

TOOLS & RESOURCES FOR SAFER CHEMICALS

BizNGO

December 9, 2015

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What is the GreenScreen?

- The GreenScreen is a comparative Chemical Hazard Assessment (CHA) method developed by Clean Production Action
 - Most current method is version 1.2
 - GreenScreen was released on March 20, 2007
- Builds on the U.S. EPA DfE Alternatives Assessment approach and other national and international precedents (OECD, GHS)
- GreenScreen is freely and publicly accessible, transparent, and peer reviewed
- GreenScreen complements other sustainability tools:
 - Based on Green Chemistry Principles
 - Supports Risk Assessment
 - Complements Life Cycle Assessment
 - A key part of Alternatives Assessment



What is the GreenScreen?

There are two levels of assessment

– GreenScreen List Translator

- Automated tool that screens the chemicals against specified authoritative and screening lists
- Scores: LT-1 (equivalent to BM-1), LT-P1, LT-U
- Quickly identifies chemicals to avoid and why
- Easily accessible, automated tool
- Useful tool for identifying “known” bads; not as useful for newly developed chemicals

– Full GreenScreen assessment

- Scientists (usually toxicologists) prepare full GreenScreen assessment
- CPA Licensed Profilers most qualified (see <http://www.greenscreenchemicals.org/>) for list of qualified profilers
- Comprises selection, review, and integration of chemical data and modeling into comprehensive assessment of a minimum of 18 hazard endpoints

The GreenScreen List Translator

GreenScreen List Translator

- Readily identifies chemicals of concern
- Based on authoritative lists
- Doesn't require toxicology expertise
- Used to identify GreenScreen Benchmark 1 Chemicals
 - LT-1 chemicals are Benchmark 1 chemicals (unless proven otherwise)
 - LT-P1 chemicals may be Benchmark 1 chemicals
 - LT-U chemicals are not known to be Benchmark 1 need further assessment to determine Benchmark score

Obtaining GreenScreen List Translator

Manual Version:

<http://www.greenscreenchemicals.org/method/greenscreen-list-translator>

Automated Tool: Incorporated into Pharos

<http://www.pharosproject.net/>

The screenshot displays the Pharos project website interface for the chemical [106-46-7] 1,4-DICHLOROBENZENE. The page is titled "Pharos" and includes navigation links for Building Products, Chemicals and Materials, Certifications, Dashboard, and Logout. The main content area shows the chemical name and a list of direct hazards with associated icons and counts:

- CANCER** (10): US NIH - Report on Carcinogens - Reasonably Anticipated to be Human Carcinogen
- REPRODUCTIVE** (2): Japan - GHS - Toxic to reproduction - Category 1B
- MAMMALIAN** (3): Japan - GHS - Specific target organs/systemic toxicity following repeated exposure - Category 1
- SKIN SENSITIZE** (1): Japan - GHS - Skin sensitizer - Category 1
- ACUTE AQUATIC** (5): EU - GHS (H-Statements) - H400 - Very toxic to aquatic life
- CHRON AQUATIC** (2): EU - GHS (H-Statements) - H410 - Very toxic to aquatic life with long lasting effects
- EYE IRRITATION** (3): EU - GHS (H-Statements) - H319 - Causes serious eye irritation
- SKIN IRRITATION** (1): New Zealand - GHS - 6.3A - Irritating to the skin
- ORGAN TOXICANT** (1): New Zealand - GHS - 6.9B (inhalation) - Harmful to human target organs or systems

On the right side, there is a "My Project Lists" section with a message: "No project lists available. Lists can be added to existing projects on your account. Visit your dashboard for more information."

1,4-Dichlorobenzene is a List Translator-1 (LT-1) Chemical

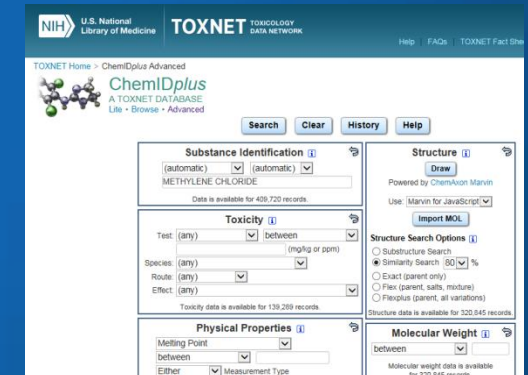


Three Steps to Safer Chemicals: GreenScreen

1. Assess and classify hazards
- 2. Apply the Benchmarks**
3. Make informed decisions

Step 1: Assess & Classify Hazards

- Identify chemical constituents along with relevant and feasible transformation products
- Collect and evaluate data from all relevant sources (using test data, literature, models, analogs, hazard lists, etc.) for the chemical under assessment
- Assign level of concern (e.g., vH, H, M, L) and level of confidence for each hazard endpoint
- Complete a hazard table for each of the 18 screened endpoints



Chemical Name	Group I Human					Group II Human						Ecotox		Fate		Physical		
	C	M	R	D	E	AT	ST	N	SnS	SnR	IrS	IrE	AA	CA	P	B	Rx	F
Chemical 1	M	<i>L</i>	L	M	<i>M</i>	L	L	<i>M</i>	L	DG	L	H	L	L	vH	M	L	L
Chemical 2	<i>L</i>	L	M	M	H	L	H	M	L	L	M	M	H	H	vH	vH	L	L
Chemical 3	L	L	M	H	DG	L	H	DG	L	DG	L	L	L	DG	M	M	L	M

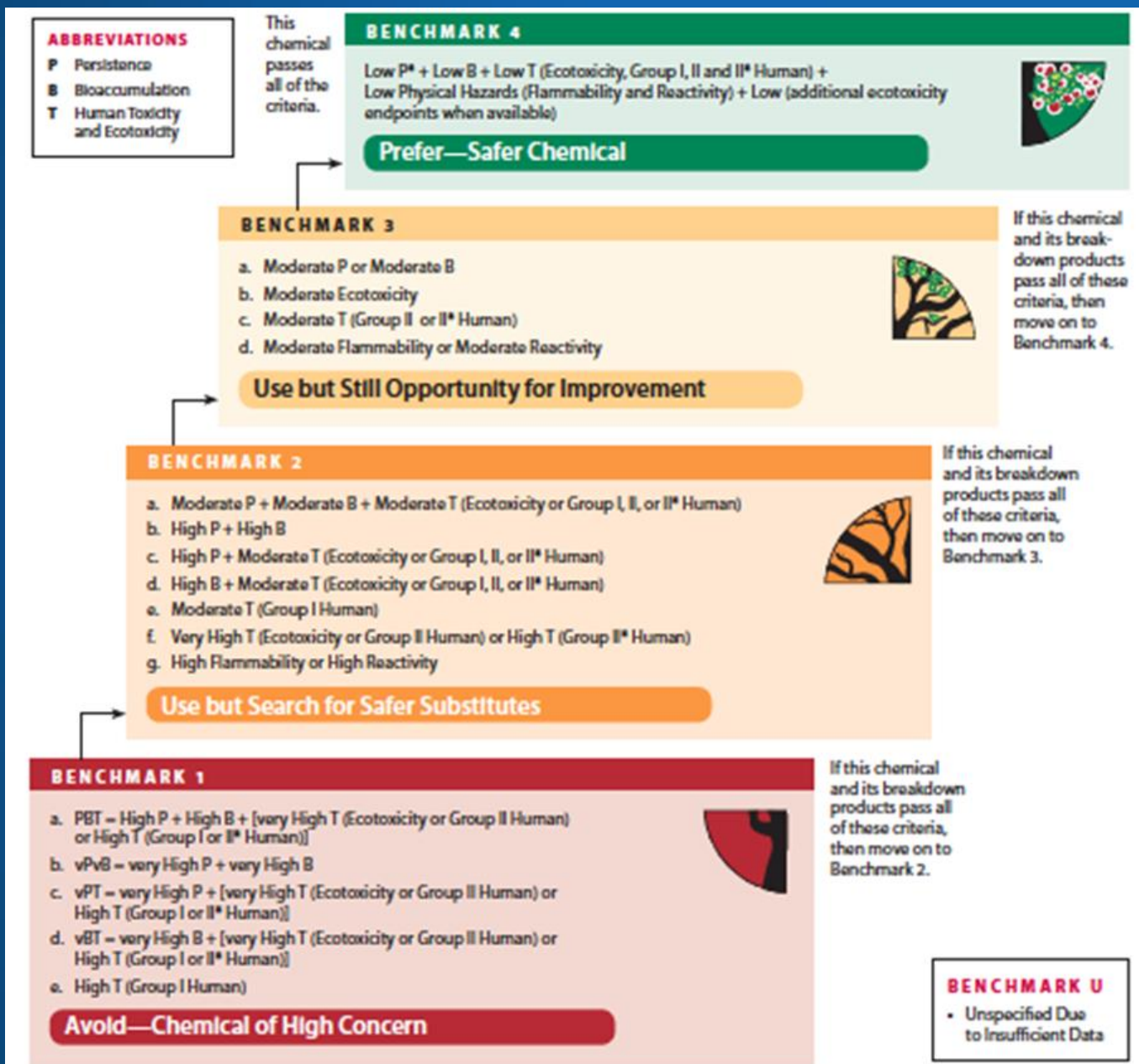
Level of Confidence

Bold H, M, or L = measured data or high quality surrogate

DG= data gap

Italic H, M, or L = estimated data (analog or model)

Step 2: Identify Benchmark Score from Hazard Classifications



The combination of hazard classifications for 18 assessed endpoints (Step 1) translates into a Benchmark score ranging from 1-4

A Benchmark score supports decision-making:

- BM1 – phase out
- BM2 – manage to use safely
- BM3 – getting there
- BM4 – inherently low hazard

Benchmark U = Undetermined due to insufficient data

← Aligned with Regulatory Drivers

Step 2, cont'd: Benchmark 2 Chemical

Group I Human					Group II and II* Human							Ecotox	Fate		Physical		
Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity	Neurotoxicity	Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Aquatic Toxicity	Persistence	Bioaccumulation	Stability	Flammability
					S	R*	S	R*	*								
L	M	L	L	L	M	H	H	M	M	L	L	H	H	M			

Chemical A is a BM 2 chemical

--Meets BM 2e classification

--Meets BM 2f classification

GS BENCHMARK 2

- a. Moderate P + Moderate B + Moderate T (Ecotoxicity or Group I, II, or II* Human)
- b. High P + High B
- c. High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)
- d. High B + Moderate T (Ecotoxicity or Group I, II, or II* Human)
- e. Moderate T (Group I Human)
- f. Very High T (Ecotoxicity or Group II Human) or High T (Group II* Human)
- g. High Flammability or High Reactivity

Use but Search for Safer Substitutes



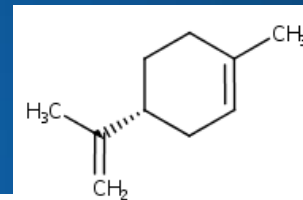
Chemical Name	GreenScreen Benchmark	Rationale
Chemical A	2 - Orange	2e. Moderate Mutagenicity/Genotoxicity 2f. High Systemic Toxicity - Repeated Exposure

Step 3: Making Informed Decisions

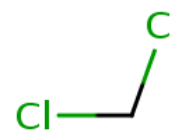
- GreenScreen scores can be used without toxicology training
- Use a chemical's full GreenScreen hazard table, not just the Benchmark score when comparing hazards of chemicals
- Consider the chemical's specific application and use
- Apply Risk Management as part of your decision-making

As we've heard earlier in the conference, all chemicals need risk management, but it's a lot easier with inherently safer chemicals...

D-Limonene, BM=2



Methylene chloride, BM=1

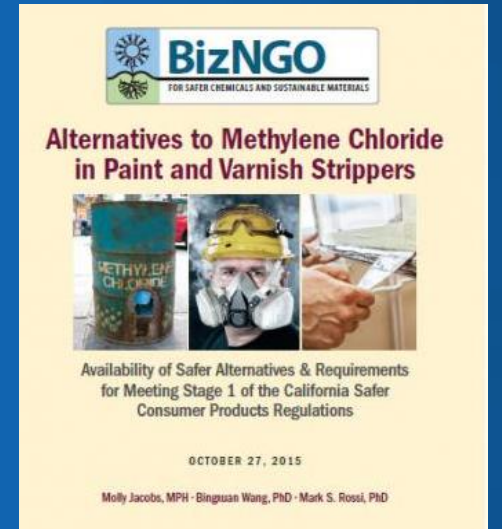
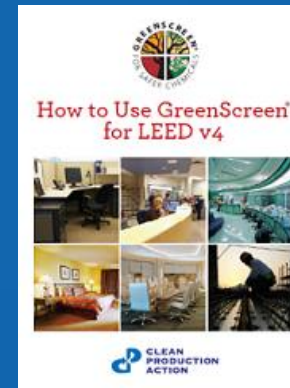


Using GreenScreen to Promote Chemical Optimization throughout the Supply Chain



GreenScreen drives chemical optimization:

- RSL/MRSL creation
- Preferred materials/positive lists
- Integral part of alternatives assessments
- Guide new product development
- Part of ecolabels and standards

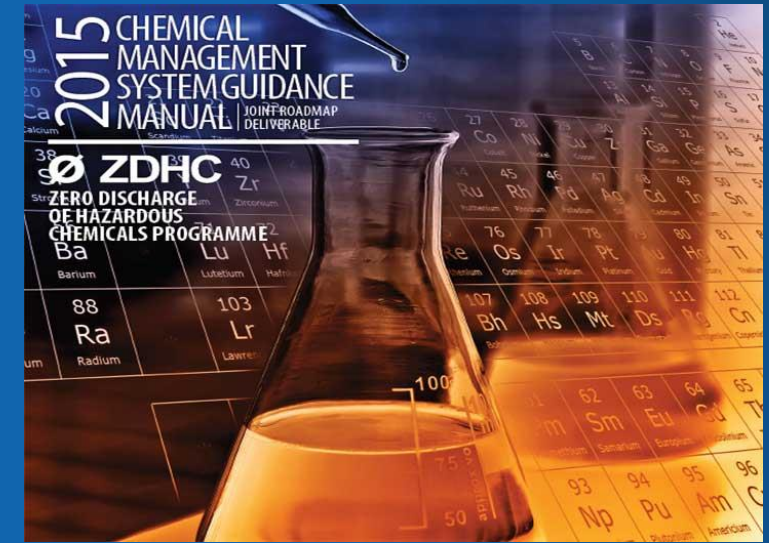


Ø ZDHC

Driving Hazard Reduction in Supply Chains: MRSL and RSL

GreenScreen is used to populate Restricted Substances Lists (RSLs) as well as Manufacturing Restricted Substances Lists (MRSLs)

- An MRSL differs from an RSL: An MRSL restricts levels of hazardous substances in formulations used and potentially discharged into the environment during manufacturing, not just chemicals present in finished products.
- MRSLs are important for industries that utilize formulations that can be released to the environment in large quantities (textile, apparel, footwear sectors)



The Zero Discharge of Hazardous Chemicals (ZDHC) coalition included GreenScreen and GreenScreen List Translator as part of creating the ZDHC MRSL

(<http://www.roadmaptozero.com/programme-documents/>)

ZDHC MRSL

CAS No.	Substance	Group A: Raw Material and Finished Product Supplier Guidance	Group B: Chemical Supplier Commercial Formulation Limit
Alkylphenol (AP) and Alkylphenol Ethoxylates (APEOs): including all isomers			
104-40-5, 11066-49-2 25154-52-3 84852-15-3	Nonylphenol (NP), mixed isomers	No intentional use	250 ppm
140-66-9 1806-26-4 27193-28-8	Octylphenol (OP), mixed isomers		250 ppm
9002-93-1 9036-19-5 68987-90-6	Octylphenol ethoxylates (OPEO)		500 ppm

Driving Hazard Reduction in Supply Chain: Positive Lists

- Levi Strauss & Co. uses GreenScreen for formulations used throughout the textile manufacturing process
 - <http://www.greenscreenchemicals.org/news/article/QA-bart-sights>



Chemical Hazard Summary Table of Chemicals Used in Formulation REDACTED																								
Chemical (FMDC#)	CAS RN	Functional use	% in Ingredient	Group 1 Human Health					Group II and II* Human Health							Ecotox.		Fate		Physical		GreenScreen® Benchmark Score, SCP Screen Results		
				Carcinogenicity	Mutagenicity	Reproductive	Developmental	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity	Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic	Chronic Aquatic	Persistence	Bioaccumulation	Reactivity		Flammability	
										s	r*													s
REDACTED																								
(FMDC-634)	[REDACTED]	Carrier	Redacted	U.S. EPA SCIL Full Green Circle		
(FMDC-604)	[REDACTED]	Mediator	Redacted	L	L	L	L	DG	L	DG	L	DG	DG	M	DG	H	H	M	M	vL	vL	M	L	Benchmark 3



GreenScreen in Alternatives Assessments

A Chemical Hazard Assessment is a critical component of a Chemical Alternatives Assessment (CAA)

- A CHA can be performed as part or independently of a full CAA

The Six Steps of a CAA are shown below:

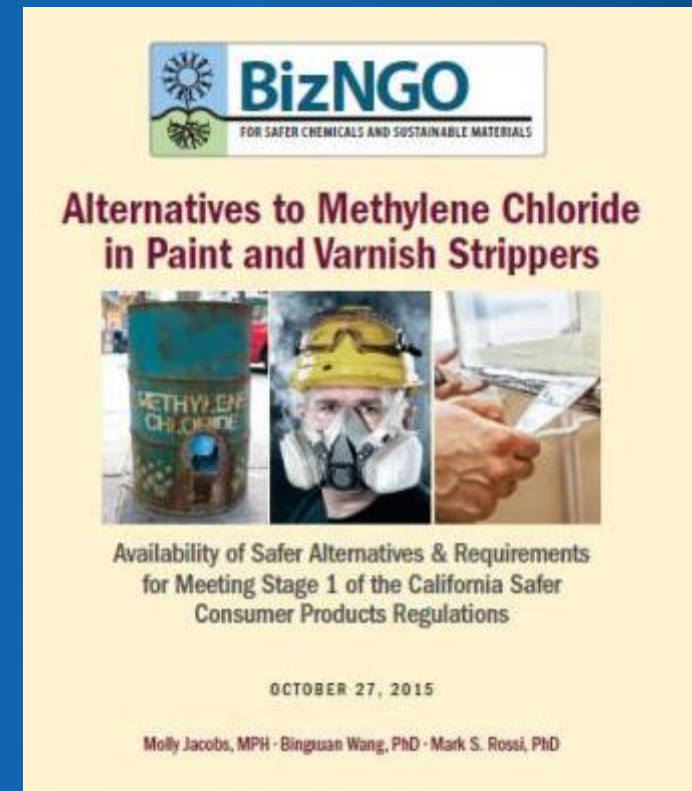
- **Chemical hazard assessment (CHA):** a systematic process of assessing and classifying hazards across an entire spectrum of endpoints and severity
- Life cycle thinking
- Exposure assessment
- Technical/functional assessment
- Economic assessment
- Social impact assessment

GreenScreen in Alternatives Assessments

GreenScreen was recently used as part of a BizNGO project to:

- (1) Identify less hazardous alternatives to methylene chloride in paint stripper products
- (2) Identify candidate alternatives for methylene chloride in paint stripping formulations that will likely be considered in actual/future Stage 1 submissions for this “priority product” in California; and
- (3) identify challenges and needs confronting compliance with the California SCP alternatives analysis process

<http://www.greenscreenchemicals.org/news/article/methylene-alternatives-assessment-new-report-webinar>



GreenScreen in Alternatives Assessments

Chemical Name	CASRN	Group I Human					Group II & II Human								Ecotox		Fate		Physical		Benchmark Score	
		C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	RX		F
								Single	repeated	Single	repeated											
Methylene chloride	75-09-2	H	NE	DG	DG	M	M	vH	H	vH	vH	L	DG	H	H	M	L	vH	vL	L	L	1
Benzyl alcohol	100-51-6	L	L	L	M	DG	M	L	L	M	H	H	L	L	H	L	L	vL	vL	L	L	2
2-(2-butoxyethoxy) ethanol	112-34-5	L	L	L	L	DG	L	L	H	DG	L	L	DG	M	H	L	L	vL	vL	L	M	2
Dimethyl sulfoxide	67-68-5	L	L	L	L	DG	L	L	L	L	L	L	L	M	M	L	L	L	vL	L	M	3
1,3-dioxolane	646-06-0	L	M	M	M	DG	L	M	M	M	L	L	DG	M	H	L	L	M	vL	L	H	2
Estasol (dibasic esters mixture)	95481-62-2	L	L	L	M	M	L	M	M	M	DG	L	DG	L	M	M	L	vL	vL	M	L	2
d-Limonene	5989-27-5	L	L	DG	L	DG	L	L	L	DG	DG	H	DG	H	H	vH	H	vL	M	L	M	2
Acetone	67-64-1	L	L	M	M	DG	L	M	M	M	M	L	DG	L	H	L	L	vL	vL	L	H	2
Methanol	67-56-1	NA	NA	NA	H	NA	H	vH	NA	NA	NA	NA	NA	NA	NA	L	L	vL	vL	NA	H	1
Toluene	108-88-3	DG	L	H	H	M	L	M	H	M	H	L	DG	H	L	H	H	H	vL	L	H	1
Formic acid	64-18-6	L	L	L	L	DG	H	vH	H	vH	DG	L	DG	vH	vH	M	M	vL	vL	L	M	2
Caustic soda	1310-73-2	L	L	L	L	L	H	vH	L	L	L	L	DG	vH	vH	M	DG	L	vL	M	L	2

GreenScreen in Alternatives Assessments

- Two alternatives (methanol and toluene) were screened out due to high developmental/reproductive toxicity (BM 1 scores for each)
- The remaining alternatives were safer, yet not free of hazards
 - DMSO has the lowest hazard profile (BM 3), but it can potentiate the hazards of other substances
- The project demonstrated that GreenScreen® is a useful tool in assessment in alternatives assessment
- Additional information about a substance – such as conditions of use – needs to be considered in addition to hazard

Chemical	Benchmark Score
Methylene chloride	1
Benzyl alcohol	2
2-(2-Butoxyethoxy) ethanol	2
Dimethyl sulfoxide (DMSO)	3
1,3-Dioxolane	2
Estasol (dibasic esters mixture)	2
d-Limonene	2
Acetone	2
Methanol	1
Toluene	1
Formic acid	2
Caustic soda	2

GreenScreen in Ecolabels and Standards



GreenScreen is now incorporated into multiple ecolabels and standards:

- TCO Certified Displays Standard 7.0 now requires all non-halogenated flame retardants to be assessed and have a Benchmark score of ≥ 2
 - <http://tcodevelopment.com/>
- U.S. Green Building Council Leadership in Energy & Environmental Design (LEED) specifies GreenScreen and GreenScreen List Translator to obtain different credits:
 - LEED v4 Option 1: Material Ingredient Reporting (1 point), and Option 2: Optimization (1 point)
 - <http://www.greenscreenchemicals.org/info/how-to-leed-report-download>

TCO DEVELOPMENT

Mandate A.6.4.3:

Non halogenated flame retardants used in plastic parts that weigh more than 25 grams shall be on the publicly available Accepted Substance List for TCO Certified. This means that the substance has been assessed by a licensed profiler according to GreenScreen™ and been assigned a benchmark score ≥ 2

The following acceptance decisions apply to substances given Benchmarks 4, 3, 2, 1 or designated U (undefined):

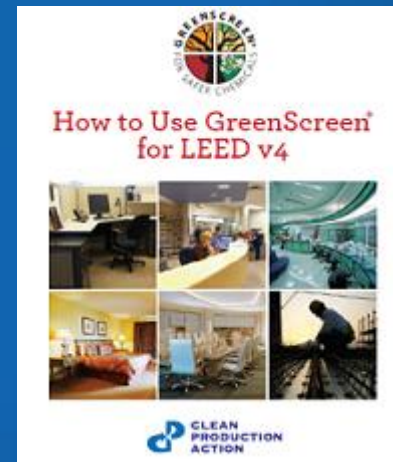
4: Accepted – (Few concerns)

3: Accepted – (Slight concern)

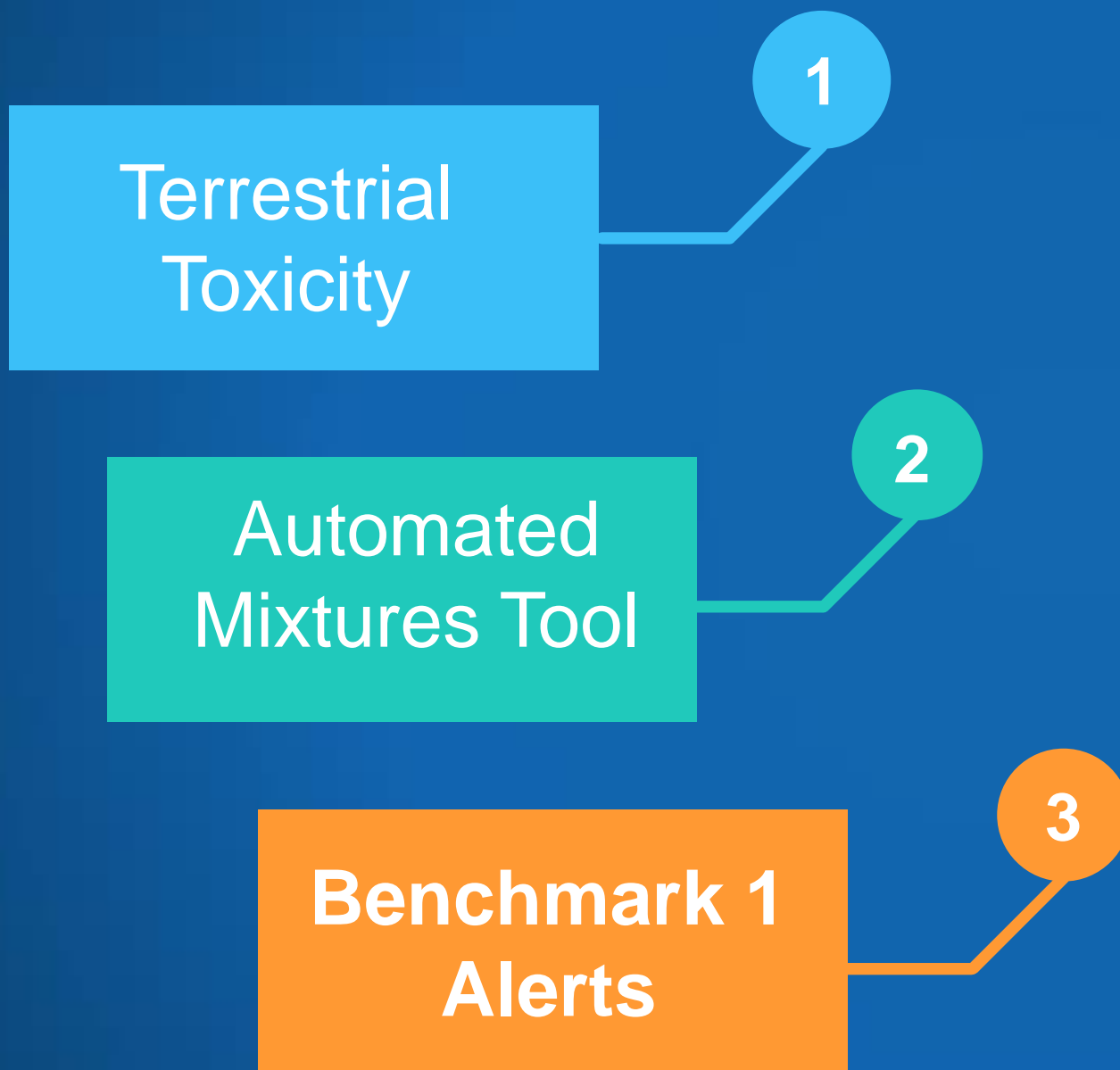
2: Accepted – (Moderate concern)

1: Not accepted - (High concern)

U: Not accepted - (Unspecified)



What are New Developments in Tools to Select Safer Chemicals?



Incorporating Terrestrial Toxicity Endpoints into GreenScreen

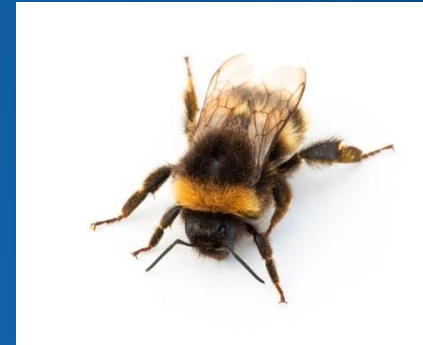
Human Health Group I	Human Health Group II and II*	Environmental Toxicity & Fate	Physical Hazards
Carcinogenicity	Acute Toxicity	Acute Aquatic Toxicity	Reactivity
Mutagenicity & Genotoxicity	Systemic Toxicity & Organ Effects	Chronic Aquatic Toxicity	Flammability
Reproductive Toxicity	Neurotoxicity	Other Ecotoxicity Studies when available*	
Developmental Toxicity	Skin Sensitization	Persistence	
	Respiratory Sensitization		
Endocrine Activity	Skin Irritation	Bioaccumulation	
	Eye Irritation		

Standard GreenScreens evaluate aquatic toxicity for environmental toxicity

- The GreenScreen procedure specifies that additional ecotoxicity endpoints may be included when relevant
- Terrestrial/Foliar Invertebrate toxicity is the ability of a chemical to pose an adverse health effect to a species that lives on land (bees, birds, soil organisms)
- Three neonicotinoid pesticides were GreenScreened and assessed terrestrial and bird and bee toxicity
 - Evaluating “other” ecotoxicity studies is relevant because these formulations are applied to crops

Incorporating Terrestrial Toxicity Endpoints into GreenScreens

- Neonicotinoids (also called “neonics”) are a relatively new type of insecticide, marketed in the last 20 years:
 - Used to control sap-feeding insects, such as aphids on cereals and root-feeding grubs
 - They are systemic pesticides and are taken up by the plant and remain active in the plant for many weeks
 - Neonics are the most widely used insecticides worldwide – their total share of the global market for insecticides is at least **30%** and is worth at least **\$2.6 billion**
 - Neonics don’t kill bees, instead they impair a bee’s ability to learn, navigate, forage for nectar, and reproduce



Environ Sci Pollut Res (2015) 22:5–34
DOI 10.1007/s11356-014-3470-y

WORLDWIDE INTEGRATED ASSESSMENT OF THE IMPACT OF SYSTEMIC PESTICIDES ON BIODIVERSITY AND ECOSYSTEMS

Systemic insecticides (neonicotinoids and fipronil): trends, uses, mode of action and metabolites

N. Simon-Delso · V. Amaral-Rogers · L. P. Belzunces · J. M. Bonmatin · M. Chagnon · C. Downs · L. Furlan · D. W. Gibbons · C. Giorio · V. Girolami · D. Goulson · D. P. Kreutzweiser · C. H. Krupke · M. Liess · E. Long · M. McField · P. Mineau · E. A. D. Mitchell · C. A. Morrissey · D. A. Noome · L. Pisa · J. Settele · J. D. Stark · A. Tapparo · H. Van Dyck · J. Van Praagh · J. P. Van der Sluijs · P. R. Whitehorn · M. Wiemers

LETTER

doi:10.1038/nature16167

Neonicotinoid pesticide exposure impairs crop pollination services provided by bumblebees

Dara A. Stanley¹, Michael P. D. Garratt², Jennifer B. Wickens², Victoria J. Wickens², Simon G. Potts² & Nigel E. Raine^{1,3}

Recent concern over global pollinator declines has led to considerable research on the effects of pesticides on bees^{1–5}. Although pesticides are typically not encountered at lethal levels in the field, there is growing evidence indicating that exposure to field-realistic levels can have sublethal effects on bees, affecting their foraging behaviour^{1,6,7}, homing ability^{8,9} and reproductive success^{2,5}. Bees are essential for the pollination of a wide variety of crops and the majority of wild flowering plants^{10–12}, but until now

pollination services¹⁸. Bumblebees are major pollinators of apples¹⁹ and many other crops across the world¹², and are exposed to low levels of pesticides when foraging in agricultural areas. Here we investigated how exposure to low, field-realistic levels of a widely used neonicotinoid insecticide (thiamethoxam) could affect the ability of bumblebees to pollinate apple trees. We pre-exposed colonies to 2.4 parts per billion (ppb) thiamethoxam, 10 ppb thiamethoxam or control solutions (containing no pesticide; rationale for selecting pesticide concentrations

Incorporating Terrestrial Toxicity Endpoints into GreenScreen

- Three neonics were GreenScreened, and DfE Alternatives Assessment terrestrial toxicity criteria were incorporated
 - All three neonics were BM 1 chemicals

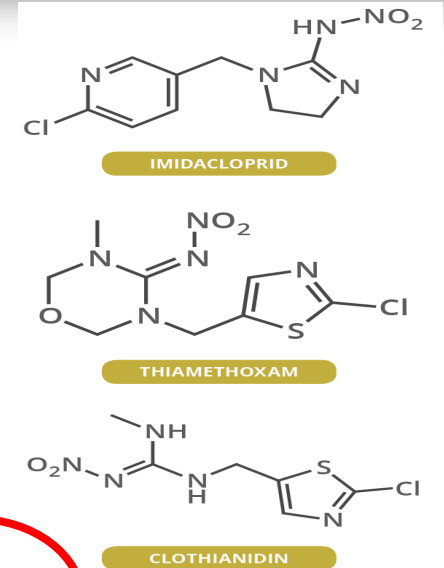


Table 15. Criteria for Other Forms of Ecotoxicity [49]

Ecotoxicity	Very High	High	Moderate	Low	Very Low
Avian (acute oral, mg/kg)	<10	10-50	51-500	501-2000	>2000
Avian (acute dietary, ppm)	<50	50-500	501-1000	1001-5000	>5000
Bees (acute, µg/bee)	--	<2	2-11	>11	--

	Group I Human					Group II and II* Human								Ecotox				Fate		Physical		
	C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	ATV	AFI	P	B	Rx	F
							single	repeated*	single	repeated*												
Imidacloprid	L	L	M	M	L	H	vH	M	vH	M	L	DG	L	L	vH	vH	H	H	vH	vL	L	L
Thiamethoxam	L	L	M	L	L	M	L	M	H	L	L	DG	L	L	vH	L	L	H	vH	vL	L	L
Clothianidin	L	L	M	M	M	M	H	M	vH	H	L	DG	L	L	vH	vH	M	H	vH	vL	L	L

Acute Terrestrial Vertebrates Toxicity Score (ATV) Score (vH, H, M, or L): Includes birds and mammals

Acute Foliar Invertebrates and Pollinators (AFI) Toxicity Score (H, M, or L): Includes bees

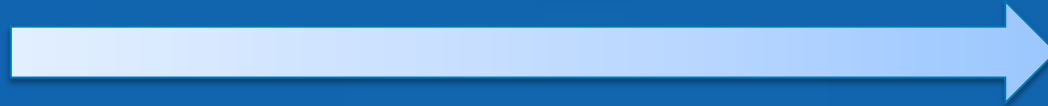
****Because the maximum score for AFI toxicity per DfE criteria is a High, a score of High was considered equivalent to a Very High for this endpoint for benchmarking purposes**

Assessing Hazards from Mixtures of Chemicals

The consideration of mixture toxicities is addressed within CLP Regulation 1272/2008 and GHS

- GHS in the EU was implemented in Regulation (EC) No. 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation) which is legally binding and directly applicable in the Member States of the EU, whereas GHS is not legally binding.
- GHS and CLP are not identical
 - Although CLP is based UN GHS “building block approach”, it does not include all the hazard categories included for a hazard class
 - e.g., category 4 of the hazard class for flammable liquids, or category 3 (mild irritant) of the hazard class for skin corrosion/irritation.

Tool #2: Incorporating CLP Mixture Criteria into GreenScreen



- Most chemical exposure occurs in the presence of multiple chemicals
 - However, most hazard and risk assessments are conducted on single chemicals
 - It is unrealistic to test every possible combination of chemicals
- GreenScreening mixtures
 - Most of the time, **data on a mixture are not available** and therefore, assessment of the GreenScreen's 18 hazard endpoints is not possible for an overall discrete chemical formulation
 - a **Benchmark score of U ("Hazard Unassignable")** is usually assigned for a mixture.
- Applying CLP's approach (additive/non-additive) of classifying hazards in a mixture is being investigated in order to assign an overall benchmark (BM) score for a mixture.

Incorporating CLP Mixture Criteria into GreenScreen

- Each of the 18 GreenScreen hazard endpoints in a mixture will receive a classification of concern ranging from High to Low based on CLP's mixture criteria for each hazard endpoint.
- The mixture score for each endpoint is automatically entered into the GreenScreen Inspector™ Tool to automatically derive an overall Benchmark score for the mixture.
 - This automated tool is undergoing peer review



Final Mixture
Benchmark

Classifying a Mixture Under CLP/GHS

Are available **test data** for the mixture sufficient for classification?

Yes

Classify the mixture for the relevant hazard

↓ **No**

Is there data available on **similar tested mixtures** and individual hazardous ingredients?

Yes

Is it possible to apply any of the **bridging principles**?

↓ **No**

Are hazard data available for all or some **ingredients**?

No

GreenScreen® tool is based on this

↓ **Yes**

Use calculation or cut-off value/concentration limits to classify?
(**Additive** and **non additive** approach)

Classification of a Mixture Based on its Components

- To assign an overall benchmark for a mixture, it is necessary to identify ingredient substances of the mixture in addition to their concentrations and CLP classifications for each hazard endpoint.
- Classification of a mixture is based on concentration thresholds which require using Cut-Off Limits (limits of concern) and a Generic Concentration Limit (GCL) which triggers the classification
 - Cut-off value: are the minimum concentrations for a substance to be taken into account for classification purposes.
 - Generic Concentration limits (GCL): are the minimum concentrations for a substance which trigger the classification of a mixture if exceeded by the individual concentration or the sum of concentrations of relevant substances
- There are two different concepts about how a substance contributes to the classification of a mixture under CLP criteria: the Additive Approach and Non-Additive Approach

CLP Mixture Rules for Each Hazard Endpoint + GreenScreen Scoring

Non-additive	Additive
<ul style="list-style-type: none"> • Carcinogenicity (C) • Mutagenicity/Genotoxicity (M) • Reproductive Toxicity (R) • Developmental Toxicity (D) • Endocrine Toxicity (E) • Systemic Toxicity/Organ Effects (ST)(Single Exposure) • Systemic Toxicity/Organ Effects (ST)(Repeated Exposure) • Neurotoxicity (N) (Single Exposure) • Neurotoxicity (N) (Repeated Exposure) • Skin Sensitization (SnS) • Respiratory Sensitization (SnR) • Reactivity (Rx) • Flammability (F) 	<ul style="list-style-type: none"> • Acute Mammalian Toxicity (AT) (additivity formula) • Skin Irritation (IrS) • Eye Irritation (IrE) • Acute Aquatic Toxicity (AA) • Chronic Aquatic Toxicity (CA) • Persistence (P) • Bioaccumulation (B)

In the **Additive Approach**, concentrations of ingredients with the same hazard are added together

- if the sum of the concentrations of one or several classified substances in the mixture equals or exceeds the a generic concentration limit (GCL) set out for this hazard class/category, the mixture is classified for that hazard.

Under the **Non-Additive Approach**, if a mixture contains two chemicals, each below the GCLs defined for that hazard class, even if the sum of the two chemicals is above the limit, the mixture will not be classified.

Assessing Hazards from Mixtures of Chemicals

Snapshot of the ToxServices' Mixture Tool

The screenshot displays the ToxServices' Mixture Tool interface, which is divided into three main worksheets:

- Data Input Worksheet (Auto GreenScreen™ Score):** This is the top worksheet. It features a table with columns for 'Inorganic Chemical?', 'Chemical Name', 'Chemical State', 'CAS#', 'Ingredient %', and 18 hazard endpoints. The endpoints are grouped into 'Group I Human' (Carcinogenicity, Mutagenicity/Genotoxicity, Reproductive Toxicity, Developmental Toxicity, Endocrine Activity, Acute Toxicity, Systemic Toxicity), 'Group II and III Human' (Neurotoxicity, Skin Sensitization*, Respiratory Sensitization, Skin Irritation, Eye Irritation), and 'Ecotox' (Acute Aquatic Toxicity, Chronic Aquatic Toxicity). Other endpoints include Persistence, Bioaccumulation, Reactivity, and Flammability. The table also includes 'Primary GreenScreen™ Benchmark Score', 'Final GreenScreen™ Benchmark Score', and 'PBT Check'. A red oval highlights the first three rows of data, and a green oval highlights the 18 hazard endpoint columns.
- Data Output Worksheet (GreenScreen® Mixture Benchmarking):** This is the middle worksheet. It shows the calculated hazard scores for the 18 endpoints for each component of the mixture. A red oval highlights the 'Formulated End Points' row, which shows scores of 1, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2. A green oval highlights the 18 hazard endpoint columns.
- ATE Calculation Worksheet (ATE Calculator):** This is the bottom worksheet. It contains a 'Hazard Summary Table' and a 'Datagap Assessment Table'. The Hazard Summary Table shows a benchmark score of 1 (No) for all endpoints. The Datagap Assessment Table shows a datagap score of 1 (No) for all endpoints. A red oval highlights the 'ATE Calculator' tab in the bottom navigation bar.

Data input worksheet: Each row represents one component of the mixture.

the GreenScreen® hazard scores for the 18 endpoints for the product mixture

Final Benchmark hazard score for the product mixture

Tool consists of three worksheets : Data input, Data output and ATE calculation

Automated Mixtures Tool: Reproductive Toxicity(R) (Non-Additive)

GreenScreen hazard classification of High (H) for Reproductive Toxicity corresponds to CLP Category 1A/1B classification

- If the final mixture contains at least one ingredient that is present in the mixture at $\geq 0.3\%$ and has a GreenScreen hazard classification of High (classified to GHS Category 1A or 1B)

GreenScreen hazard classification of Moderate (M) corresponds to CLP Category 2 classification

- If the final mixture contains at least one ingredient that is present in the mixture at $\geq 3.0\%$ and has a GreenScreen hazard classification of Moderate (classified to GHS Category 2 for this endpoint).

Ingredient Classified as:	Cut-off/concentration limits triggering classification of a mixture as:		
	Category 1 reproductive toxicant		Category 2 reproductive toxicant
	Category 1A	Category 1B	
Category 1A	$\geq 0.3\%$	--	--
Category 1B	--	$\geq 0.3\%$	
Category 2 Carcinogen	--	--	$\geq 0.1\%$ [Note 1]
			$\geq 3.0\%$ [Note 2]

Note 1: If a Category 2 reproductive toxicant ingredient is present in the mixture at a concentration between 0.1% and 3.0%, every regulatory authority would require information on the SDS for that product. However a label warning would be optimal.

Note 2: If a Category 2 reproductive toxicant ingredient is present in the mixture at a concentration of $\geq 3\%$, both an SDS and a label would generally be expected.

Example: Calculating Overall Mixture Hazard Classification for Reproductive Toxicity



Auto GreenScreen™ Score



Table 1: Hazard Table

Enter Material Name :

Inorganic Chemical?	Chemical Name	Chemical State	CAS#	Ingredient %	Auto GreenScreen™ Score																		Preliminary GreenScreen™ Benchmark Score	Final GreenScreen™ Benchmark Score	PBT Check		
					Group I Human					Group II and II+ Human								Ecotox		Fate		Physical					
					Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*		Respiratory Sensitization*		Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity				Persistence	Bioaccumulation
C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F								
No		Liquid	1	38%	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	4	4			
No		Solid	2	12%	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	4	4			
No		Liquid	3	1%	L	L	M	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	2	2			
No			4	7%	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	4	4			
No			5	3%	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	4	4			
No			6	15%	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	4	4			

GreenScreen® Mixture Benchmarking

Inorganic?	vh	L (DG Threshold)	25.00%	25.00%	10.00%	25.00%	25.00%	25.00%	25.00%	0.10%	5.00%	1.00%											
M	1.00%	1.00%	20.00%	10.00%	1.00%	0.20%	1.00%	0.20%	1.00%	1.00%	5.00%	5.00%											
H	0.10%	0.30%	1.00%	1.00%	1.00%	0.20%	1.00%	0.20%	1.00%	1.00%	5.00%	5.00%											
Formulated End Points	C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F	L	L	L
assessed for this endpoint due to data gaps	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	No	No	No		
2	No	No	No	No	No	No	No
3	No	No	No	No			
4	STOP						

Chemical Name	Preliminary GreenScreen® Benchmark Score
	4

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Final GreenScreen® Benchmark Score
4

After Data Gap Assessment
Note: No Data Gap Assessment Done if Preliminary GS Benchmark Score is 1.

Datagap Assessment Table

atagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2												
3												
4	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	4

The mixture was classified as Low (L) for reproductive toxicity based on not meeting the criteria for Moderate scoring.

Although the mixture contains one ingredient (CAS# 3) with a Moderate (M) classification for reproductive toxicity, it is present below the threshold set for Moderate (3%) and is not considered in the final Benchmark score.

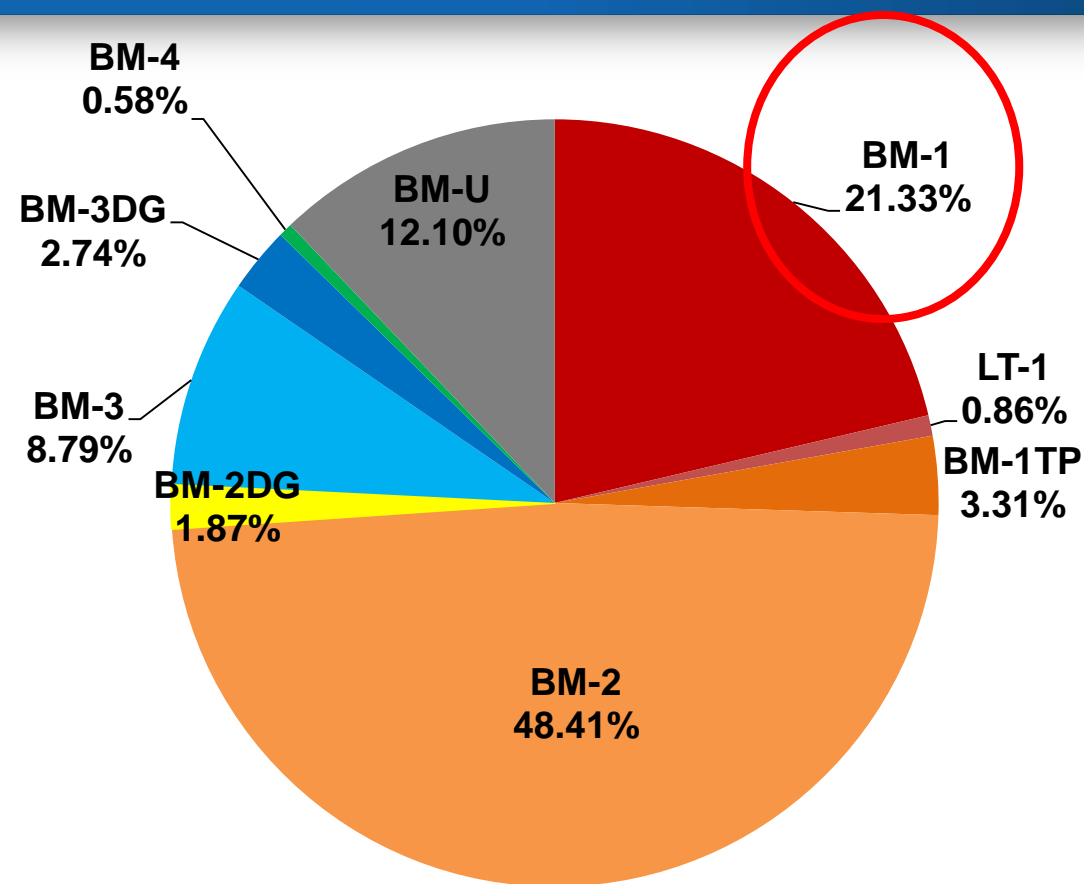
The mixture was assigned an overall Benchmark score of 4

New Development #3: Benchmark 1 Structural Alert Project

To date, approximately 20% of GreenScreened chemicals are classified as Benchmark 1 chemicals:

- Many of these are CMRs/PBTs and total >150 chemicals

A project with the Univ. of Mass-Lowell is underway to assess the chemical structures of Benchmark 1 chemicals in order to create an overall Benchmark 1 composite structure



GS BENCHMARK 1

- PBT = High P + High B + [very High T (Ecotoxicity or Group II Human) or High T (Group I or II* Human)]
- vPvB = very High P + very High B
- vPT = very High P + [very High T (Ecotoxicity or Group II Human) or High T (Group I or II* Human)]
- vBT = very High B + [very High T (Ecotoxicity or Group II Human) or High T (Group I or II* Human)]
- High T (Group I Human)



Avoid—Chemical of High Concern

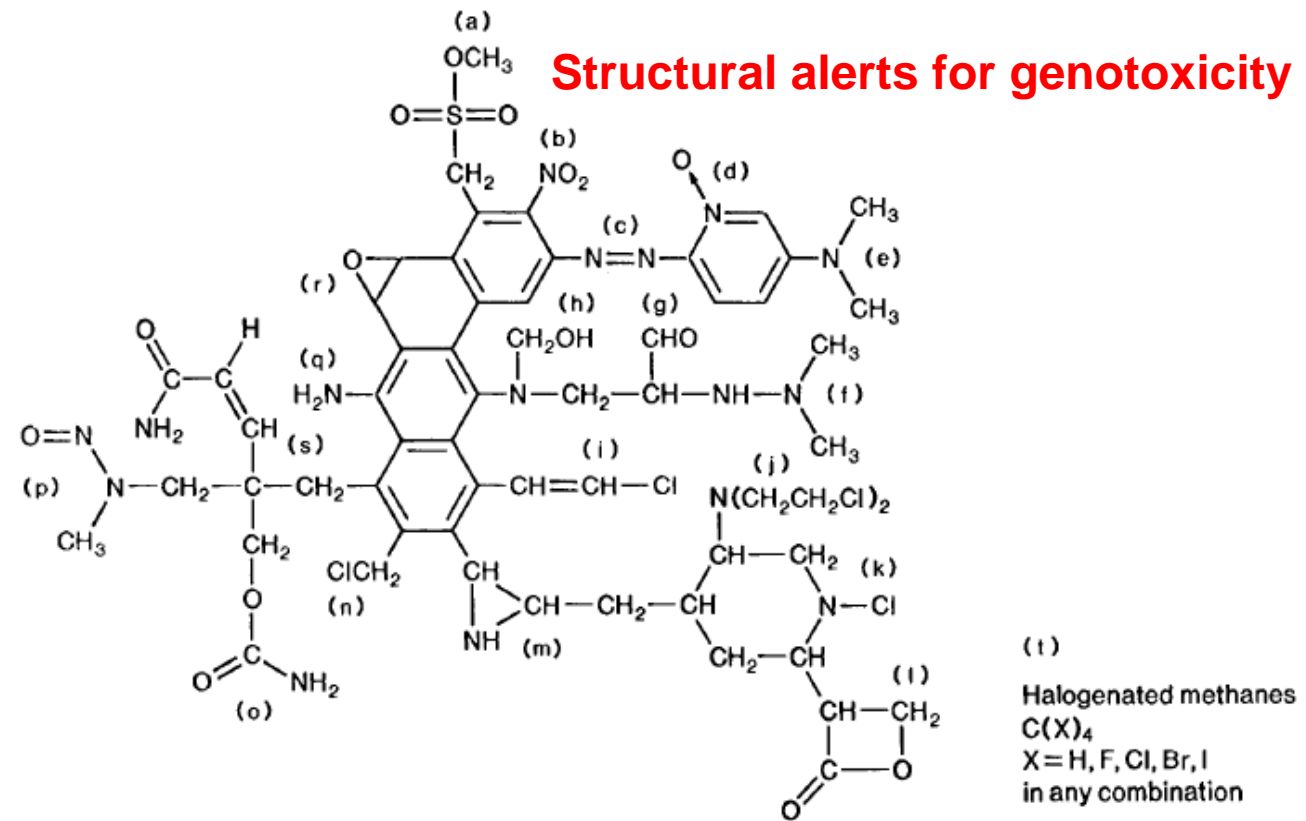
Benchmark 1 Structural Alert Project

In toxicology, the Ashby and Tennant composite structure for genotoxic alerts is well-known

- Easily depicts potential genotoxins, and is useful for carcinogenicity prediction

The 148 chemicals currently classified as BM-1 chemicals come from numerous chemical classes

- In a manner similar to Ashby and Tennant, the BM-1 structural alert project will identify an overall structure useful for predicting significant human health and environmental hazards
- Such a structure would be helpful during the chemical formulation process and easily flag potential problems



Ashby and Tennant (1988, 1989)

Conclusions

- The GreenScreen continues to evolve in order to incorporate best practices associated with assessing human health and environmental hazards
- Work is underway to incorporate mixtures assessment rules into the GreenScreen Inspector™, which is a freely available tool
 - Peer review of the tool is expected to take 8-12 months
- Future action items:
 - Securing on-going funding to make the >700 GreenScreens publicly accessible

Thank you!

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