MAKING THE CASE FOR REPLACING HAZARDOUS CHEMICALS WITH SAFER SOLUTIONS

Margaret H. Whittaker, Ph.D., M.P.H., C.Biol., F.R.S.B., E.R.T., D.A.B.T.
ToxServices LLC
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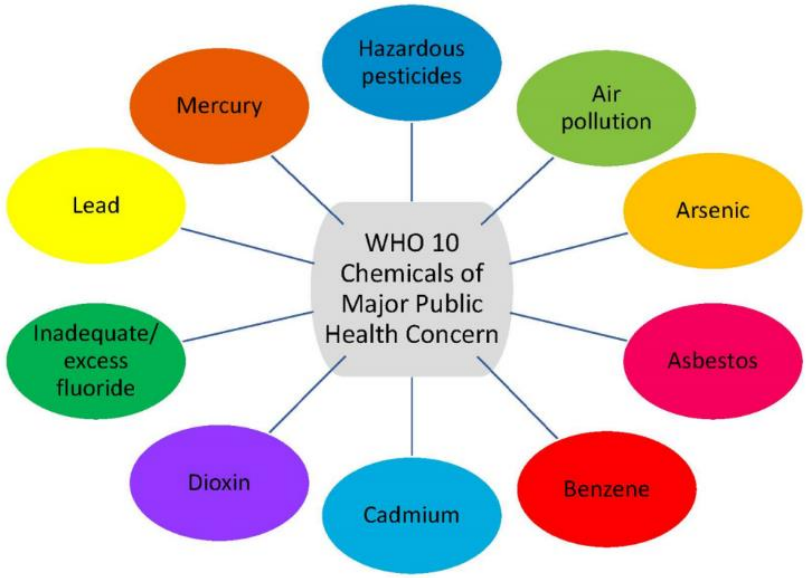
PRESENTATION OVERVIEW

- Introduction
- Overview: Is there a need to replace hazardous chemicals with safer solutions?
- Textbook example of why hazard avoidance is better: Today's darling child can be tomorrow's nightmare
- The road less traveled on the path to safer solutions: Stay the course!
- Useful methods to identify safer solutions
- Resources to learn more!

INTRODUCTION: LET'S GET ACQUAINTED!

- I am a toxicologist with ToxServices LLC, a U.S.-based consulting firm
- I have 25 years of experience as a human health risk assessor, and a chemicals alternatives assessor
- I have a Ph.D. in Toxicology from The University of Maryland, Baltimore and an M.P.H. in Environmental Health from The University of Michigan
- I am a Diplomate of the American Board of Toxicology, a U.K./EuroTox Registered Toxicologist, and a Chartered Biologist and Fellow of the U.K. Royal Society of Biology



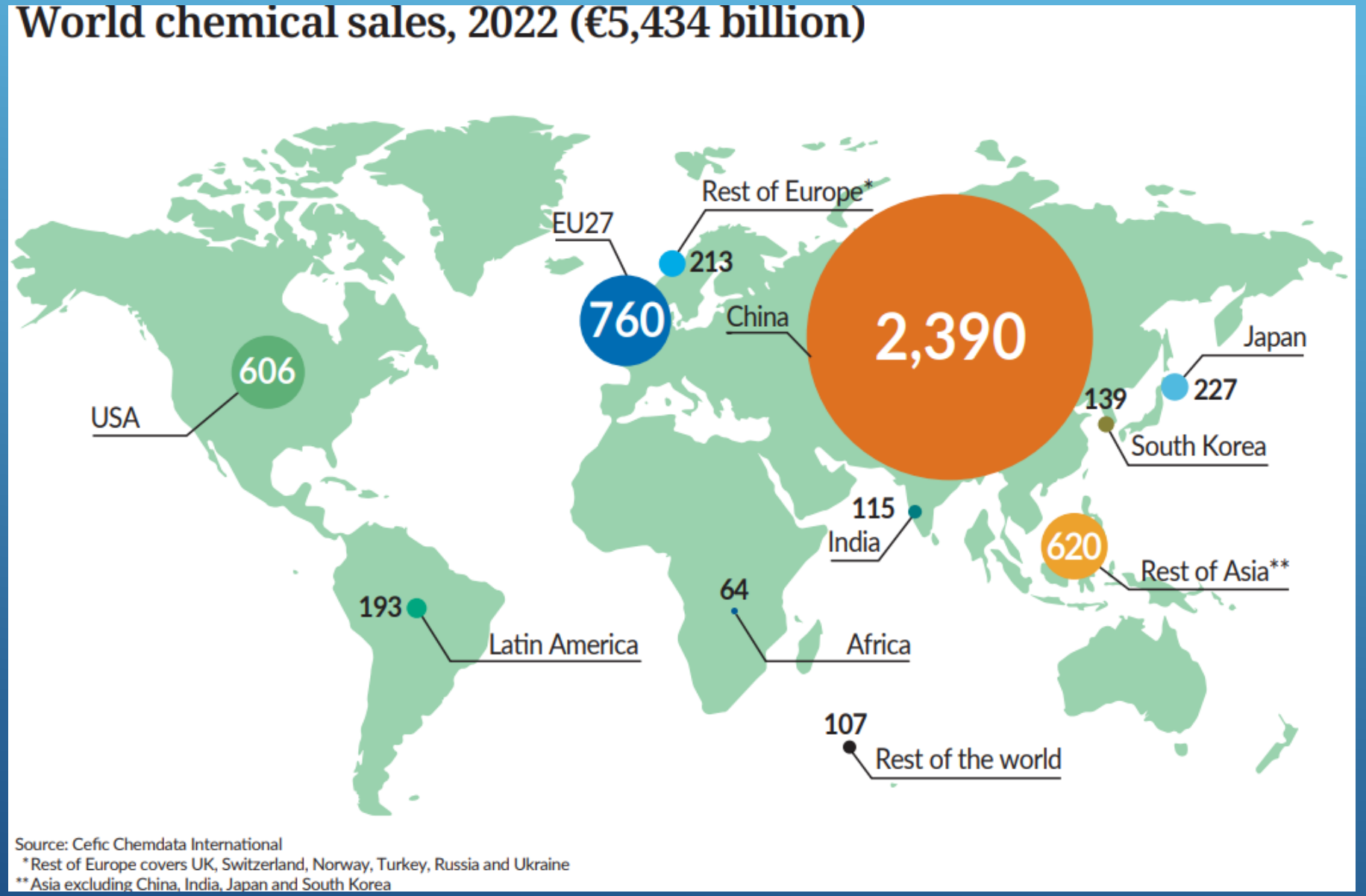
- What chemicals are hazardous?
- What are the impacts of hazardous chemicals?
  - Hazardous chemicals can impact humans, other living organisms, and/or the environment
  - **Health:** WHO Western Pacific: The environment determines a child's future: early life exposures impact on adult health as fetal programming and early growth may be altered by environmental risk factors (WHO Western Pacific Region)
  - **Health:** Between 2000 and 2020, the WHO estimates there were > 1,000 technological incidents involving chemicals worldwide, affecting > 1.85 million people.

SNAPSHOT OF CHEMICAL HAZARDS AROUND THE WORLD

Table 1: Examples of Regrettable Substitutions		
Chemical Category	**Chemical of Concern (Primary hazards)**	**Regrettable Substitute (Primary hazards)**
Flame retardants	Polybrominated diphenyl ethers (PBDEs) (Neurotoxicity, reproductive toxicity, and carcinogenicity, e.g., DecaBDE)	Tris(2,3-dibromopropyl) phosphate (Carcinogenicity, aquatic toxicity)
Solvents	Trichloroethylene (Carcinogenicity)	Bromopropane (Carcinogenicity, neurotoxicity)
Commercial Refrigerants	Chlorofluorocarbon (CFCs) such as R-12 (Dichlorodifluoromethane) (Ozone depletion, Greenhouse gas)	Hydrofluorocarbons (HFCs) such as HFC-23 (aka Fluoroform) (Greenhouse gas)
Plastics and Coatings Ingredients	Bisphenol A (BPA) (Endocrine disruption)	Bisphenol S (BPS) (Endocrine activity)

IS THERE A NEED TO REPLACE HAZARDOUS CHEMICALS?

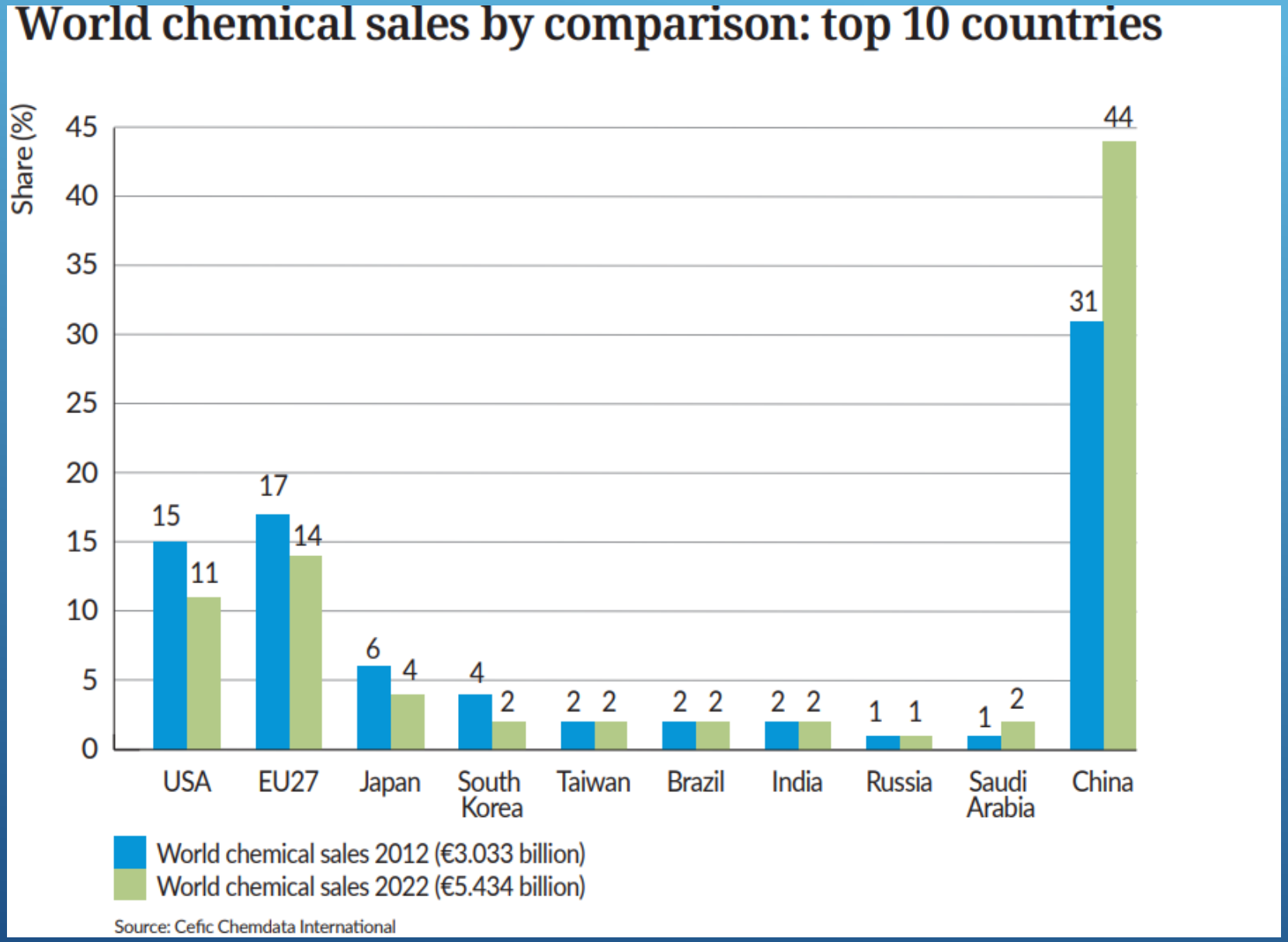
- Short answer. Yes (end of discussion).
- Where are we with chemical usage?
- The WHO estimates that more than 160 million chemicals are known
  - 40,000 to 60,000 chemical are used in commerce
  - 6,000 chemicals account for >99% of the total volume of chemicals in commerce globally
  - From 1950-2000, global chemical production increased 50-fold
  - The WHO estimates that chemical sales will **double** globally by 2030
- We repeat past mistakes
  - Regrettable substitution is avoidable.



Snapshot of global chemical use

2022 Figures

CEFIC WORLDWIDE CHEMICAL USE REPORT: YEAR 2022



GLOBAL TRENDS IN CHEMICAL PRODUCTION

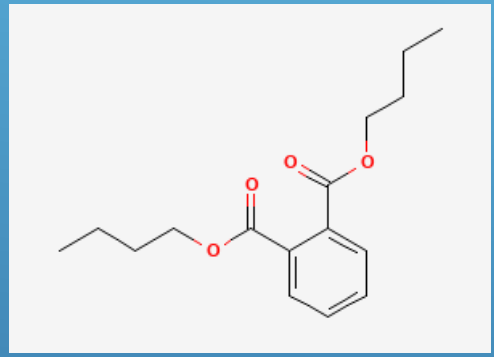
Recognizing geographical trends in chemical production is key to advancing safer chemical use

How do we connect with formulators overseas who choose to use hazardous chemicals?

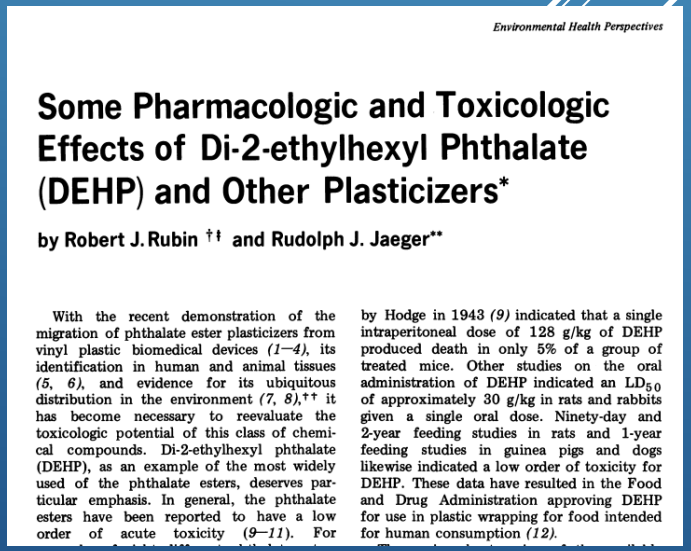
CEFIC WORLDWIDE CHEMICAL USE REPORT: YEAR 2012 VS. 2022

HAZARDOUS CHEMICAL CASE STUDY: WORLDWIDE USE OF DIBUTYL PHTHALATE (DBP)

- DBP was discovered inadvertently in the late 1920s by Dr. Waldo L. Semon of B.F. Goodrich when searching for PVC softeners
- DBP was the first *ortho*-phthalate added to PVC
  - 1 billion pounds of *ortho*-phthalates manufactured in 1972 ballooned to 12.3 billion pounds in 2019
- DBP and di(2-ethylhexyl)phthalate (DEHP) were detected in ambient waters and in plasma of patients receiving blood transfusions or who had undergone dialysis
- Rubin and Jaeger (1973) called out the data gaps in toxicological dataset on ortho-phthalates
- Despite the growing recognition of the DBP's toxicity (notably, in males), more than 50 years passed before manufacturers started phasing out DBP.



Dibutyl phthalate (CAS#84-74-2)



Environmental Health Perspectives

Some Pharmacologic and Toxicologic Effects of Di-2-ethylhexyl Phthalate (DEHP) and Other Plasticizers*

by Robert J. Rubin †‡ and Rudolph J. Jaeger**

With the recent demonstration of the migration of phthalate ester plasticizers from vinyl plastic biomedical devices *(1—4)*, its identification in human and animal tissues *(5, 6)*, and evidence for its ubiquitous distribution in the environment *(7, 8)*,†† it has become necessary to reevaluate the toxicologic potential of this class of chemical compounds. Di-2-ethylhexyl phthalate (DEHP), as an example of the most widely used of the phthalate esters, deserves particular emphasis. In general, the phthalate esters have been reported to have a low order of acute toxicity *(9—11)*. For

by Hodge in 1943 *(9)* indicated that a single intraperitoneal dose of 128 g/kg of DEHP produced death in only 5% of a group of treated mice. Other studies on the oral administration of DEHP indicated an LD_{50} of approximately 30 g/kg in rats and rabbits given a single oral dose. Ninety-day and 2-year feeding studies in rats and 1-year feeding studies in guinea pigs and dogs likewise indicated a low order of toxicity for DEHP. These data have resulted in the Food and Drug Administration approving DEHP for use in plastic wrapping for food intended for human consumption *(12)*.

HAZARDOUS CHEMICAL CASE STUDY: HAZARD CLASSIFICATION OF DIBUTYL PHTHALATE (DBP) OVER TIME

1950s

DBP low acute toxicity in male rats
(4 g/kg)
(47)

DBP no chronic toxicity in male rats
(125 mg/kg)
(47)

1970s/1980/1990s

DBP shown to harm male reproductive tract in rats, mice, guinea pigs

Testicular toxicity reported in multiple studies
(50, 51, 52, 53, 55, 57, 58)

2000s

GHS Health Hazard Classification
GHS Category 1B Reprotoxic (May damage unborn child. Suspected of damaging fertility)
Hazard Statement H360Df
(58)

GHS Environmental Hazard Classification
GHS Category 1 Acute Aquatic Toxicity (H400)(58)

Worldwide Regulatory Bans, Reporting, and Disclosure Requirements
In 2005, DBP banned from toys /child care products in EU
In 2005, DBP added to California's Proposition 65
In 2008, U.S. CPSC banned DBP in children's toys/child care products with >0.1% DBP
In 2011, DBP was added to the State of WA's Chemicals of High Concern for Children List
In 2017, DBP added to the State of OR's High Priority Chemicals of Concern for Children's Health List

Timeline of DBP Classification (Whittaker and Heine 2023)

DBP initially thought to have low toxicity (1950s), but later testing identified male reproductive hazards

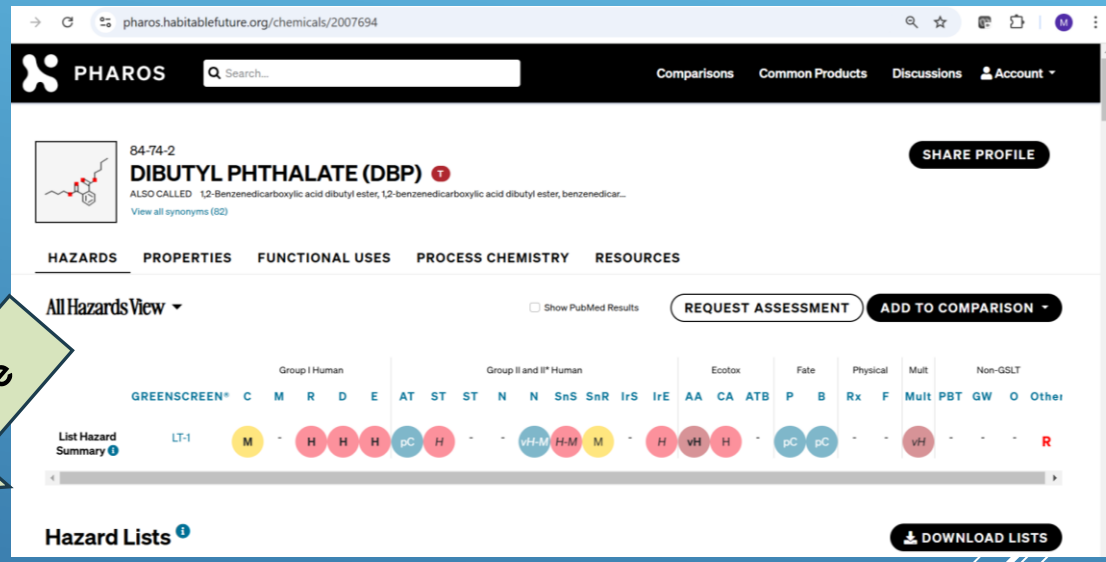
When classified using a current-day chemical hazard assessment framework such as GHS, DBP is classified as:
--Highly reprotoxic (GHS Category 1B, GHS Hazard Statement H360D)

--Acutely toxic to aquatic organisms (GHS Category 1, GHS Hazard Statement H400)

HAZARDOUS CHEMICAL CASE STUDY: HAZARD CLASSIFICATION OF DIBUTYL PHTHALATE (DBP)

Pharos record for DBP:

--DBP is listed on 89 RSLs (bad!)
--DBP listed on 2 Positive Lists, including Cosmetic Ingredient Review (CIR)'s 2024 Quick Reference Table



Safe

CIR Reference Table (2024)

Dibutyl Phthalate	S

†S - Safe in the present practices of use and concentration. Ingredient, concentration, and use information are available in documents discoverable at https://cir-reports.cir-safety.org; SQ - safe for use in cosmetics, with qualifications; I - the available data are insufficient to support safety; Z - the available data are insufficient to support safety, but the ingredient is not used; U - the ingredient is unsafe for use in cosmetics; UNS - ingredients for which the data are insufficient and their use in cosmetics is not supported

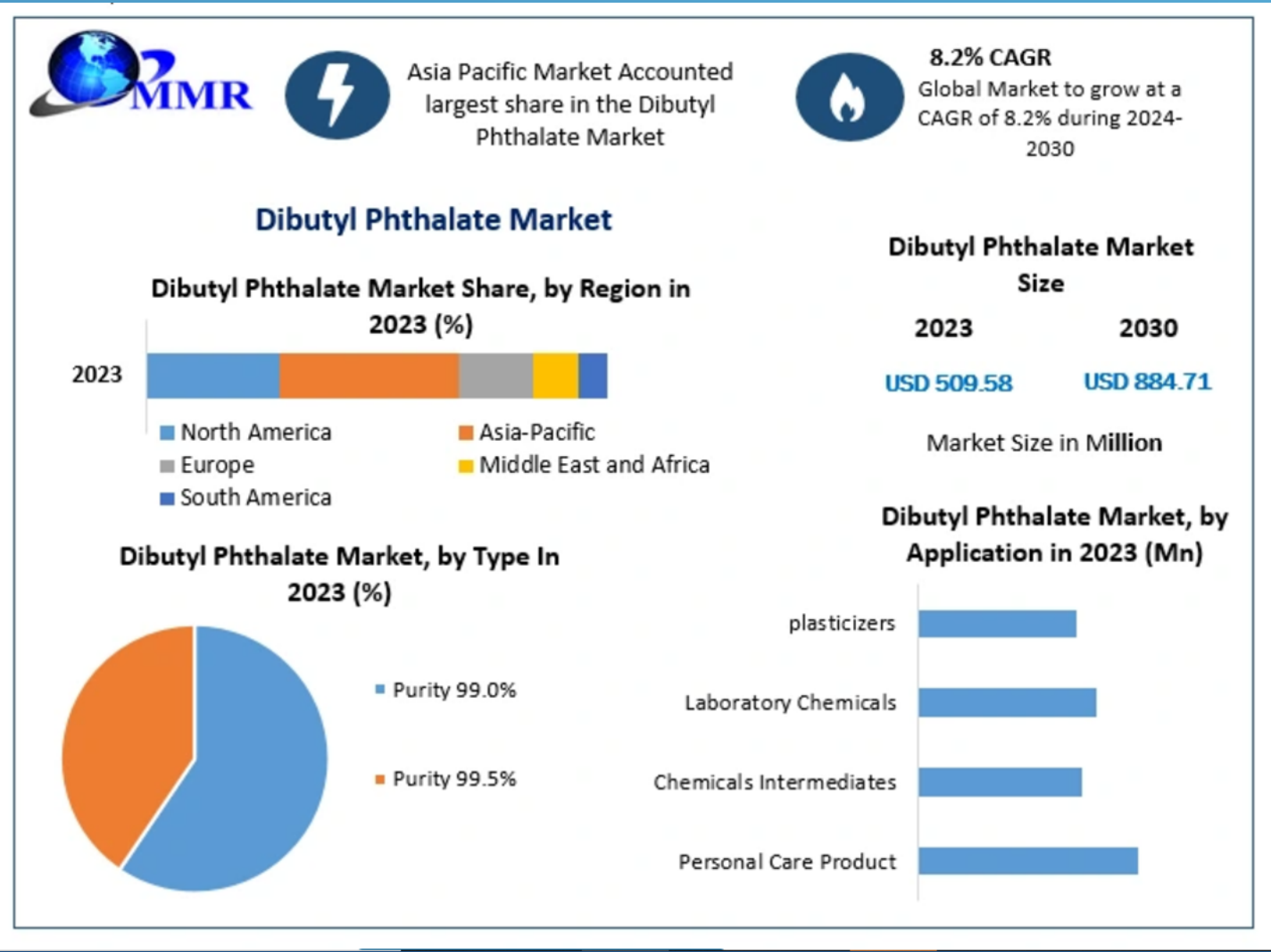
EU Cosmetic Regulation Annex II listing for DBP:

--DBP is prohibited from use in cosmetics in the EU (meaning no intentional use!)

Which List Should be Believed?!

Prohibited

HAZARDOUS CHEMICAL CASE STUDY: DBP, CONT'D



Despite the H360d and H400 hazard classifications, DBP's global market size continues to grow!

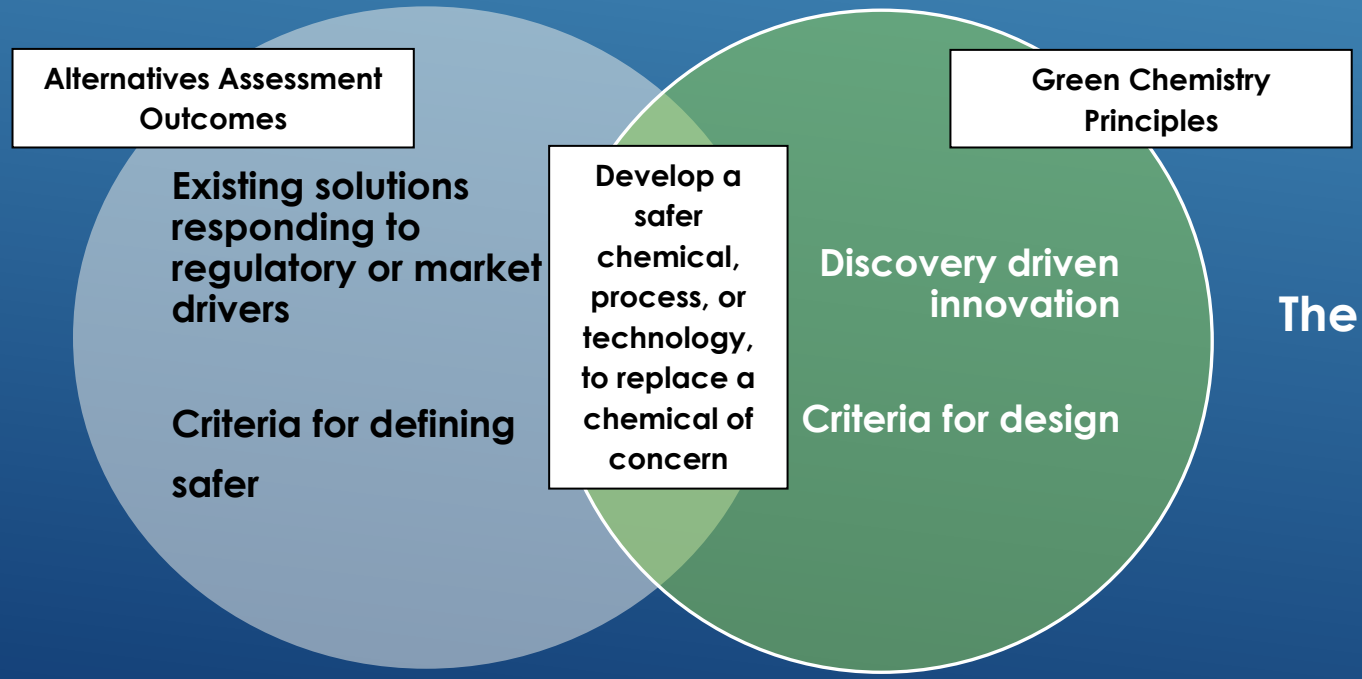
DBP's CAGR (compound annual growth rate) is 8.2%!

Asia Pacific market is largest share of DBP

Source: MMR 2024

ONWARDS TO SAFER SOLUTIONS: WHICH PATH(S) TO CHOOSE?

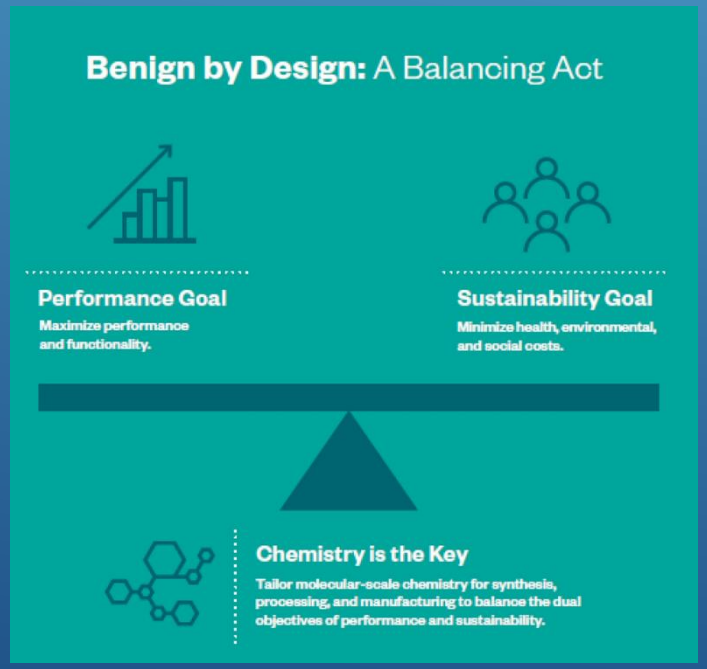
- **POP QUIZ!**
  - Is it easier to replace hazardous chemicals using Green Chemistry or an Alternative Assessment (AA)?
  - Answer: You need **both**.
- Green chemistry uses new chemistries that reduce or eliminate use or generation of hazardous substances
- AA evaluates alternatives to ensure they are less hazardous, and perform, are cost-effective, and don't have adverse social, environmental, or economic impacts at any life cycle stage!

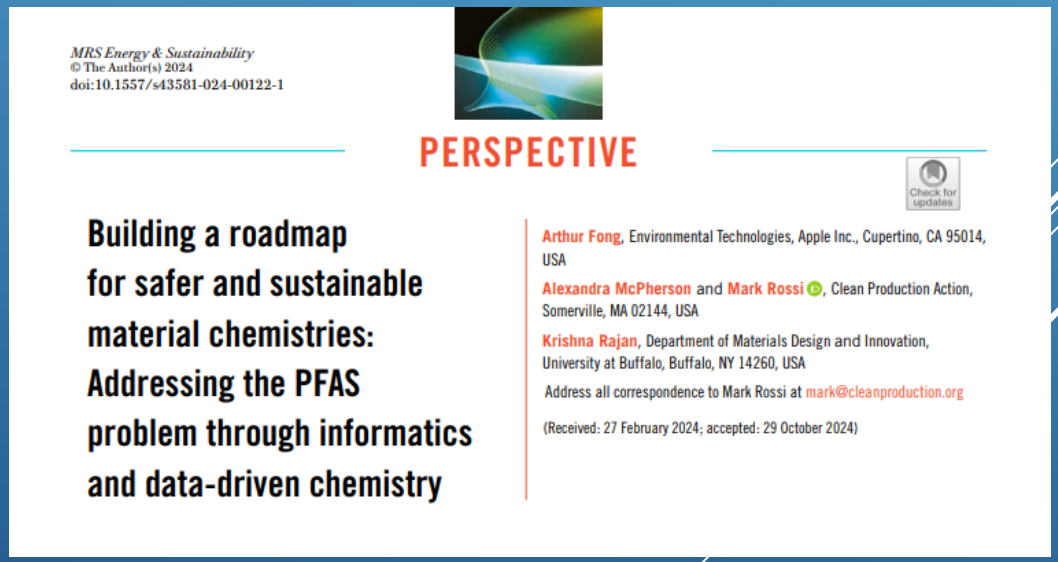


The Nexus Between Alternatives Assessment and Green Chemistry (Tickner et al. 2020)

SAFER SOLUTIONS: DESIGN CORRECTLY FROM THE BEGINNING!

- The Ellen MacArthur Foundation (2023) estimates that more than 80% of a product's environmental impact is determined at the design stage
- Future is big data and AI to design safer and sustainable: New open-access article by Art Fong, CPA, and Univ. of Buffalo!





Fong et al. (2024): Balance Safer and Sustainable Chemistries

https://link.springer.com/article/10.1557/s43581-024-00122-1

SAFER SOLUTIONS: DESIGN CORRECTLY FROM THE BEGINNING USING CORRECT TOOLS FOR THE JOB!

- **It is critical to assess hazards of input chemicals at the design stage**
- **How to assess to confirm a safer solution?**
  - **List-based screening:** Using on-line lists indexed in on-line databases is a first-approach, but the example of DBP (CIR vs. EU Cosmetics Regulation) demonstrates that a list-based approach may lead you down the wrong path!
  - **Ecolabels and transparency reports:** Important to recognize their limitations
  - **Third-party verified chemical assessments:** Chemical hazard assessments undertaken by impartial third-party is becoming increasingly important to avoid use of hazardous substances

ARE ECOLABELS THE SOLUTION? MAYBE. RECOGNIZE THEIR DIFFERENCES

Inventory	Characterize	Screen	Social	Energy/Water
1, 2. Declare Label, Health Product Declaration (HPD) Chemical Inventory		Screening against lists. No non-list screening.		
3. ChemFORWARD Chemical Inventory, Hazard Characterization, and Chemical Screening				
4. ChemFORWARD SAFER Tradename Chemical Inventory, Hazard Characterization, and Chemical Screening				
5. GreenScreen® Certified: Chemical Inventory, Hazard Characterization, Chemical Screening				
6. U.S. EPA Safer Choice Certification: Chemical Inventory, Hazard Characterization, Chemical Screening, and Optional Energy/Water Assessment				Updated 2024 Safer Choice Standard includes this as optional endpoints
7. Cradle to Cradle Certified®: Chemical Inventory, Hazard Characterization, Chemical Screening, Social Fairness, Material Reutilization, and Energy and Water Usage				

Updated Estimated Cost and Time of Example Third Party Evaluations

Program	Cost Range	Completion Time Estimate	Comment/Links
Declare Label	$2,000-$3,000	6-8 weeks	A Declare label is valid for 1 year and compares a product's ingredients list against ILFI's RED List of chemicals. License fees are paid to ILFI (included in the cost range).
Health Product Declaration (HPD)	$1,500-$3,000	6-8 weeks	An HPD is valid for 3 years. An HPD is a disclosure tool that inventories chemical composition and discloses known hazards and chemical benchmarks (such as GreenScreen scores)
GreenScreen® for Safer Chemicals Certification	$15,000-$20,000	6-8 weeks	A GreenScreen certification is valid for 5 years with annual renewals; there is a certification fee paid to CPA. Analytical testing is required.
U.S. EPA Safer Choice Certification	$4,000-$9,000	6-8 weeks	A Safer Choice certification is valid for 3 years, with on-site audit, a desk audit, and a renewal audit occurring during the cycle. Performance testing is required. No certification fee is paid to EPA.
Cradle to Cradle Certified® Full Certification	$20,000 - $60,000	6 Months	A Cradle to Cradle Certification is valid for 3 years. An on-site audit is required at inception. Analytical testing (RSL compliance and recycled content, if applicable) is required). Certification fees are paid to C2CPII.
ChemFORWARD Safer Assessment	$6,000- $15,000	3 Months	A ChemFORWARD Safer assessment is valid for 2 years. Costs may be significantly lower if chemicals are already in the ChemFORWARD repository.

The primary reason that most Third Party Evaluations are focused on "safer" and regrettable substitution avoidances is time and cost.

SPOTLIGHT: THIRD-PARTY ASSESSMENTS CHEMFORWARD AND CHEMFORWARD SAFER

- ChemFORWARD (https://www.chemforward.org/) and ChemFORWARD SAFER (https://www.chemforward.org/safer)
  - **ChemFORWARD** is a repository of chemical assessments (non-tradename level)
  - **ChemFORWARD Safer** is a program that assesses tradename ingredients

CEA venebio GRADIENT NSF REACH24H TOXSERVICES TOXICOLOGY RISK ASSESSMENT CONSULTING ToxStrategies

1. Ensure safety of all chemical constituents while **protecting CBI**
2. Leverage existing CHAs to **reduce the cost** and increase consistency
3. Build customer confidence with rigorous **third-party** process
4. Provides a portable claim to **distinguish** trade name material

INOLEX

Aromastat™

CHEM FORWARD SAFER chemforward.org

Product Summary | Contents | Product Details

Chemical Name	CAS	Function	Hazard Band	Concentration
2-phenylethanol	60-12-8		C	70.00%
Caprylhydroxamic acid	7377-03-9		C	15.00%
Glycerin	56-81-5		A	15.00%

https://www.chemforward.org/safer-product-listing

CHEMFORWARD: COMPREHENSIVE ENDPOINTS ASSESSED

- Example of a ChemFORWARD Assessment for TPO-L
- TPO-L, is a photoinitiator in adhesives, sealants, coatings, paints and printing inks
- Screening shows numerous data gaps, numerous hazards to human health and environmental endpoints

GHS Hazard Summary Table for Ethyl Phenyl(2,4,6-trimethylbenzoyl)phosphinate (CAS #84434-11-7)

Endpoint	Route Specific Conclusions		
	Oral	Dermal	Inhalation
Carcinogenicity	CNP	CNP	CNP
Mutagenicity	NC		
Reproductive Toxicity	CNP	CNP	CNP
Developmental Toxicity	NC	CNP	CNP
Lactation Toxicity	CNP		
Acute toxicity	NC	NC	NC
Specific Target Organ Toxicity - Single Exposure	NC	NC	NC
Specific Target Organ Toxicity - Repeated Exposure	NC	CNP	CNP
Neurotoxicity - Single Exposure	CNP	NC	NC
Neurotoxicity - Repeated Exposure	NC	CNP	CNP
Skin Sensitization	GHS Cat. 1B		
Respiratory Sensitization	NC		
Skin Corrosion / Irritation	NC		
Eye Damage / Irritation	NC		
Respiratory Irritation	CNP		
Aspiration	NC		
Acute Aquatic Toxicity - Vertebrate	GHS Cat. 2		
Acute Aquatic Toxicity - Crustacea	GHS Cat. 2		
Acute Aquatic Toxicity - Algae	GHS Cat. 2		
Chronic Aquatic Toxicity - Vertebrate	GHS Cat. 2		
Chronic Aquatic Toxicity - Crustacea	GHS Cat. 2		
Chronic Aquatic Toxicity - Algae	GHS Cat. 2		
Persistence and Biodegradation	Not rapidly degradable		
Bioaccumulation	Not bioaccumulative		
Hazards to the Ozone Layer	NC		
Physical Properties: Reactivity and Flammability	Reactivity: NC Flammability: NC		

Note: GHS Category rating is reported for each endpoint, if available, with lower ratings indicating a higher hazard. In instances when there are no data or insufficient data, the term "CNP" (classification not possible) is applied. NC is the best GHS rating possible, indicating Not Classified.
Note: Persistence and bioaccumulation do not have specific GHS hazard ratings, however, their characterization is used to assign the aquatic toxicity hazards.

CHEMFORWARD OUTPUT

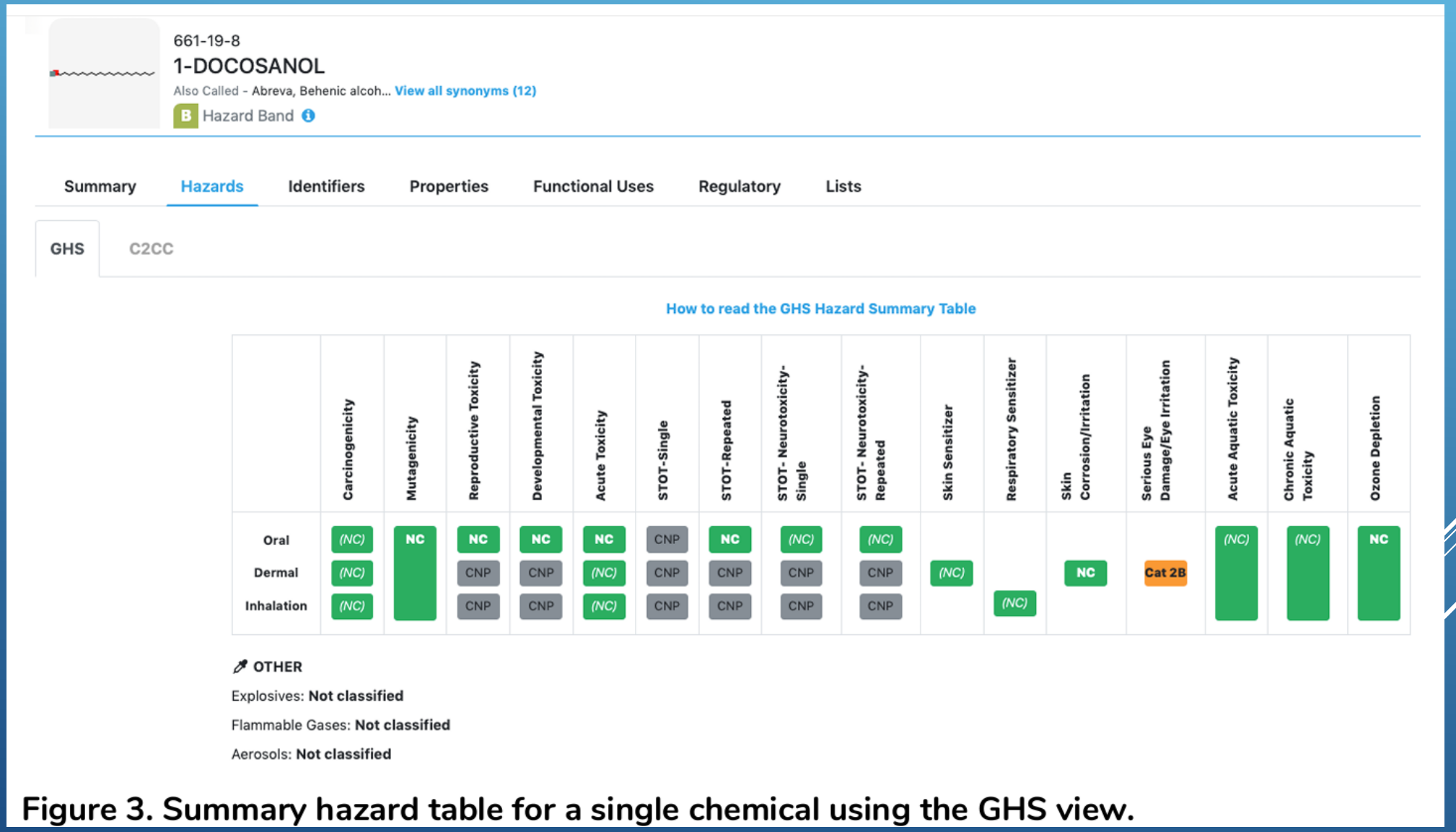
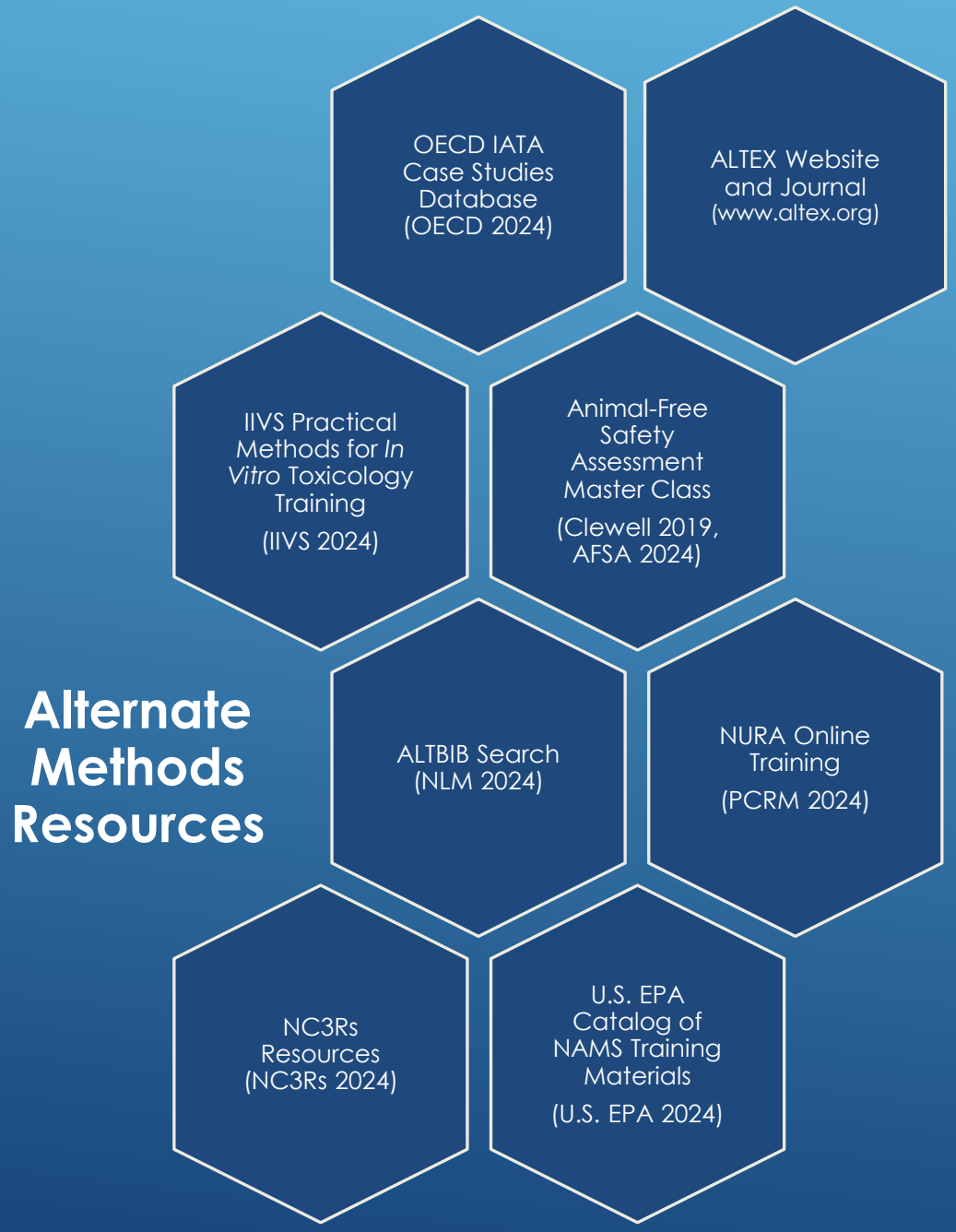


Figure 3. Summary hazard table for a single chemical using the GHS view.

ChemFORWARD assigns hazard bands based on the results of detailed assessments

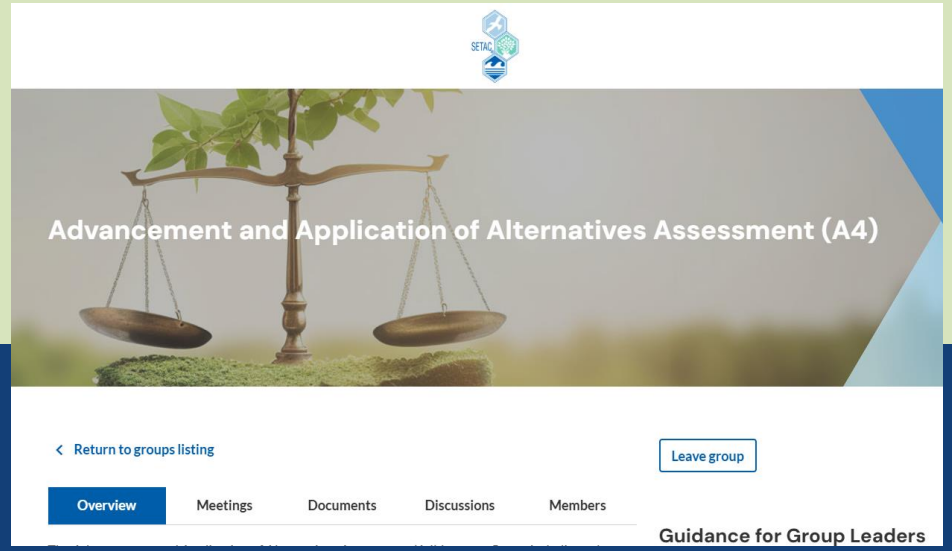
RESOURCES/TOOLS TO CONQUER SAFER CHEMICAL EVALUATION

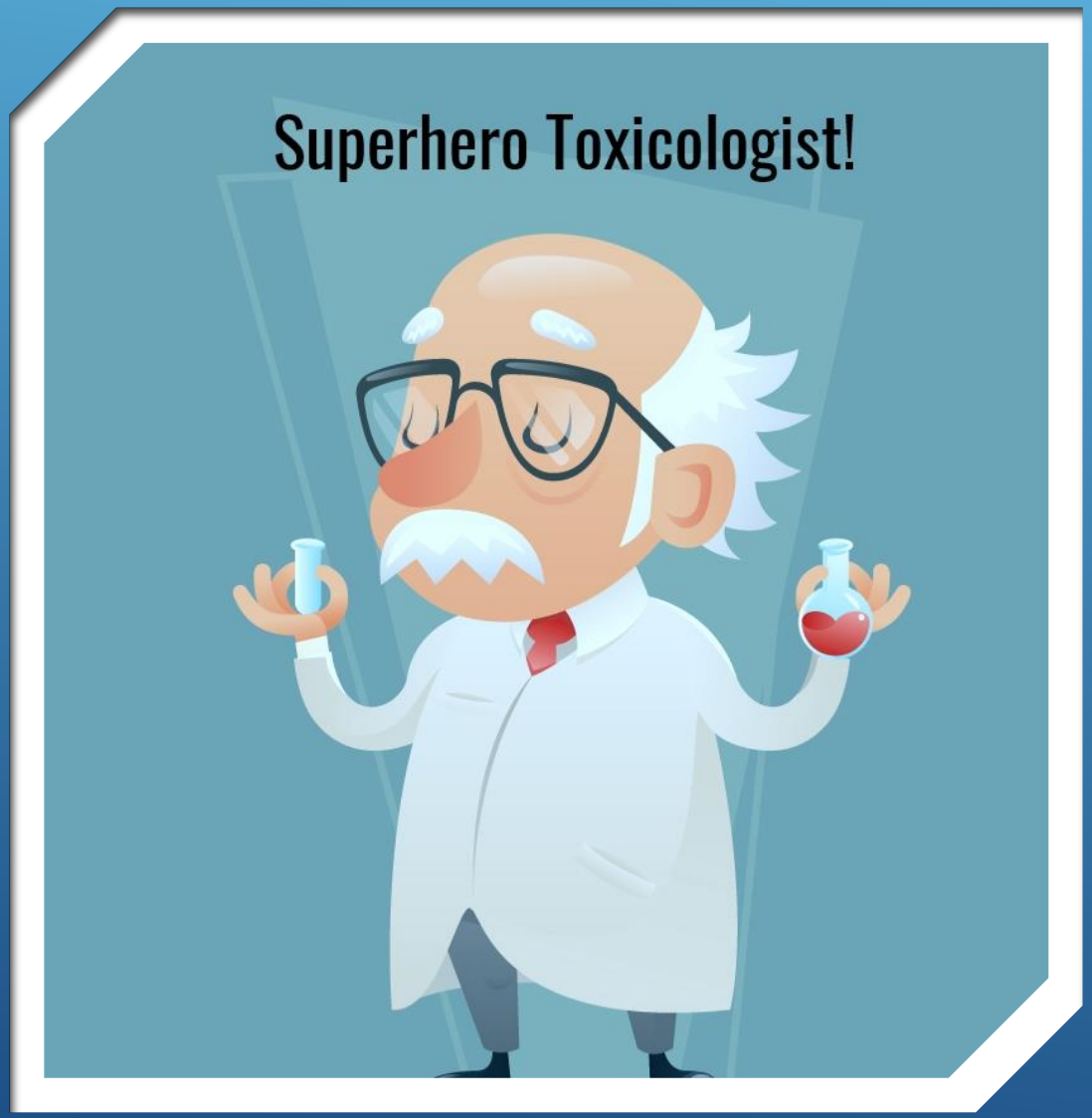


There are many in-person and virtual training opportunities and databases in hazard assessment and methods involving non-animal testing to assess chemical hazards

CONCLUSION

- Hazardous chemical usage continues around the world
- The changing geographical distribution of chemical manufacturing will influence how and if hazardous chemicals enter the supply chain
- There are a variety of approaches that can be implemented to avoid hazardous chemical use, including list-based screening, ecolabels, and CHAs
- Interested in the topic of AA? Join SETAC's newest Interest Group, the Advancement and Application of Alternatives Assessment (A4) and get involved in the AA community!
  - https://www.setac.org/group/advancement-and-application-of-alternatives-assessment-a4.html





THANK YOU!
PLEASE CONTACT ME WITH QUESTIONS

MWHITTAKER@TOXSERVICES.COM

202-429-8787