

Redefining possible®

Recent Developments in Hazard Assessment

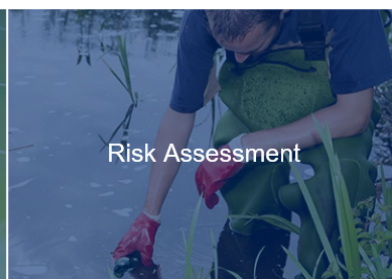
Catherine Rudisill, M.S.
SRC, Inc.



Defense > Environment > Intelligence

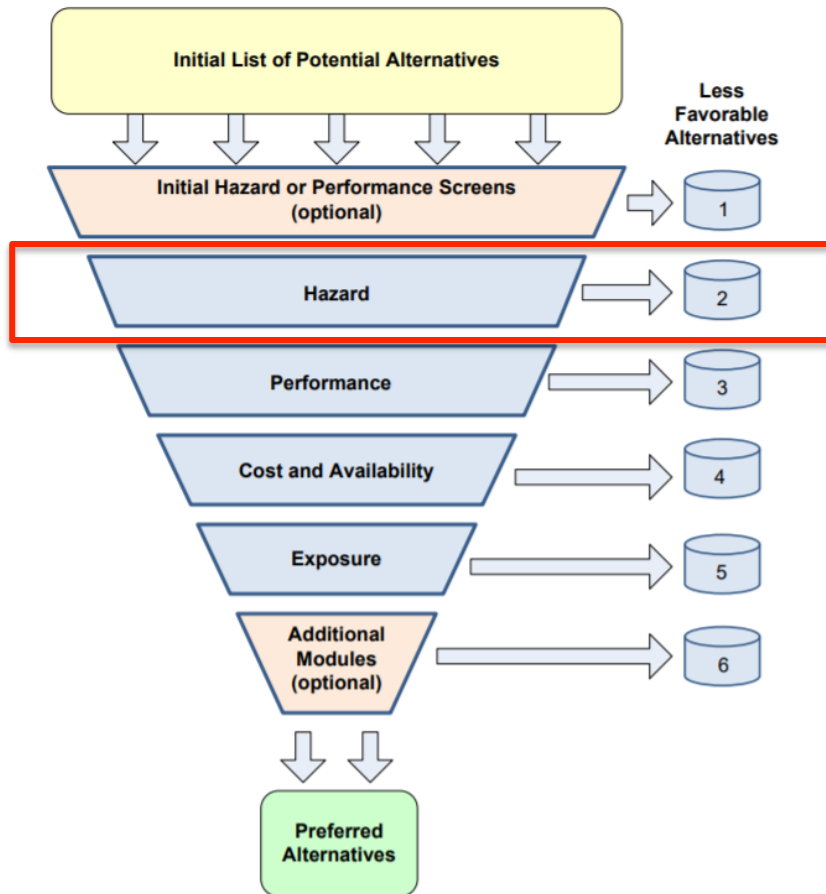
SRC Background

- Environmental Health Analysis (EHA)
- Providing Technical Support for >40 years
- Leader in Green Chemistry, pollution prevention (P2), and sustainability initiatives
- Not-for-Profit, Research & Development Organization



Hazard Assessment in AA's

IC2 Guide for Alternatives Assessment v1.1



Principle: Focus on reducing hazard

New Approach Methodologies (NAM's)

- Reduce the need for vertebrate testing

AA's uniquely positioned to incorporate these methodologies:

- Emerging field, establishing best practices
- Alternatives identified at the design-phase, requiring verification
- Existing substances (often data poor) utilized for new uses

New Approach Methodologies (NAM's)

Cost Advantage

Type of Toxicity		Study Cost (\$US)
Genetic toxicity		
	Chromosome aberration	
	animal test	\$30,000
	<i>in vitro</i> test	\$20,000
Sister chromatid exchange		
	animal test	\$22,000
	<i>in vitro</i> test	\$8,000
Unscheduled DNA synthesis		
	animal test	\$32,000
	<i>in vitro</i> test	\$11,000

*Humane Society International: http://www.hsi.org/issues/chemical_product_testing/facts/time_and_cost.html

Ethical Considerations

Propionic acid (undiluted)

Rabbit Eye Irritation Study (1975):

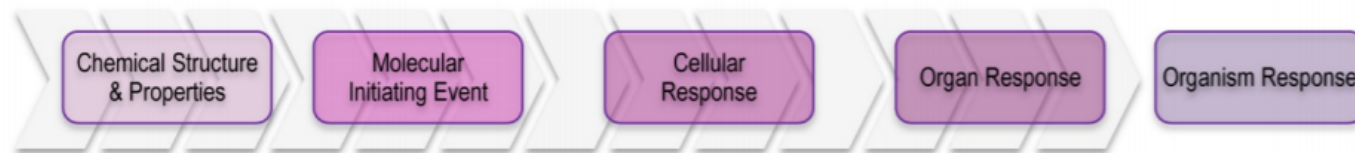
“...Clinical signs included severe discomfort recorded as squealing, pawing and thrashing...”

The Future Is Now!

EPA's NAM for Skin Sensitization

- ▶ **April 2018** - *Interim Science Policy: Use of Alternative Approaches for Skin Sensitization as a Replacement for Laboratory Animal Testing*

Proteins (Adapted from Strickland et al. 2018)



- ▶ Defined Approaches:
 - AOP “2 out of 3”
 - KE 3/1 sequential testing strategy (STS)
 - ▶ Validity must be at least that for reliable animal methods. For Mouse LLNA:
 - **70-80% Hazard prediction**
 - **60-70% Potency prediction**
- ➔ NAM should be just as accurate

EPA Chemistry Dashboard v3.0

Released August 2018



United States
Environmental Protection
Agency

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Di(2-ethylhexyl) phthalate

117-81-7 | DTXSID5020607

Searched by DSSTox Substance Id.

DETAILS

EXECUTIVE SUMMARY

PROPERTIES

ENV. FATE/TRANSPORT

HAZARD

▶ ADME

▶ EXPOSURE

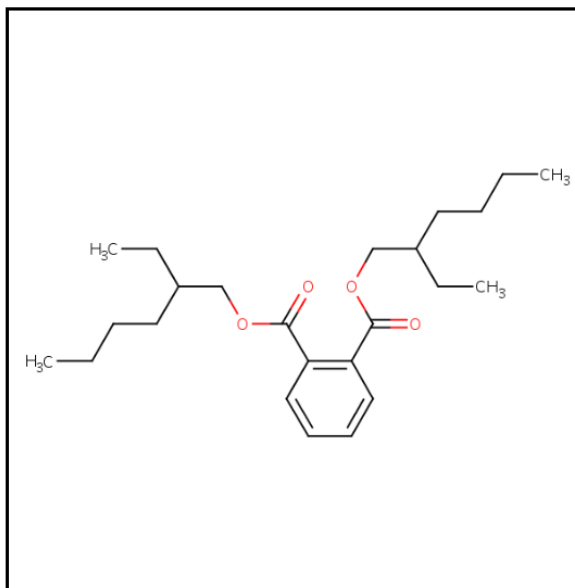
▶ BIOACTIVITY

SIMILAR COMPOUNDS

GENRA (BETA)

RELATED SUBSTANCES

SYNONYMS



Wikipedia

Bis(2-ethylhexyl) phthalate (**di-2-ethylhexyl phthalate**, **diethylhexyl phthalate**, **DEHP**; **dioctyl phthalate**, **DOP**) is an organic compound with the formula $C_{24}H_{38}(CO_2C_8H_{17})_2$. DEHP is the most common member of the class of phthalates, which are used as plasticizers. It is the diester of phthalic acid and the branched-chain 2-ethylhexanol. This colorless viscous liquid is soluble in oil, but not

...
[Read more](#)

Intrinsic Properties

Molecular Formula: $C_{24}H_{38}O_4$ Mol File

Find All Chemicals

Average Mass: 390.564 g/mol

Isotope Mass Distribution

Monoisotopic Mass: 390.27701 g/mol

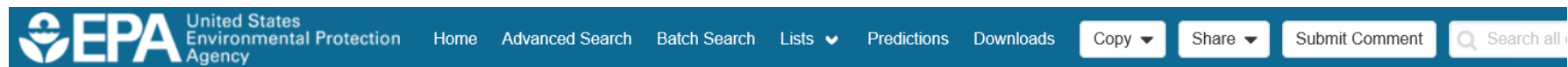
<https://epa.gov/>



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EPA Chemistry Dashboard v3.0

▶ Access the TOXCAST data summaries and model outputs!



Di(2-ethylhexyl) phthalate

117-81-7 | DTXSID5020607

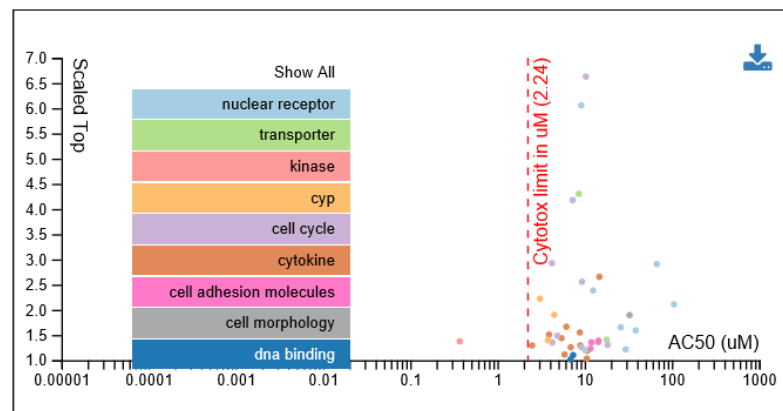
Searched by DSSTox Substance Id.

- DETAILS
- EXECUTIVE SUMMARY
- PROPERTIES
- ENV. FATE/TRANSPORT
- HAZARD
- ▶ ADME
- ▶ EXPOSURE
- ▼ BIOACTIVITY
 - TOXCAST: SUMMARY**

PUBCHEM

Chemical Activity Summary i

i TOXCAST DATA



i ASSAY DETAILS

Select a data point in the plot to see associated details

NURA meeting in RTP

A promotional poster for the NURA meeting. The background is red with a blurred image of laboratory glassware on the left and a computer monitor on the right. The NURA logo, a white circle with a red network diagram, is at the top left. The word "NURA" is in large white letters. A white banner with "FREE" in red is at the top right. The text "New Approach Methodology Use for Regulatory Application (NURA):" is in white, followed by "Integrating new approaches into your TSCA testing" in white italics. The dates "October 1-2, 2018" and location "Research Triangle Park, NC" are at the bottom in white.

NURA **FREE**

New Approach Methodology Use
for Regulatory Application (NURA):
*Integrating new approaches
into your TSCA testing*

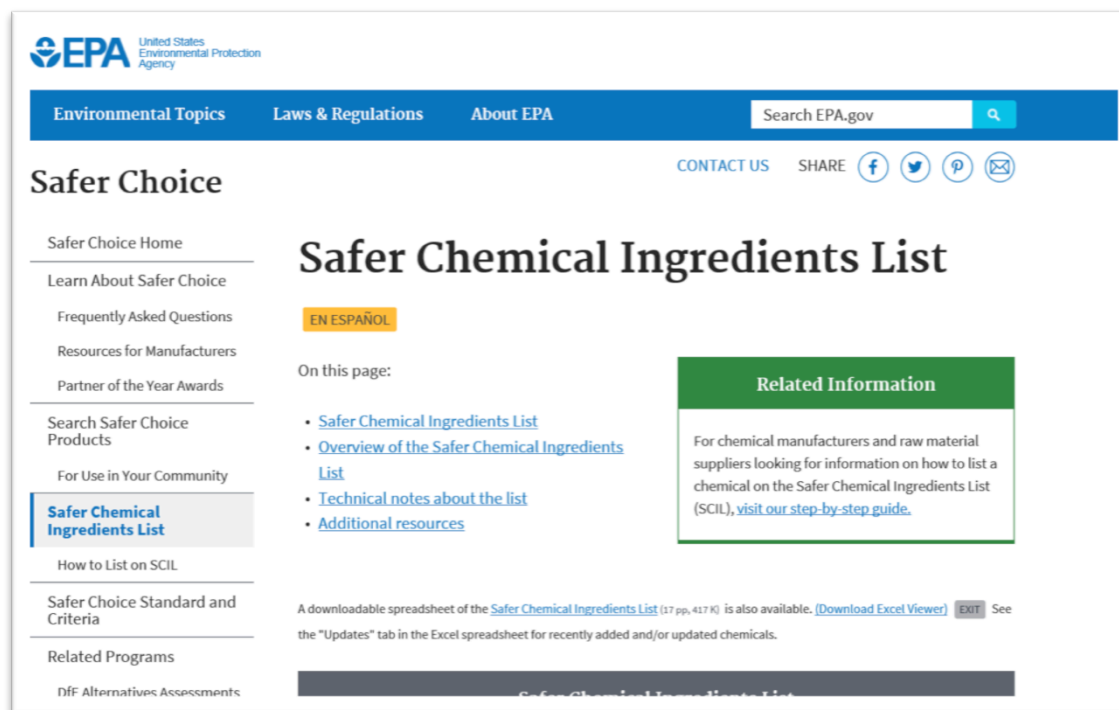
October 1-2, 2018
Research Triangle Park, NC

- In vitro Methods
- QSAR's
- High-Throughput Screening Data
- Etc.

What's Old is New Again!

EPA Safer Chemicals Ingredients List

- Started with 500 in 2012, Last updated in September 2018
- Now with 1,000 listings (>950 unique)
- Functional & evaluated against standard hazard criteria
- Positive list: <https://www.epa.gov/saferchoice/safer-ingredients>



GreenScreen®



- ▶ Updated March 2018
- ▶ Includes new hazard criteria for polymers and products (mixtures)

Fun Fact:

TSCA Public Inventory contains:

~25% - UVCB's

~25% - Polymers

The World of QSARs



norden

Nordic Council of Ministers



Ministry of Environment and Food
The Danish Environmental Protection Agency

DTU Food
National Food
Institute

Danish (Q)SAR Database

The Danish (Q)SAR Database includes estimates from more than 200 (Q)SARs from free and commercial platforms and related to physicochemical properties, ecotoxicity, environmental fate, ADME and toxicity. (Q)SAR predictions for more than 600,000 chemical substances can be searched, sorting can be made on chemical similarity, and profiles for individual substances can be downloaded.

The database is developed by the National Food Institute, Technical University of Denmark, with support from the Danish Environmental Protection Agency, the Nordic Council of Ministers and the European Chemicals Agency.

Search

User manual

Contact



FREE!

<http://qsar.food.dtu.dk/>



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OECD QSAR Toolbox: v4.2 (Feb 2018)

OECD.org | Data | Publications | More sites ▼ | News | Job vacancies

OECD
BETTER POLICIES FOR BETTER LIVES

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[OECD Home](#) > [Chemical safety and biosafety](#) > [Assessment of chemicals](#) > The OECD QSAR Toolbox

- > Testing of chemicals
- > Assessment of chemicals
- > Risk management of chemicals
- > Chemical accident prevention, preparedness and response

The OECD QSAR Toolbox

To increase the regulatory acceptance of (Q)SAR methods, the OECD is developing a QSAR Toolbox to make (Q)SAR technology readily accessible, transparent, and less demanding in terms of infrastructure costs.

[Download the Toolbox](#) | [Guidance Documents and Training Materials](#) | [Webinar](#) | [Help Desk](#) | [Public Discussion Forum](#)

WHAT'S NEW?

4 October 2018 - A patch for QSAR Toolbox version 4.2 was released to fix several bugs. It is

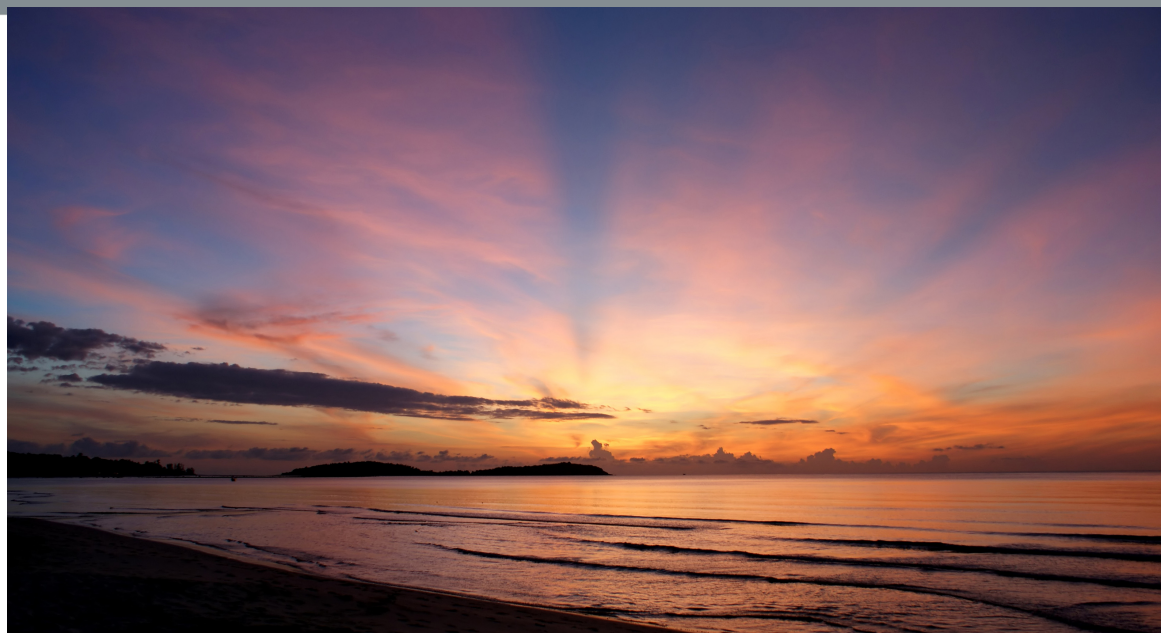
FREE!

ECOSAR v2.0 (Nov 2017)



FREE!

Conclusions



Pamela Spencer & Cathy Rudisill - Co-chairing afternoon session on Hazard Assessment in Alternatives Assessment Methods

Time: 1:15-3:15 PM

Location: Coastal Room

And Posters Too!