RapidTox in the CompTox Chemicals Dashboard

Practical Example Application-Emergency Response

Setting the stage-hypothetical situation

- Multiple rail cars transporting semi-volatile organic materials involved in accident near major source waterway for local utility

- Seven compromised cars spill over 200,000 gallons of Hexadecanoic acid (CASRN 57-10-3), also known as palmitic acid, down an embankment into the waterway

- No RSL value; no IRIS, PPRTV, CalEPA, ATSDR or other known human health assessment/toxicity value

- Municipal and State governments issue call for support in dealing with the emergency; water utility intake shut down; information on hexadecanoic acid needed within 12 hrs

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X   📄 Convert   ▼   📑 Select

⭐ ▶ Suggested Sites ▼   🔷 OHR Intranet - Leave Man...   🔷 Benchmark Dose Software...   ⚗ One EPA Workplace   🌐 Web Slice Gallery ▼   📑 My Workplace - LandingP...

🌱 EPA   United States
Environmental Protection
Agency

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Step One   Step Two   Step Three   Step Four   Step Five   Step Six

●━━━━━━━━━●━━━━━━━━━●━━━━━━━━━●━━━━━━━━━●━━━━━━━━━●

Step One: Select Input

Chemicals   Product/Use Categories   Assay/Gene

🔍 Hexadecanoic acid   ✕

Hexadecanoic acid
DTXSID20...

click

HEXADECANOIC ACID DER (FR. LAVANDULA) A
DTXSID50321651

HEXADECANOIC ACID NONYL ESTER
DTXSID30437345

Hexadecanoic acid--1-aminopropan-2-ol (1/1)
DTXSID30981959

Hexadecanoic acid--1,1'-azanediyldi(propan-2-ol) (1/1)
DTXSID401004744

Hexadecanoic acid--1,1',1"-nitrilotri(propan-2-ol) (1/1)
DTXSID101004745
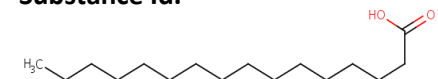
Hexadecanoic acid--2-(diethylamino)ethan-1-ol (1/1)
DTXSID80918098

Hexadecanoic acid--2,4a,8,9b-tetramethyl-2,3,4,4a,5,9b-hexahydro-1H-pyrido[4,3-b]indole (1/1)
DTXSID10914821

4

Chemistry Dashboard

Aa ▼   Aa   Aa ▲

762 Thousand Chemicals

**Hexadecanoic acid
57-10-3 | DTXSID2021602
Searched by DSSTox
Substance Id.**

| Step One | Confirm Outputs | Step Three | Step Four | Step Five | Step Six |

Emergency Response: Pre-populated Outputs and Additional User-defined Options

Emergency Response-Phase 1 Outputs

(Pre-selected)

(e.g., PAL, EL, MEG, TLV)

✅ Acute or Short-term Human Health values

🚫 Acute or Short-term Ecotoxicology values   hover

click

✅ Subchronic or Chronic Human Health values

🚫 Subchronic or Chronic Ecotoxicology values

click

✅ Existent Points-of-Departure (all species)

✅ Physicochemical Properties

✅ Fate and Transport

Additional Options Available

Pre-selected)

🚫 Literature Survey Heat Map

🚫 ToxCast/ToxPi profile
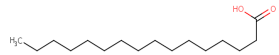
🚫 GenRA predictions

🚫 QSAR predictions

click   RUN

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5

Chemistry Dashboard

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**Hexadecanoic acid
57-10-3 |
DTXSID2021602
Searched by DSSTox
Substance Id.**

Step One

Existent Toxicity Values

Information Availability	Evaluate Information
● ○ Acute Oral	Review
○ ● Subchronic Oral	Review
○ ● Chronic Oral	Review
● ○ Acute Inhalation	Review
● ○ Subchronic Inhalation	Review
● ○ Chronic Inhalation	Review

ToxVal type	Value	Units	Exposure route	Duration Class	Species	Source
Air quality standard (background)	10	mg/m^3	Inhalation	Chronic	-	DE AGOF Dust
Air quality standard (normal)	650	mg/m^3	Inhalation	Chronic	-	DE AGOF Dust
Air quality standard (attention value)	1500	mg/m^3	Inhalation	Chronic	-	DE AGOF Dust
Air quality standard (background)	10	mg/m^3	Inhalation	Chronic	-	DE AGOF SVOCs
Air quality standard (normal)	650	mg/m^3	Inhalation	Chronic	-	DE AGOF SVOCs
Air quality standard (attention value)	1500	mg/m^3	Inhalation	Chronic	-	DE AGOF SVOCs

Evaluate Information

Review   Select
Review   Select

Evaluate Information

Review   Select
Review   Select

● ○   Fate and Transport   Review   Remove

● ○   GenRA   Review   Select

click

click

Generate Pre-Report

click

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Pre-Report Review (Emergen

- ✓ Acute or Short-term human health values (**6**)
- ✓ Subchronic or Chronic Human Health value (**7**)
- ✓ Existent Points-of-Departure (in vivo all species)(
- ✓ Physicochemical Properties
- ✓ Fate and Transport

Data Acquisitio   click

Generate Report   click

Acute or Short-term Human Health Values

Acute Oral

Acute Oral Human Health Values include any quantitative value derived from

Subch

Subch

Subchro
derived
and/or

	To
☐	M

Chron

Chronic
derived
and/or

	Tox
☐	Air std (ba
☐	Air quality standard (normal)

Hexadecanoic acid
57-10-3 | DTXSID2021602
Searched by DSSTox
Substance Id.

Dossier: End-user session R8.11.20.18

Oral
Acute Oral Value(s):
    Rat LD50 = 10,000 mg/kg

Inhalation
Acute Inhalation Value(s):
    Protective Action Criteria-1 = 2 mg
    Protective Action Criteria-2 = 12 mg

Existent Point-of-departure:

Fate and Transport:

Physicochemical Properties:

Appendix A – Human Health Values

Oral-Acute/Short-term

ToxVal type	Value	Units	Exposure route	Duration Class	Species	Source
LD50	10000	mg/kg	Oral	Acute	Rat	Acute Tox

Oral-Subchronic
- There are no existent oral subchronic human health values for hexadecanoic acid (57-10-3)

Oral-Chronic
- There are no existent oral chronic human health values for hexadecanoic acid (57-10-3)
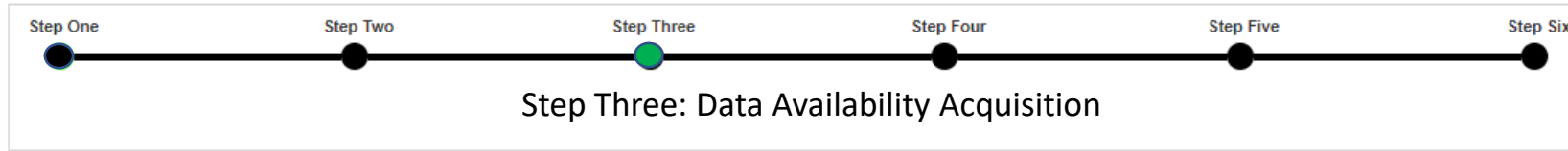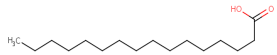
Inhalation-Acute/Short-term

ToxVal type	Value	Units	Exposure route	Duration Class	Species	Source
PAC-1	2	mg/m³	Inhalation	Acute	-	DOE
PAC-2	12	mg/m³	Inhalation	Acute	-	DOE
PAC-3	12	mg/m³	Inhalation	Acute	-	DOE
Air quality standard	0.15	mg/m³	Inhalation	Acute (30 mins)	-	Canada Ontario JSL
Air quality standard	0.15	mg/m³	Inhalation	Acute (24 hrs)	-	Canada Ontario JSL

Inhalation-Subchronic

ToxVal type	Value	Units	Exposure route	Duration Class	Species	Source
MEG	50	mg/m³	Inhalation	Subchronic	-	DOD Air-MEGs Short-Term
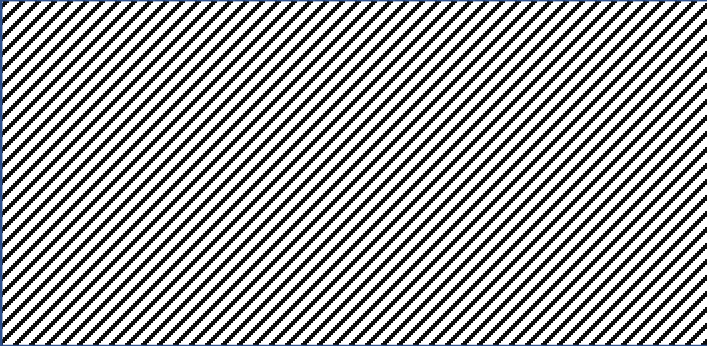
| | | 650 | mg/m³ | Inhalation | Chronic | - | DE AGOF Dust |

7

Chemistry Dashboard

Aa▾ Aa Aa▴

**Hexadecanoic acid
57-10-3 |
DTXSID2021602
Searched by DSSTox
Substance Id.**

Step One — Step Two — Step Three — Step Four — Step Five — Step Six

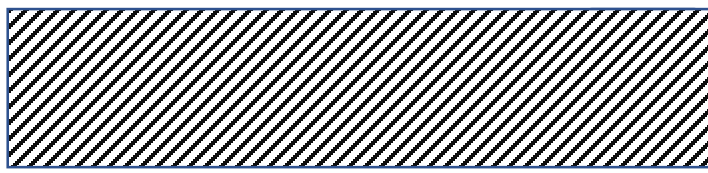Step Three: Data Availability Acquisition

Data Landscape for Output Generation-Emergency Response

Existent Toxicity Values

Information Availability   Evaluate Information

Points-of-Departure (in vivo)

Information Availability   Evaluate Information

Environmental Chemistry

● ○	PhysChem	
● ○	Fate and Transport	[Review] [Remove]

Ecotoxicology Values

Information Availability		Evaluate Information
○ ●	Acute/Short-term	[Review] [Select]
○ ●	Subchronic/Chronic	[Review] [Select]

New Approach Methods

Information Availability		Evaluate Information
● ○	Automated lit search	[Review] [Select]
● ○	ToxCast / Tox21 (in vitro)	[Review] [Select]
● ○	GenRA	[Review] [Select]

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8

Bioactivity

New Approach Methods

Information Availability	Evaluate Information
● ○ Automated lit search	Review · Select
● ○ ToxCast / Tox21 (in vitro)	Review · Select
● ○ GenRA	Review · Select

click

ⓘ TOXCAST DATA   ⓘ ASSAY DETAILS
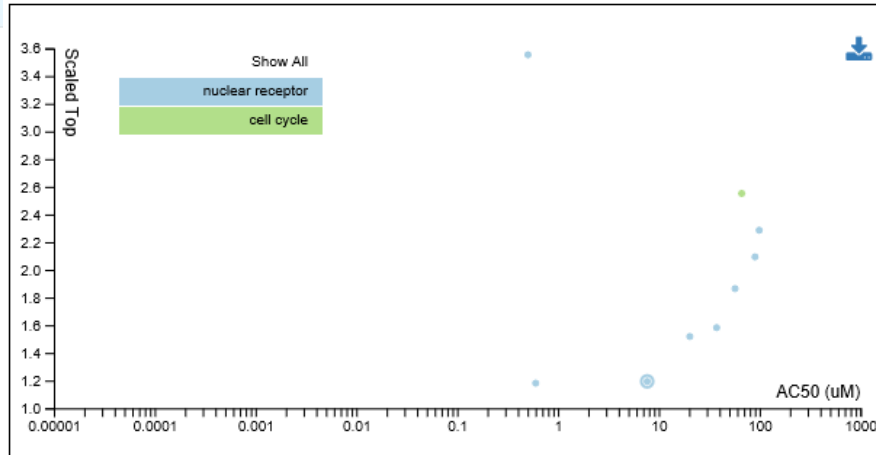
ASSAY DETAILS

AC50 (uM): 7.68
Scaled top: 1.19
Assay Endpoint Name: ACEA_T47D_80hr_Positive
Assay Description: 2
Gene Symbol: ESR1
Organism: human
Tissue: breast
Assay Format Type: cell-based
Biological Process Target: cell proliferation
Detection Technology: RT-CES
Analysis Direction: positive
Intended Target Family: nuclear receptor
Description: Data from the assay component ACEA_T47D_80hr was analyzed into 2 assay endpoints. This assay endpoint, ACEA_T47D_80hr_Positive, was

	Modal	Description	SeqaPASS	Gene Name	AOP	Event	Hit Call	Top	Scaled Top	AC50	logAC50	Intended Target Family
_T47D_80hr_Negative	📄	-	-	-	-	-	ACTIVE	54.9	2.55	66.5	1.82	cell cycle
_T47D_80hr_Positive	📄	2	NP_000116.2 ⬇	ESR1	200	1181	ACTIVE	29.1	1.19	7.68	0.885	nuclear receptor
ERE_CIS_up	📄	75	NP_000116.2 ⬇	ESR1	200	1181	ACTIVE	0.777	1.58	37.5	1.57	nuclear receptor
PPARa_TRANS_up	📄	132	NP_005027.2 ⬇	PPARA	58	468	ACTIVE	1.80	1.52	20.3	1.31	nuclear receptor
RORg_TRANS_up	📄	-	NP_005051.2 ⬇	RORC	-	-	ACTIVE	1.40	1.18	0.602	-0.220	nuclear receptor
XR_FXRSRC1_0480	📄	753	NP_001193922.1 ⬇	NR1H4	61	479	ACTIVE	52.1	2.09	90.2	1.96	nuclear receptor
XR_FXRSRC1_1440	📄	754	NP_001193922.1 ⬇	NR1H4	61	479	ACTIVE	93.4	2.29	99.2	2.00	nuclear receptor
ERa_LUC_BG1_Agonist	📄	788	NP_000116.2 ⬇	ESR1	200	1181	ACTIVE	90.2	3.55	0.505	-0.297	nuclear receptor
PXRE_CIS_dn	📄	-	-	-	-	-	ACTIVE	1.25	1.86	57.2	1.76	nuclear receptor

Generalized read-across

1 Chemical of interest entered via name, synonym(s), CASRN, and/or SMILES

2 Existent human health reference value(s) are identified in ToxValDB

3 End-user selects **non-cancer and/or cancer value(s)** for fit-for-purpose application

4 Existent human health relevant in vivo-based PODs are identified in ToxRefDB

5 A human health toxicity value may be derived using selected POD in conjunction with automated and/or expert-driven application of UFs

6 **HER(s)** may be calculated using selected POD(s) and exposure data

7 Literature search/survey using Sifter module

8
- **Compendium of identified literature**
- **Heat map of potential health outcomes**

9 Expert-evaluation of studies
- Assign weights to studies
- Collect/array study author based effect levels
- Identify d-r datasets for modeling; model; array BMDs

10 RapidTox Dashboard modules provide empirically-based and/or predicted NAM outputs. For ex:
- GenRA
- QSAR
- In vitro data (ToxCast)
- IVIVE (rTK)
- Chemical properties

11 Identify analogue chemicals based on structural and bioactivity similarity via GenRA module

12 Identify in vitro-based bioactivity information

13 Identify QSAR estimates

14 Identify empirically and/or predicted Pchem or environmental fate properties

15 Identify **potential PODs** from information across dashboard generated, NAM-based datastreams to calculate a HER, BER and/or screening toxicity value?
- Surrogate POD from selected analogue
- POD derived from reverse dosimetry (IVIVE) of ToxCast bioactivity data
- QSAR outputs
- Collated empirical ± EpiSuite ± other model outputs (Pchem; environ. fate)

BER = Bioactivity-Exposure ratio
GenRA = generalized read-across
HER = Hazard-Exposure ratio
IVIVE = in vitro to in vivo extrapolation (reverse toxicokinetics)
NAM = New Approach Methods
Pchem = Physicochemical
SMILES = Simplified molecular-input line-entry system
ToxRefDB = Toxicity Reference Database
ToxValDB = Toxicity Value Database

12

If you need further assistance or have questions about RapidTox please contact:
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