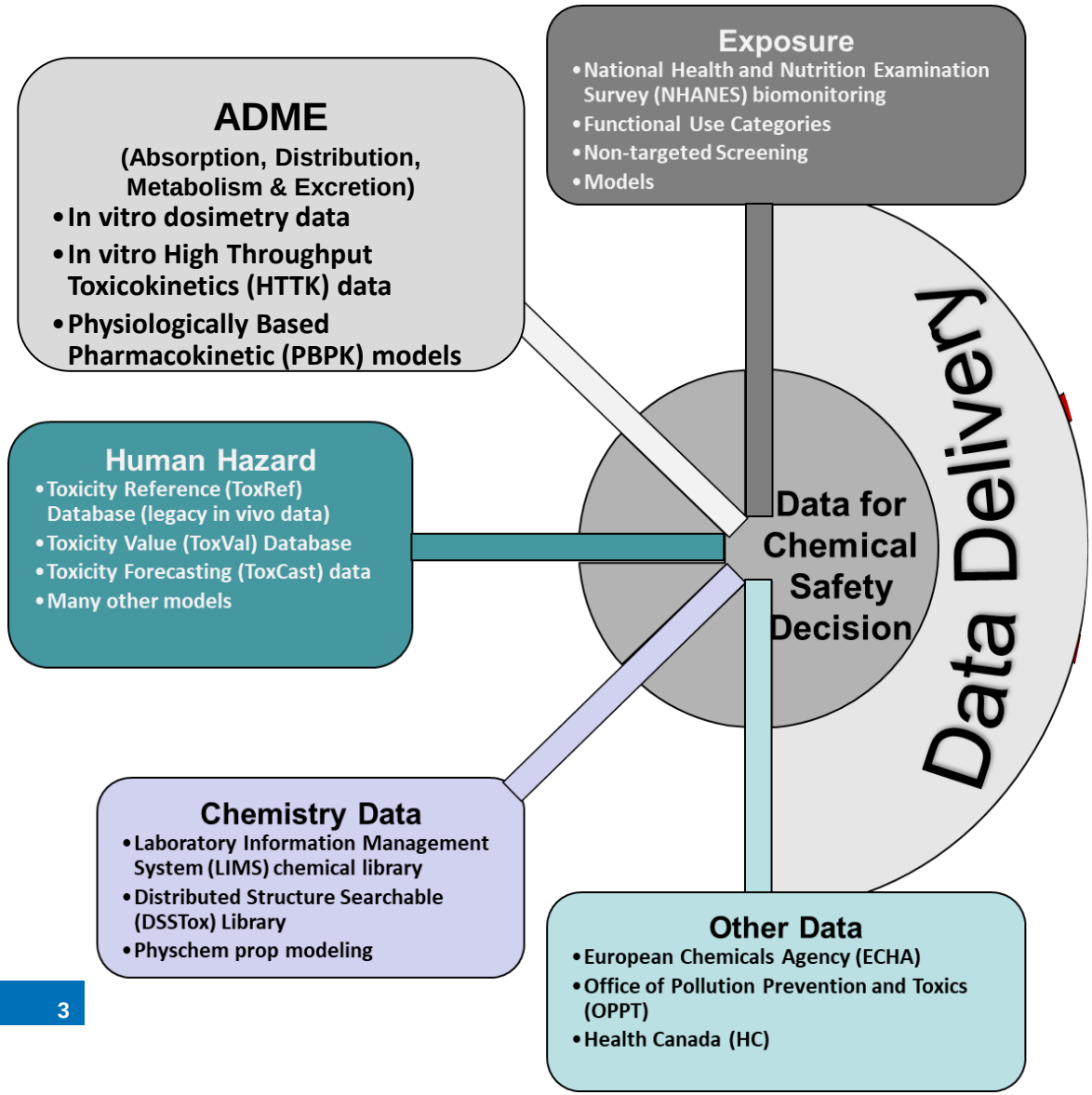


Modified from Judson *et al.*, EHP 2010

Approach

- **Develop a "one-stop-shop" for data as an integration node for environmental chemical data to support EPA and partner decision making:**
  - Centralized location for relevant chemical safety data:
    - Chemistry, exposure, hazard, dosimetry
  - Combination of existing data and predictive models
  - Publicly accessible, periodically updated, curated
- **Ease of access to data results in efficiency and accelerates chemical risk assessment**

Approach


Exposure
• National Health and Nutrition Examination Survey (NHANES) biomonitoring
• Functional Use Categories
• Non-targeted Screening
• Models
ADME
(Absorption, Distribution, Metabolism & Excretion)
• In vitro dosimetry data
• In vitro High Throughput Toxicokinetics (HTTK) data
• Physiologically Based Pharmacokinetic (PBPK) models
Human Hazard
• Toxicity Reference (ToxRef) Database (legacy in vivo data)
• Toxicity Value (ToxVal) Database
• Toxicity Forecasting (ToxCast) data
• Many other models
Data for Chemical Safety Decision
Data Delivery
Chemistry Data
• Laboratory Information Management System (LIMS) chemical library
• Distributed Structure Searchable (DSSTox) Library
• Physchem prop modeling
Other Data
• European Chemicals Agency (ECHA)
• Office of Pollution Prevention and Toxics (OPPT)
• Health Canada (HC)

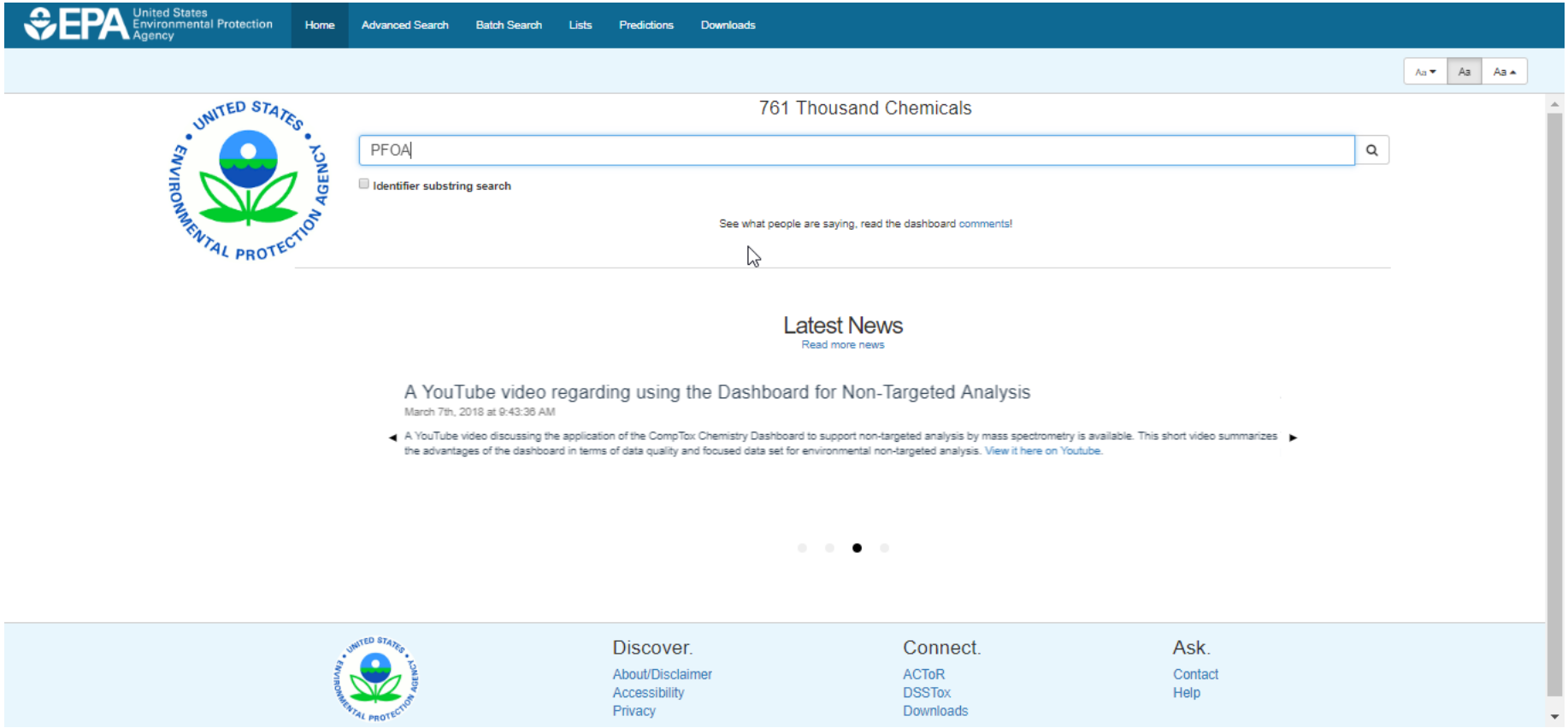
Results: EPA's CompTox Dashboard

United States Environmental Protection Agency

A publicly accessible website delivering:

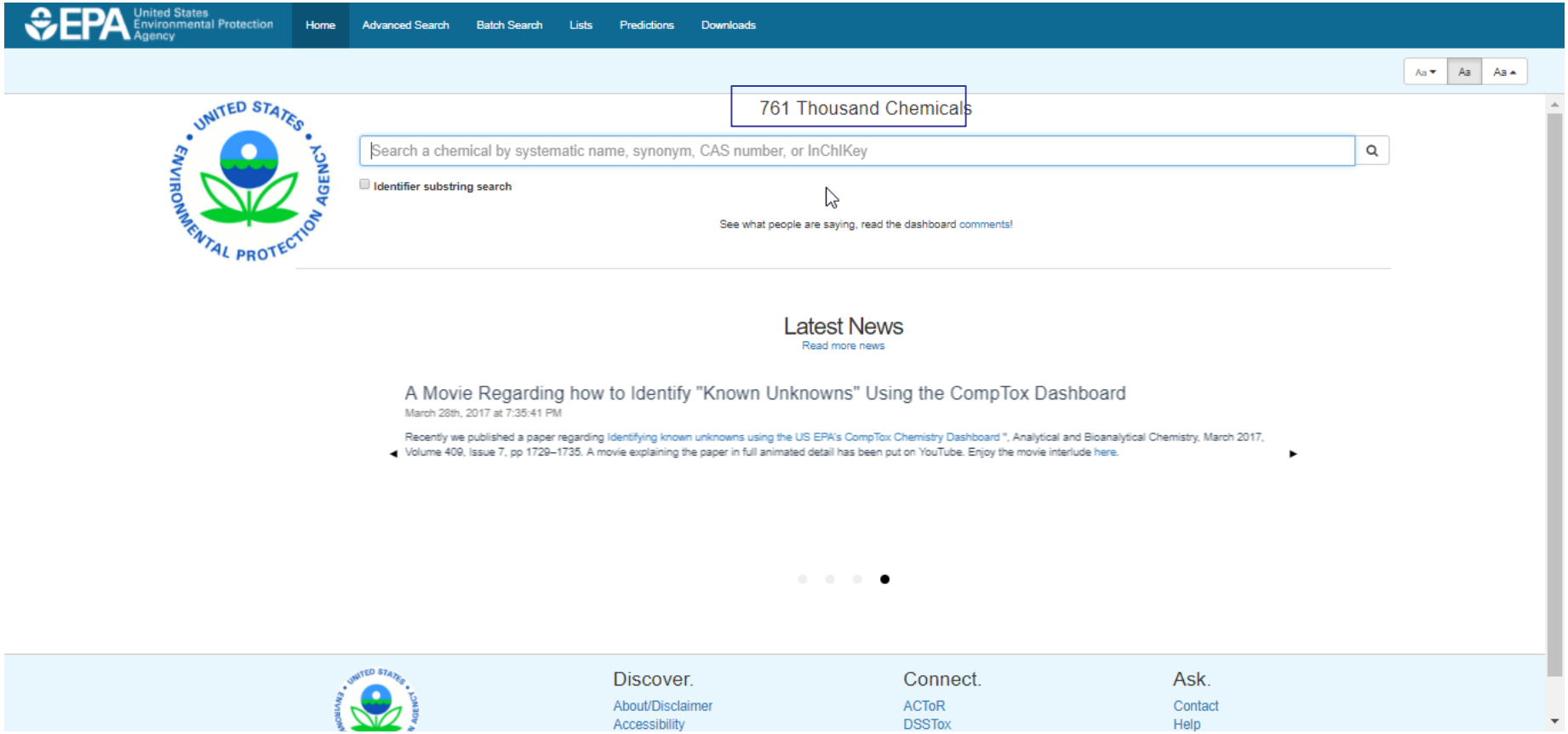
- ~760,000 chemicals with related property data
- Experimental and predicted physicochemical property data
- Integration to "biological assay data" for 1000's of chemicals
- Information regarding consumer products containing chemicals
- Generalized Read-Across (GenRA) module
- Links to other agency websites and public data resources
- "Literature" searches for chemicals using public resources
- "Batch searching" for thousands of chemicals
- Downloadable Open Data for reuse and repurposing
- Many features (only highlighting a few)
- Access to multiple tools (direct data interpolation and predictive) for multiple disciplines

EPA CompTox Dashboard: Live Demo

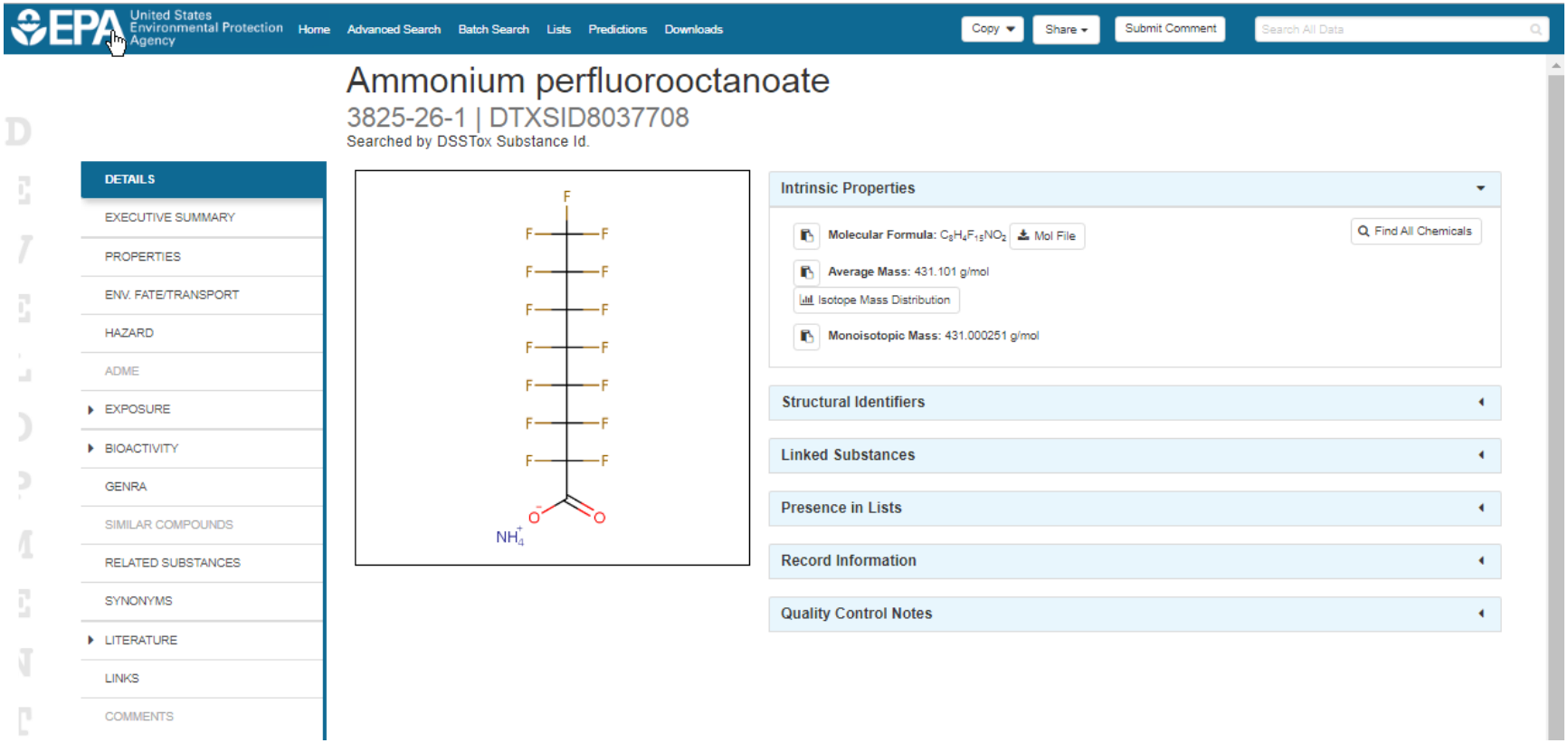


CompTox Dashboard

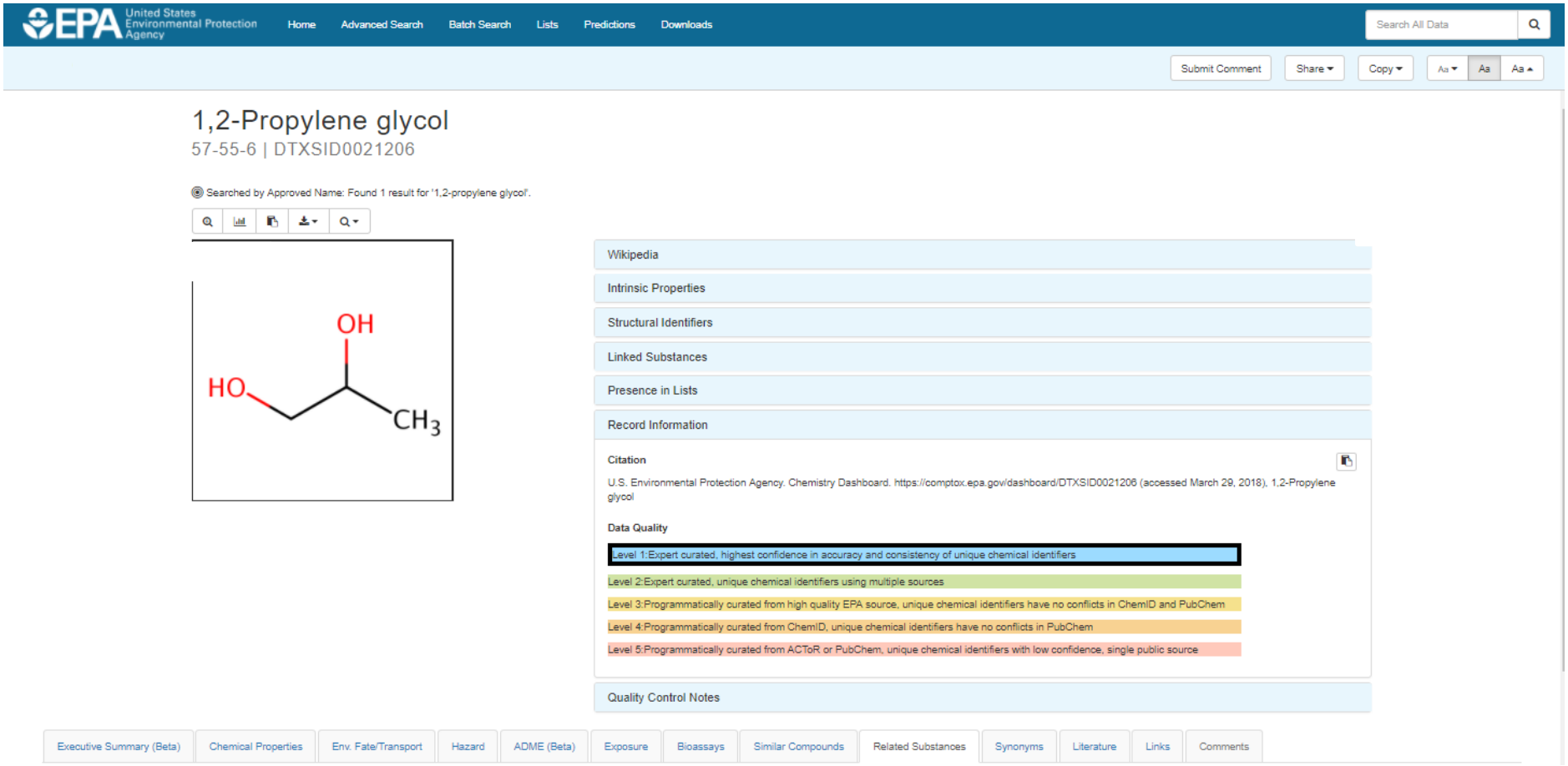
https://comptox.epa.gov/dashboard



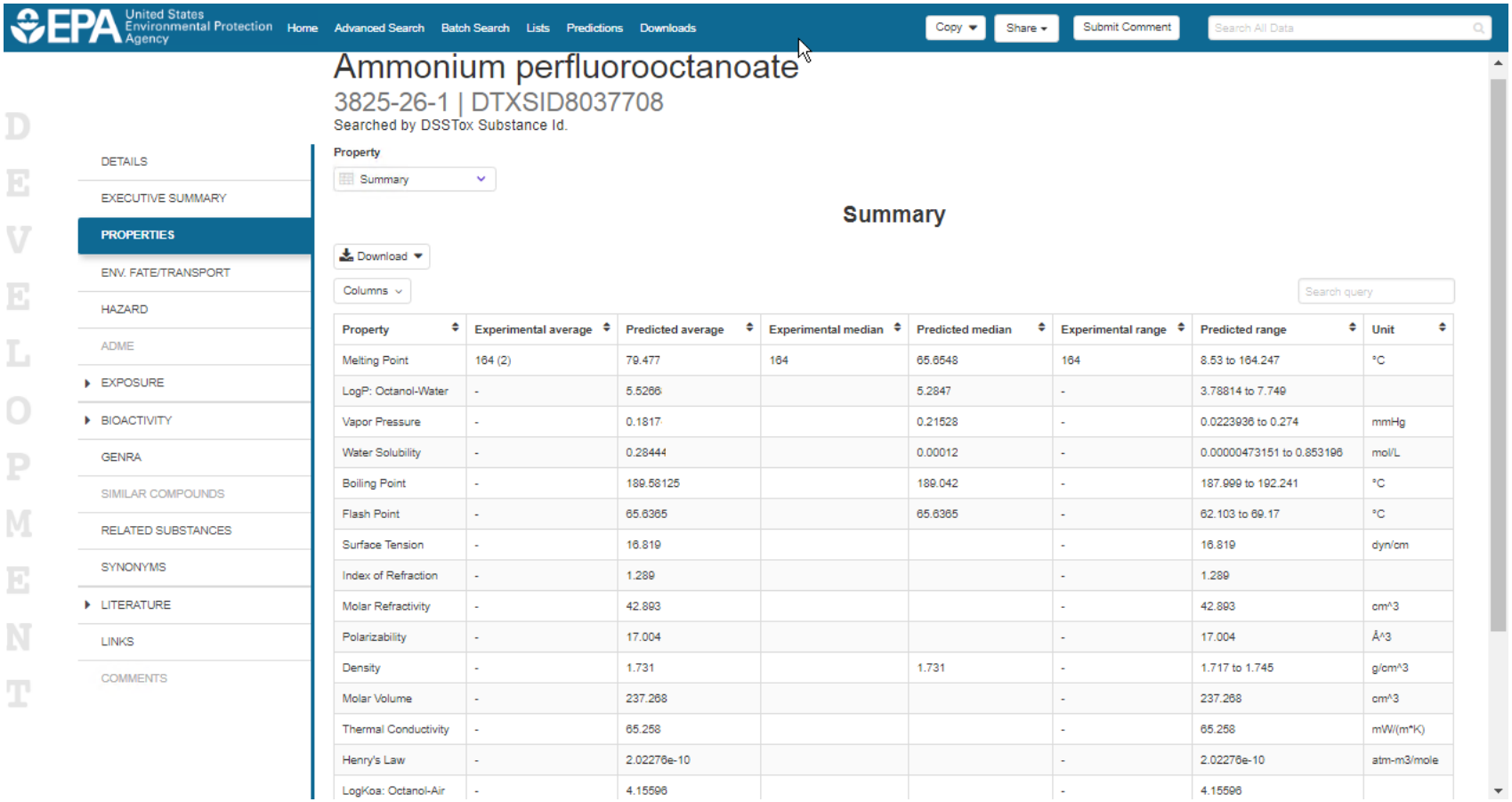
Detailed Chemical Pages



Data Quality

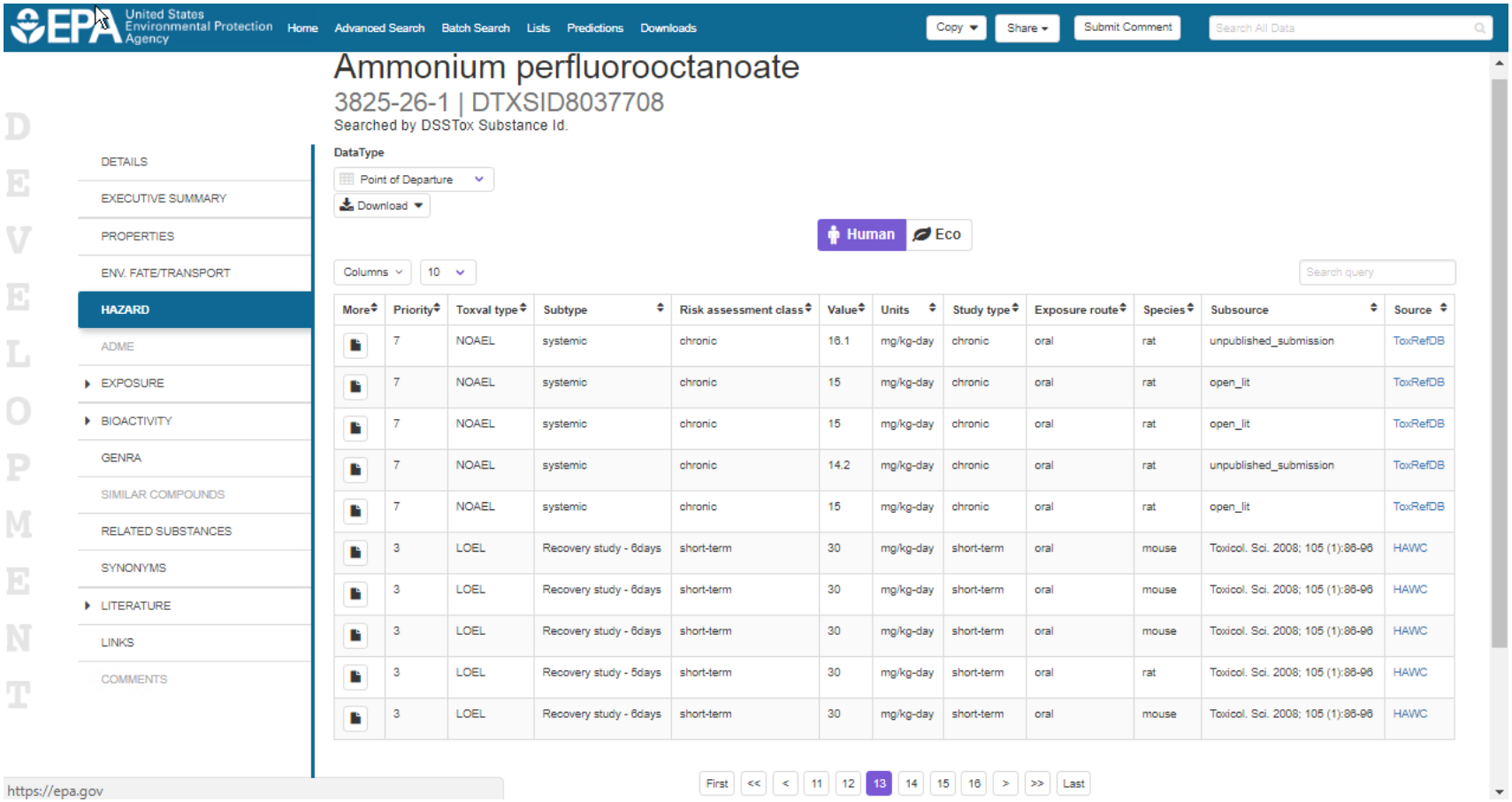


Properties, Fate and Transport



Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Melting Point	164 (2)	79.477	164	65.6548	164	8.53 to 164.247	°C
LogP: Octanol-Water	-	5.5266		5.2847	-	3.78814 to 7.749	
Vapor Pressure	-	0.1817		0.21528	-	0.0223936 to 0.274	mmHg
Water Solubility	-	0.28444		0.00012	-	0.00000473151 to 0.853196	mol/L
Boiling Point	-	189.58125		189.042	-	187.999 to 192.241	°C
Flash Point	-	65.6365		65.6365	-	62.103 to 69.17	°C
Surface Tension	-	16.819			-	16.819	dyn/cm
Index of Refraction	-	1.289			-	1.289	
Molar Refractivity	-	42.893			-	42.893	cm^3
Polarizability	-	17.004			-	17.004	Å^3
Density	-	1.731		1.731	-	1.717 to 1.745	g/cm^3
Molar Volume	-	237.268			-	237.268	cm^3
Thermal Conductivity	-	65.258			-	65.258	mW/(m*K)
Henry's Law	-	2.02276e-10			-	2.02276e-10	atm-m3/mole
LogKoa: Octanol-Air	-	4.15596			-	4.15596	

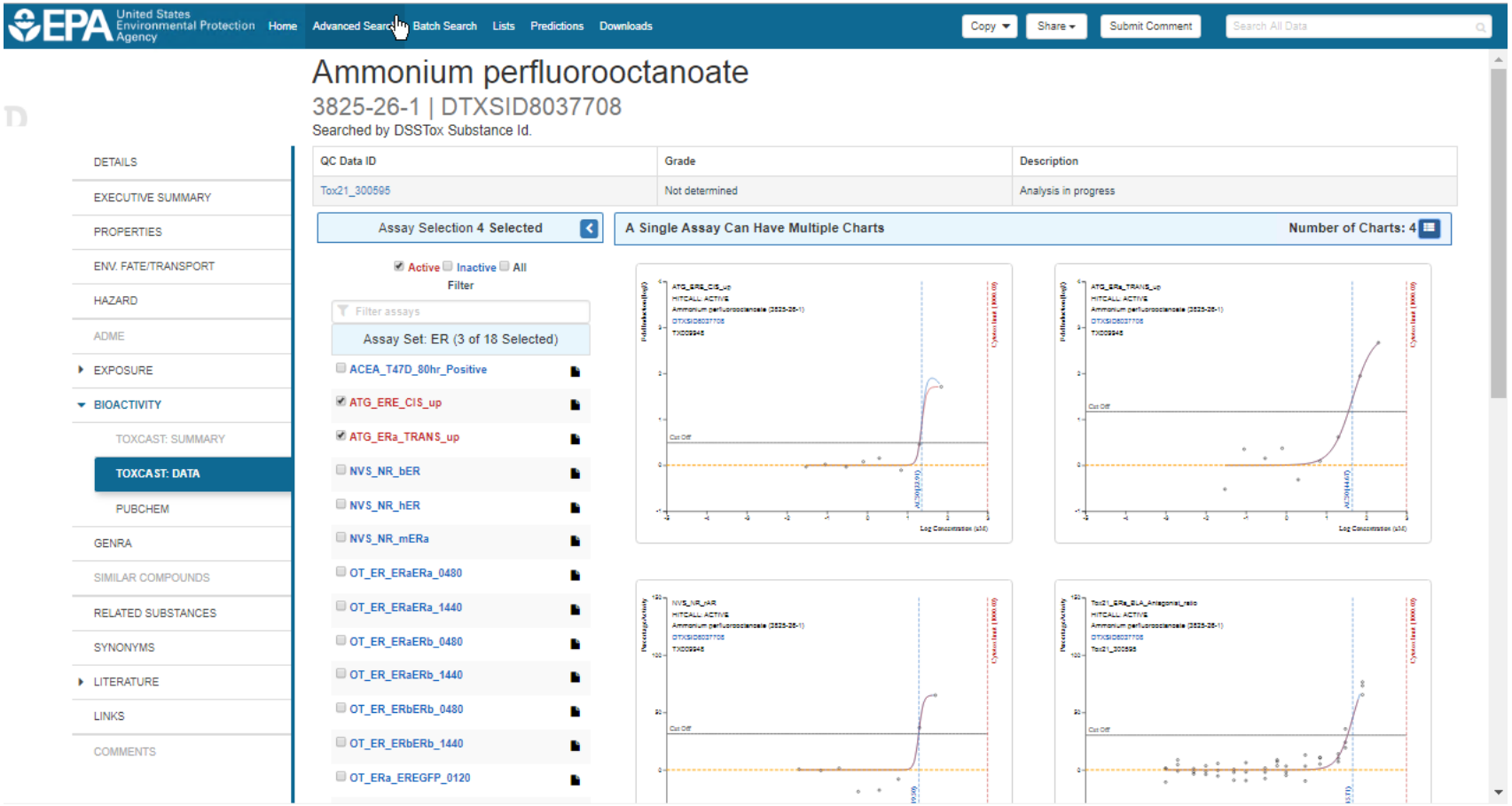
Chemical Hazard Data



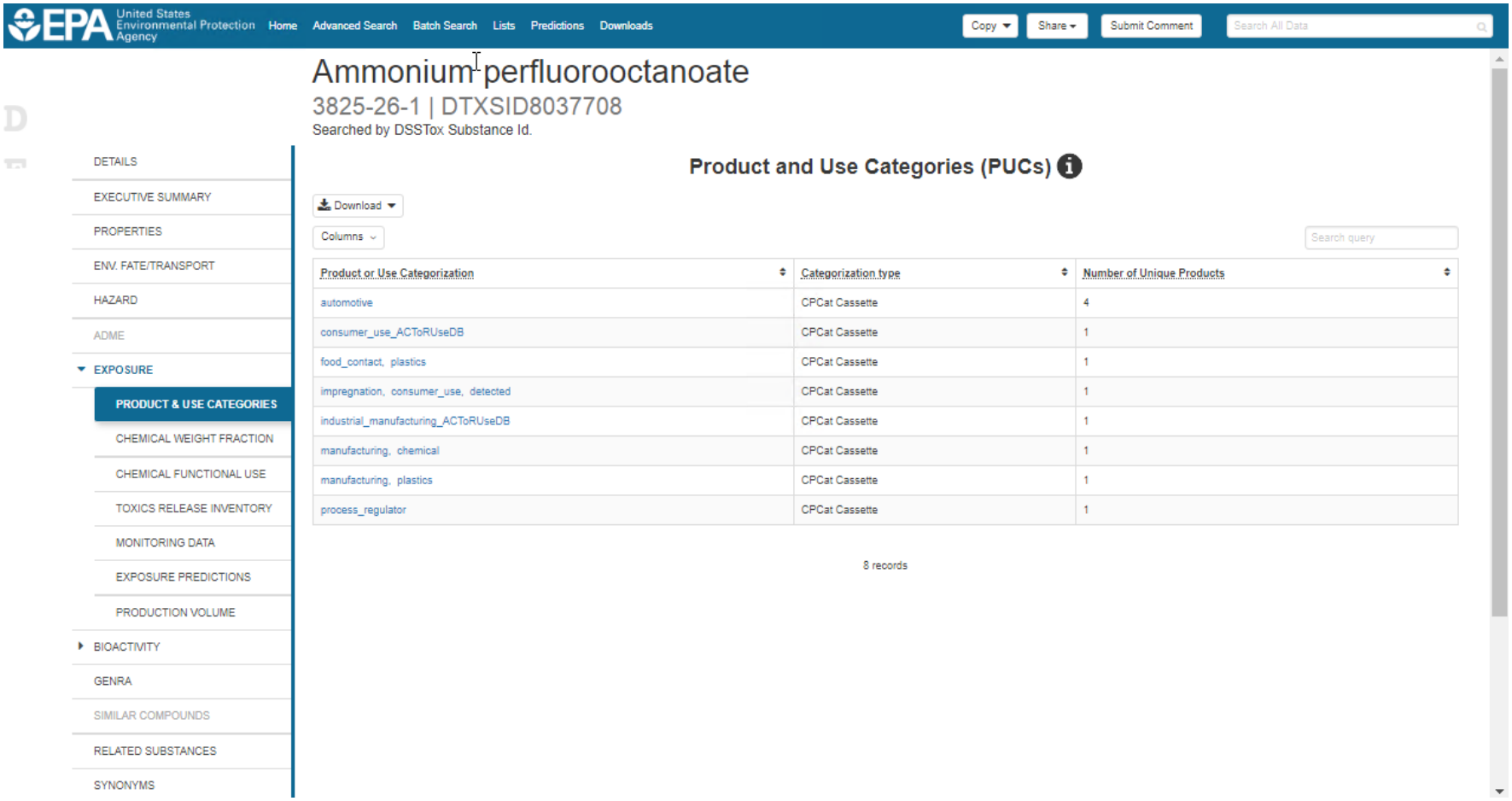
More	Priority	Toxval type	Subtype	Risk assessment class	Value	Units	Study type	Exposure route	Species	Subsource	Source
	7	NOAEL	systemic	chronic	16.1	mg/kg-day	chronic	oral	rat	unpublished_submission	ToxRefDB
	7	NOAEL	systemic	chronic	15	mg/kg-day	chronic	oral	rat	open_lit	ToxRefDB
	7	NOAEL	systemic	chronic	15	mg/kg-day	chronic	oral	rat	open_lit	ToxRefDB
	7	NOAEL	systemic	chronic	14.2	mg/kg-day	chronic	oral	rat	unpublished_submission	ToxRefDB
	7	NOAEL	systemic	chronic	15	mg/kg-day	chronic	oral	rat	open_lit	ToxRefDB
	3	LOEL	Recovery study - 6days	short-term	30	mg/kg-day	short-term	oral	mouse	Toxicol. Sci. 2008; 105 (1):86-96	HAWC
	3	LOEL	Recovery study - 6days	short-term	30	mg/kg-day	short-term	oral	mouse	Toxicol. Sci. 2008; 105 (1):86-96	HAWC
	3	LOEL	Recovery study - 6days	short-term	30	mg/kg-day	short-term	oral	mouse	Toxicol. Sci. 2008; 105 (1):86-96	HAWC
	3	LOEL	Recovery study - 5days	short-term	30	mg/kg-day	short-term	oral	rat	Toxicol. Sci. 2008; 105 (1):86-96	HAWC
	3	LOEL	Recovery study - 6days	short-term	30	mg/kg-day	short-term	oral	mouse	Toxicol. Sci. 2008; 105 (1):86-96	HAWC

In Vitro Bioassay Screening

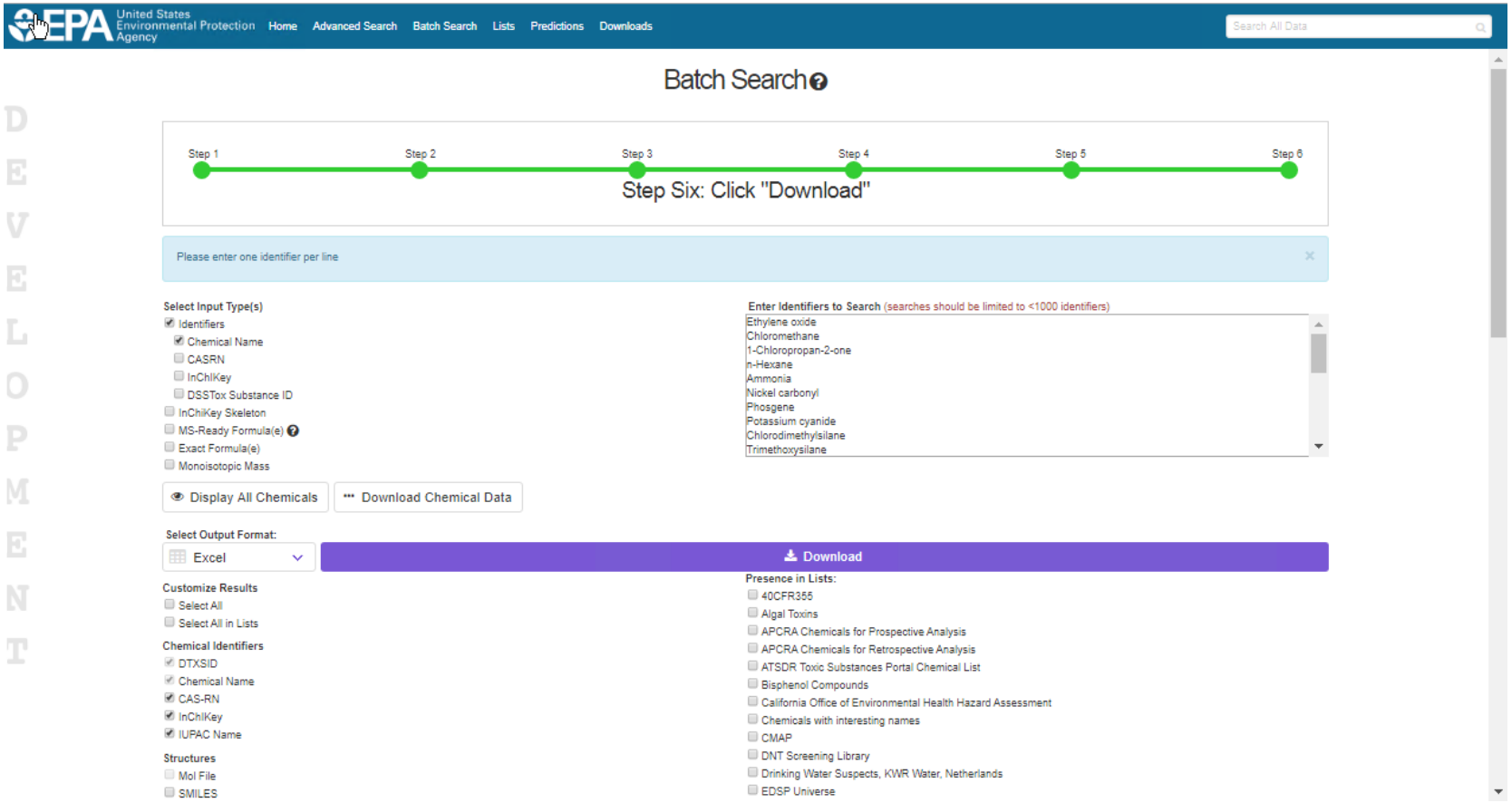
ToxCast and Tox21



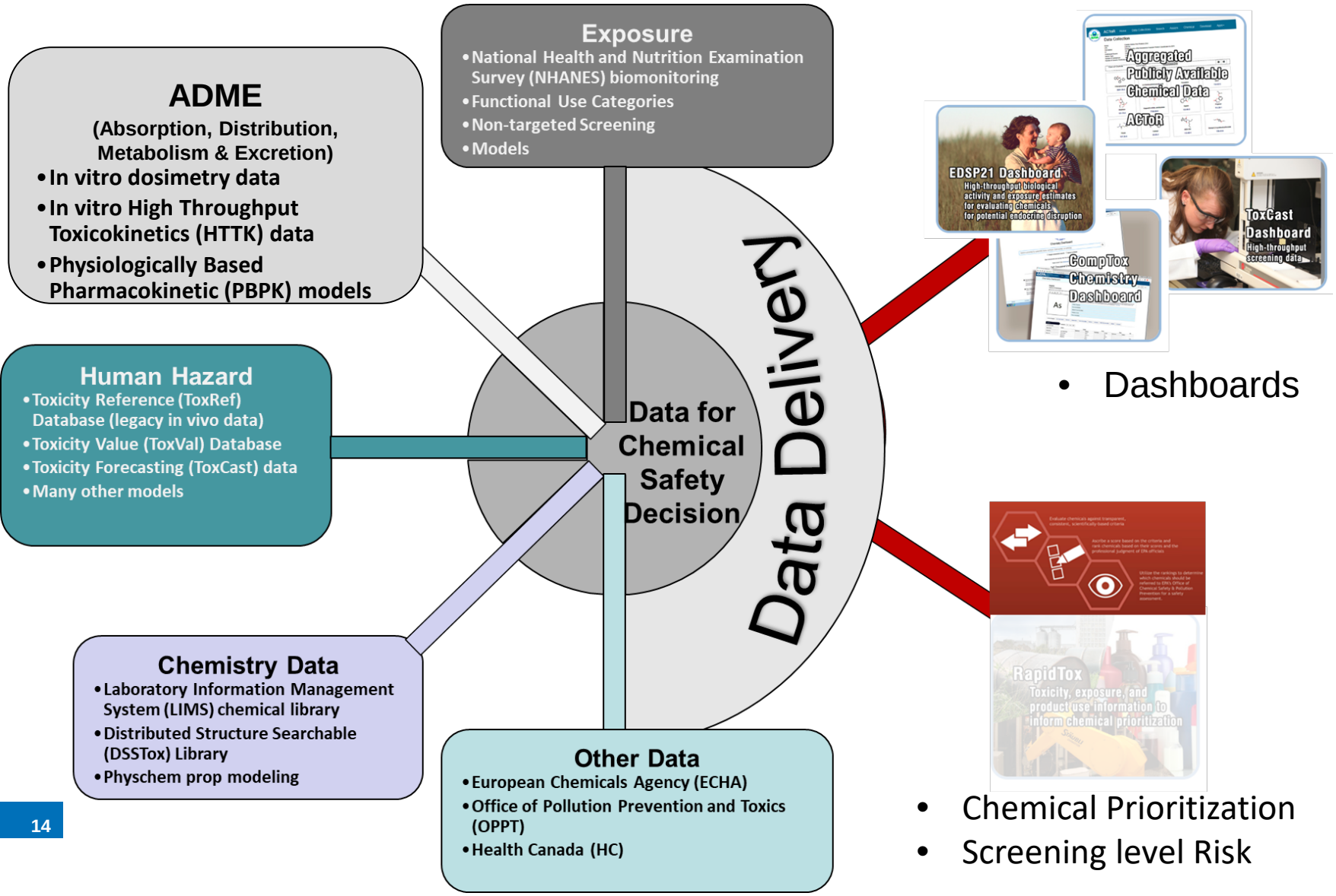
Sources of Exposure to Chemicals



Searching for more than one Chemical: Batch Searching



Impact



- Dashboards

- Chemical Prioritization
- Screening level Risk

Impact

- An integration hub for multiple “modules”
  - Experimental and predicted properties
  - Human and Ecological Hazard data
  - Exposure data – products, data in the environment
  - *In vitro* bioassay data – ToxCast/Tox21
  - Literature searching – Google Scholar and PubMed
  - Specialized searches – mass/formula for analytical support
  - Batch searching and Real Time Predictions
- CompTox Dashboard integrates chemical data
- Used by EPA and others to support chemical safety decisions
  - EPA examples: Endocrine Disruptor Screening Program in the 21st Century (EDSP21), Future (RapidTox)

Impact

United States Environmental Protection Agency

Minnesota Dept Health Risk Assessments for Water Contaminant

MDH Minnesota Department of Health

First Quarter Report
FISCAL YEAR 2016
July - September 2015

Drinking Water Contaminants of Emerging Concern Program

The mission of the Drinking Water Contaminants of Emerging Concern (CEC) program is to investigate and communicate the health and exposure potential of contaminants of emerging concern in drinking water. The CEC program supports the Clean Water Fund mission to *protect drinking water sources* and the Minnesota Department of Health (MDH) mission to *protect, maintain, and improve the health of all Minnesotans.*

Chemical Review

Using ToxCast to Compare Activity of Pesticide Active Ingredients with their Environmental Degradates

Three chemicals were nominated to the CEC program this quarter:

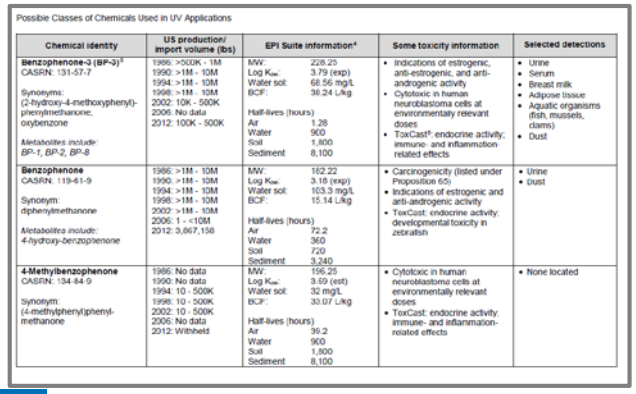
- Anatoxin-a, a toxin produced naturally by blue-green algae (cyanobacteria),
- Bifenthrin, an insecticide known to be toxic to aquatic organisms, and
- Tetrahydrofuran, an industrial solvent.

Chemicals Screened by the CEC Program

Chemical Review Process

- Pilot study to utilize ToxCast data in Drinking Water Contaminants of Emerging Concern

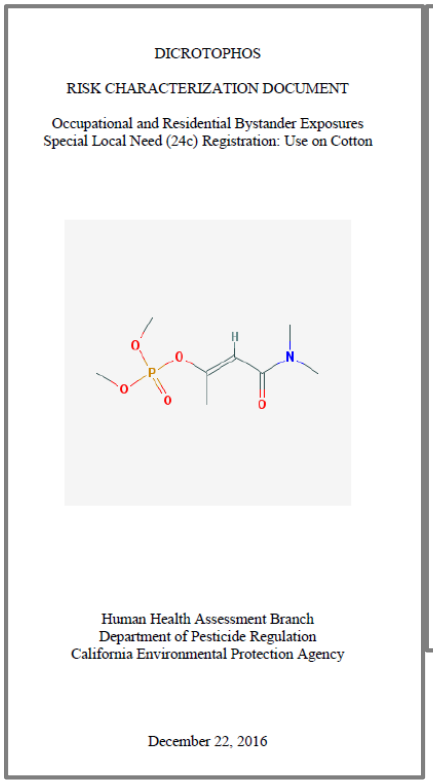
Prioritization for Biomonitoring CA


Possible Classes of Chemicals Used in UV Applications

Chemical identity	US production/ import volume (lbs)	EPI Suite information[4]	Some toxicity information	Selected detections
Benzophenone-3 (BP-3)[5] CASRN: 131-57-7 Synonyms: (2-hydroxy-4-methoxyphenyl)-phenylmethanone; oxybenzone *Metabolites include: BP-1, BP-2, BP-8*	1986: >500K - 1M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: 10K - 500K 2006: No data 2012: 100K - 500K	MW: 228.25 Log K_{ow}: 3.79 (exp) Water sol: 68.56 mg/L BCF: 38.24 L/kg Half-lives (hours) Air 1.28 Water 900 Soil 1,800 Sediment 8,100	• Indications of estrogenic, anti-estrogenic, and anti-androgenic activity • Cytotoxic in human neuroblastoma cells at environmentally relevant doses • ToxCast®: endocrine activity; immune- and inflammation related effects	• Urine • Serum • Breast milk • Adipose tissue • Aquatic organisms (fish, mussels, clams) • Dust
Benzophenone CASRN: 119-61-9 Synonym: diphenylmethanone *Metabolites include: 4-hydroxy-benzophenone*	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: >1M - 10M 2006: 1 - <10M 2012: 3,067,158	MW: 182.22 Log K_{ow}: 3.18 (exp) Water sol: 103.3 mg/L BCF: 15.14 L/kg Half-lives (hours) Air 72.2 Water 360 Soil 720 Sediment 3,240	• Carcinogenicity (listed under Proposition 65) • Indications of estrogenic and anti-androgenic activity • ToxCast: endocrine activity; developmental toxicity in zebrafish	• Urine • Dust
4-Methylbenzophenone CASRN: 134-84-9 Synonym: (4-methylphenyl)phenyl-methanone	1986: No data 1990: No data 1994: 10 - 500K 1998: 10 - 500K 2002: 10 - 500K 2006: No data 2012: Withheld	MW: 196.25 Log K_{ow}: 3.89 (est) Water sol: 32 mg/L BCF: 33.07 L/kg Half-lives (hours) Air 39.2 Water 900 Soil 1,800 Sediment 8,100	• Cytotoxic in human neuroblastoma cells at environmentally relevant doses • ToxCast: endocrine activity; immune- and inflammation-related effects	• None located

- Data surfaced through the EPA CompTox Dashboard utilized to prioritize biomonitoring for of emerging contaminants

CalEPA Pesticide Assessments


DICROTOPHOS

RISK CHARACTERIZATION DOCUMENT

Occupational and Residential Bystander Exposures
Special Local Need (24c) Registration: Use on Cotton

Human Health Assessment Branch
Department of Pesticide Regulation
California Environmental Protection Agency

December 22, 2016

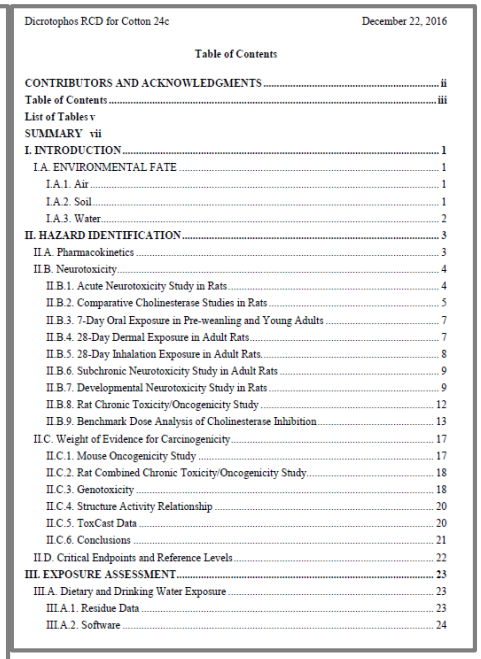

Dicrotophos RCD for Cotton 24c December 22, 2016

Table of Contents

CONTRIBUTORS AND ACKNOWLEDGMENTS ii
Table of Contents iii
List of Tables v
SUMMARY vii
I. INTRODUCTION 1
I.A. ENVIRONMENTAL FATE 1
I.A.1. Air 1
I.A.2. Soil 1
I.A.3. Water 2
II. HAZARD IDENTIFICATION 3
II.A. Pharmacokinetics 3
II.B. Neurotoxicity 4
II.B.1. Acute Neurotoxicity Study in Rats 4
II.B.2. Comparative Cholinesterase Studies in Rats 5
II.B.3. 7-Day Oral Exposure in Pre-weanling and Young Adults 7
II.B.4. 28-Day Dermal Exposure in Adult Rats 7
II.B.5. 28-Day Inhalation Exposure in Adult Rats 8
II.B.6. Subchronic Neurotoxicity Study in Adult Rats 9
II.B.7. Developmental Neurotoxicity Study in Rats 9
II.B.8. Rat Chronic Toxicity/Oncogenicity Study 12
II.B.9. Benchmark Dose Analysis of Cholinesterase Inhibition 13
II.C. Weight of Evidence for Carcinogenicity 17
II.C.1. Mouse Oncogenicity Study 17
II.C.2. Rat Combined Chronic Toxicity/Oncogenicity Study 18
II.C.3. Genotoxicity 18
II.C.4. Structure Activity Relationship 20
II.C.5. ToxCast Data 20
II.C.6. Conclusions 21
II.D. Critical Endpoints and Reference Levels 22
III. EXPOSURE ASSESSMENT 23
III.A. Dietary and Drinking Water Exposure 23
III.A.1. Residue Data 23
III.A.2. Software 24

- ToxCast data used for weight of evidence decisions regarding health effects for pesticides

*Not a comprehensive list

Conclusion

- EPA's CompTox Dashboard provides access to data for ~760,000 chemicals
- High quality data from ongoing curation efforts
- An integration hub for multiple "modules" and tools to support multiple environmental applications
- Major Update to EPA CompTox Dashboard released in August 2018
  - Endocrine Disrupting Compounds (EDCs)
  - Per- and Polyfluoroalkyl Substances (PFAS)
  - Generalized **Read-Across** (GenRA) module

Contacts

Antony Williams (*Dashboard Architect*)
National Center for Computational Toxicology
US EPA Office of Research and Development
919-541-1033
williams.antony@epa.gov

Monica Linnenbrink (Communications Director)
National Center for Computational Toxicology
US EPA Office of Research and Development
919-541-1522
linnenbrink.monica@epa.gov

Reeder Sams (Deputy Director, Acting)
National Center for Computational Toxicology
US EPA Office of Research and Development
919-541-0661
sams.reeder@epa.gov

The views expressed in this presentation are those of the author and do not necessarily reflect the views or policies of the US EPA