

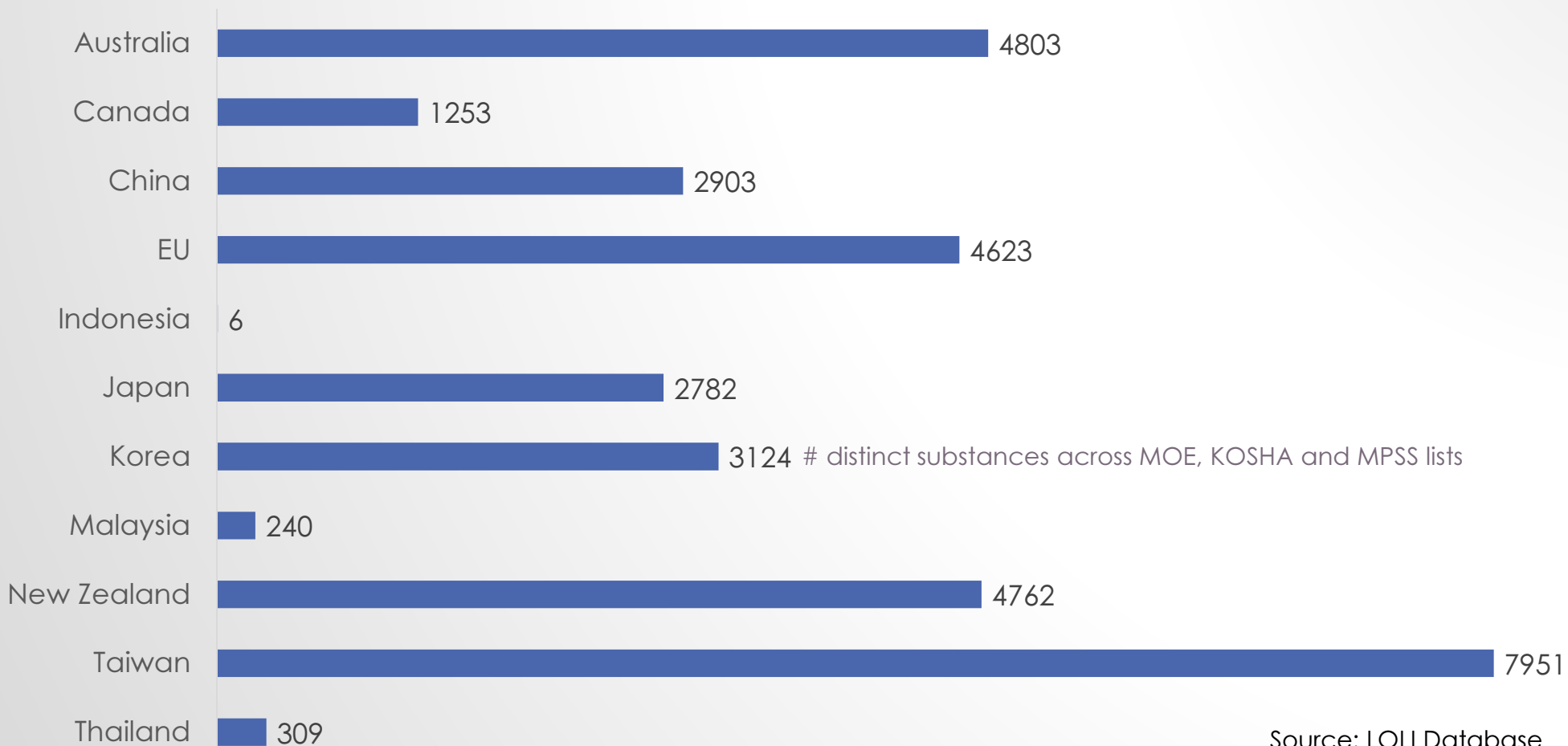
# Observations: UN Global List Pilot Project versus Published GHS Classifications

**Darlene Susa-Anderson**

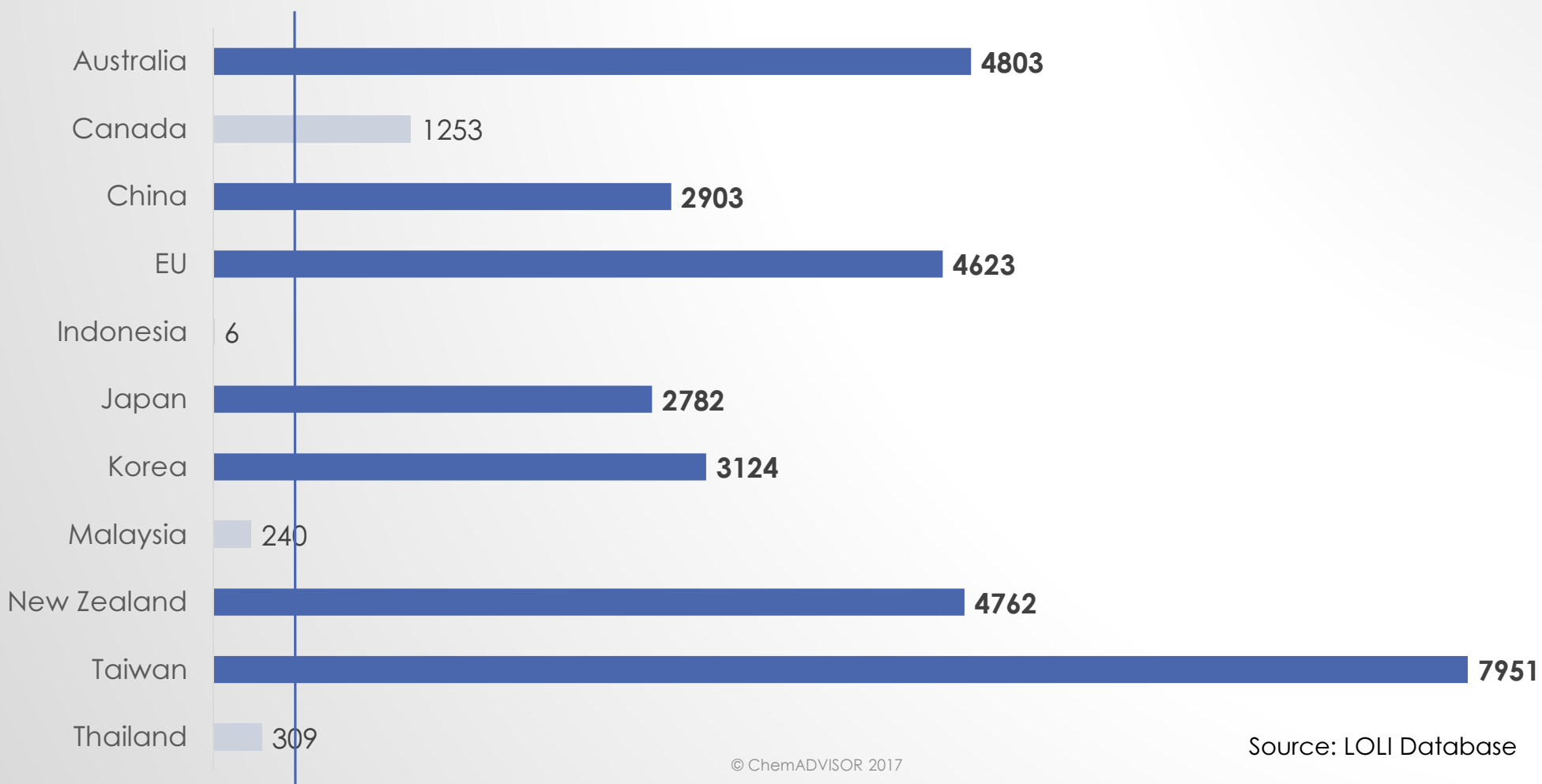
March 28, 2017



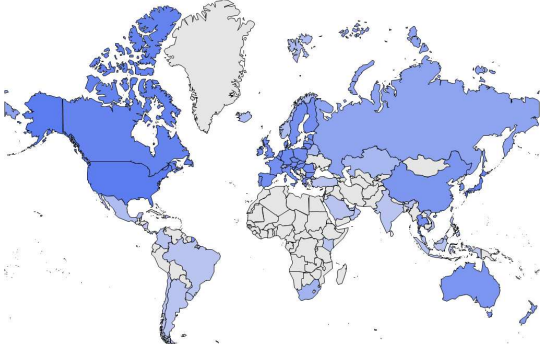
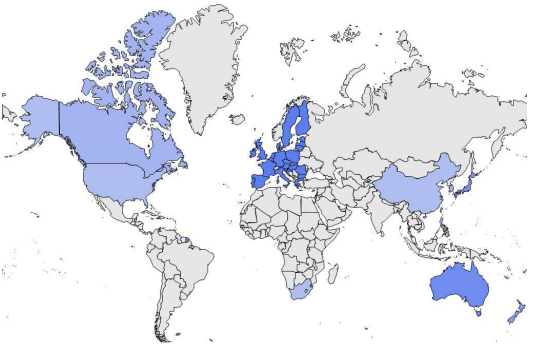
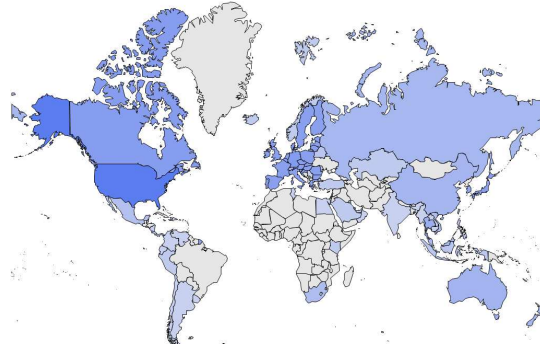
## Published GHS Classifications



## Published GHS Classifications



# Pilot Project: Chemical Selection

Dicyclopentadiene	Dimethyltin dichloride	Di-n-butyl phthalate
77-73-6	753-73-1	84-74-2
 <p>Source: LOLI Database</p>	 <p>Source: LOLI Database</p>	 <p>Source: LOLI Database</p>
Russia	European Chemicals Agency	United States of America
Flammable Liquid – Cat. 3 Acute Toxicity – Oral – Cat. 3 Acute Toxicity – Dermal – Cat. 5 Acute Toxicity – Inhalation – Cat. 2 Skin Corrosion/Irritation – Cat. 2 Reproductive Toxicity – Cat. 2 STOT - SE – Cat. 3 STOT – RE – Cat. 2 Aspiration – Cat. 1 Aquatic Environment - Acute 1 Aquatic Environment – Chronic 2	Acute Toxicity – Dermal – Cat. 3 Acute Toxicity – Inhalation – Cat. 2 Acute Toxicity – Oral – Cat. 3 Skin Corrosion/Irritation – Cat. 1 Serious Eye Damage/Eye Irritation – Cat. 1 Reproductive Toxicity – Cat. 2 STOT – RE – Cat. 1 Aquatic Environment – Acute 3 Aquatic Environment – Chronic 3	Reproductive Toxicity – Cat. 1B Aquatic Environment – Acute 1 Aquatic Environment – Chronic 1

For each substance we will compare published country classifications to those of the pilot project and explore reasons for their discrepancies where possible.

New Zealand publishes source data for showing justifications for classifications in its Hazardous Substances and New Organisms Chemical Classification and Information Database (HSNO CCID):

<http://www.epa.govt.nz/search-databases/Pages/HSNO-CCID.aspx>

Japan publishes data on chemicals in the National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHRIP):

[http://www.nite.go.jp/en/chem/chrip/chrip\\_search/systemTop](http://www.nite.go.jp/en/chem/chrip/chrip_search/systemTop)

# Dicyclopentadiene (DCPD)



	Australia	Canada	Canada HPR	China	European Union	Indonesia	Japan	Korea MOE	Korea MOEL	Korea MPSS	Malaysia	New Zealand	Taiwan	Thailand	Worst Case
Flammable liquids	2	3		2	2		3			3		3	3	3	2
<b>Flammable solids</b>							<b>1</b>							<b>1</b>	<b>1</b>
<b>Acute Toxicity - Dermal</b>							<b>5</b>					<b>5</b>		<b>5</b>	<b>5</b>
Acute Toxicity - Inhalation	4	2			4							3	2	2	2
Acute Toxicity - Oral	4	4			4		4	4				3	4	4	3
<b>Skin corrosion/irritation</b>	<b>2</b>	<b>2</b>		<b>2</b>	<b>2</b>		<b>2</b>	<b>2</b>				<b>2</b>	<b>2</b>	<b>2</b>	<b>2</b>
Serious eye damage/eye irritation	2			2	2		2B					2	2A	2B	2A
Specific target organ toxicity - Single exposure	3			3	3		1,3	1,3						1,3	1,3
Specific target organ toxicity - Repeated exposure							1,2	1,2				2	2	1,2	1,2
<b>Aspiration hazard</b>							<b>1</b>	<b>1</b>						<b>1</b>	<b>1</b>
<b>Hazardous to aquatic environment - acute hazard</b>				<b>2</b>			<b>2</b>							<b>2</b>	<b>2</b>
Hazardous to aquatic environment - chronic hazard	2			2	2		2	2				2,3	2	2	2
<b>Acute Toxicity - Inhalation - Vapour</b>							<b>2</b>	<b>2</b>							<b>2</b>
<b>Terrestrial vertebrate ecotoxicity</b>												<b>2</b>			<b>2</b>

# Dicyclopentadiene (DCPD)



Hazard Class	Australia	Canada	China	EU	Japan	Korea	NZ	Taiwan	Thailand	Joint	
Flammable Liquid	2	3	2	2	3		3	3	3	3	<a href="#">Slide 8</a>
Flammable Solid					1				1		
Acute Toxicity - Dermal					5		5		5	5	
Acute Toxicity - Inhalation	4	2		4			3	2	2	2	<a href="#">Slide 10</a>
Acute Toxicity - Inhalation - Vapor					2	2					
Acute Toxicity - Oral	4	4		4	4	4	3	4	4	3	<a href="#">Slide 10</a>
Skin Corrosion/Irritation	2	2	2	2	2	2	2	2	2	2	
Serious Eye Damage/Eye Irritation	2		2	2	2B		2	2A	2B		<a href="#">Slide 11</a>
Reproductive Toxicity										2	
Specific Target Organ Toxicity - Single Exposure	3		3	3	1, 3	1, 3			1, 3	3	
Specific Target Organ Toxicity - Repeated Exposure					1, 2	1, 2	2	2	1, 2	2	
Aspiration hazard					1	1			1	1	
Hazardous to the Aquatic Environment - Acute			2		2				2	1	<a href="#">Slide 13</a>
Hazardous to the Aquatic Environment - Chronic	2		2	2	2	2	2, 3	2	2	2	

Source: ChemADVISOR compiled

## Dicyclopentadiene – a Flammable ..?

Hazard Class	Australia	Canada	China	EU	Japan	Korea	NZ	Taiwan	Thailand	Joint
Flammable Liquid	2	3	2	2	3		3	3	3	3
Flammable Solid					1				1	

Within the flammable liquid classification countries the discrepant countries were Australia, China, and the EU so no justification is available to review. Japan and Thailand classified for liquid and solid states. Japan provided a rationale of flashpoint 23 to 60°C for Flammable Liquid Category 3, and a flashpoint of 32°C for Flammable Solid Category 1.

Table 2.6.1: Criteria for flammable liquids

Category	Criteria
1	Flash point < 23 °C and initial boiling point ≤ 35 °C
2	Flash point < 23 °C and initial boiling point > 35 °C
3	Flash point ≥ 23 °C and ≤ 60 °C
4	Flash point > 60 °C and ≤ 93 °C

Table 2.7.1: Criteria for flammable solids

Category	Criteria
1	Burning rate test: Substances or mixtures other than metal powders: (a) wetted zone does not stop fire; and (b) burning time < 45 s or burning rate > 2.2 mm/s Metal powders: burning time ≤ 5 min
2	Burning rate test: Substances or mixtures other than metal powders: (a) wetted zone stops the fire for at least 4 min; and (b) burning time < 45 s or burning rate > 2.2 mm/s Metal powders: burning time > 5 min and ≤ 10 min

**NOTE 1:** For classification tests on solid substances or mixtures, the tests should be performed on the substance or mixture as presented. If for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that which was tested and which is considered likely to materially alter its performance in a classification test, the substance must also be tested in the new form.

**NOTE 2:** Aerosols should not be classified as flammable solids. See Chapter 2.3.

Source: UN GHS Rev 6



## Dicyclopentadiene – a Flammable ..?

Purity	Melting Point	Boiling Point	Flash Point
97-100%	32.2C	172.2C	32.2C
<97%	<20C	172.2C	32.2C

Source Dow DCPD product handling guide as referenced in OECD comments of October 2015:

<http://www.dow.com/hydrocarbons/aromatics/srh/safety.htm>

### *Short summary and overall relevance of the provided information on flammable liquids*

No information on the primary sources of this data or the methods used for most studies is available. However, most of the data are taken from a reliable government source and is therefore considered to be suitable for use. The lowest flash point was measured for commercial DCPD (>80%) as >23 °C. The highest flash point was reported as 41°C. Apart from company data, the study reports don't provide information on physical state of the tested substances and its purity which also affects the physical state: the pure substance is a waxy solid at room temperature. Commercial grades with purity < 97% are liquid at room temperature. For the purpose of this exercise it is proposed to be assumed that flash points were obtained by testing a liquid substance: DCPD with purity < 97%.

### *Comparison with the GHS criteria*

In comparison with the GHS criteria all data on flash point of DCPD is within the range of Category 3:  $23^{\circ}\text{C} \leq (23^{\circ}\text{C} \div 41^{\circ}\text{C}) \leq 60^{\circ}\text{C}$ .

### *Conclusion on classification and labelling for flammable liquids*

According to the GHS criteria Category 3 for flammable liquids is proposed for liquid DCPD, including DCPD with purity < 97% based on the flash point.

Symbol: Flame.

Signal word: Warning.

Hazard statement: H226: Flammable liquid and vapour.

Source: REPORT ON THE PROPOSAL FOR CLASSIFICATION AND LABELLING (C&L) OF DICYCLOPENTADIENE

## Dicyclopentadiene (DCPD)

Acute Toxicity - Inhalation	4	2		4		3	2	2	2
-----------------------------	---	---	--	---	--	---	---	---	---

- New Zealand classified this substance as *Acute Toxicity Inhalation Category 3 (dust/mist)* and used a mouse LC<sub>50</sub> value for dust/mist.
- The pilot project referenced numerous animal studies (rat, mouse, rabbit, guinea pig, beagle dog) but did not include the mouse value used by NZ. They utilized the most reliable data and treated the material as a liquid with a vapor, leading to a classification as *Acute Toxicity Inhalation Category 2 (vapor)*.

Acute Toxicity - Oral	4	4		4	4	4	3	4	4	3
-----------------------	---	---	--	---	---	---	---	---	---	---

- Japan used a rat LD<sub>50</sub> range of 346.5-590 mg/kg to classify this substance as an *Acute toxicity oral category 4*.
- The pilot project referenced numerous animal studies (rat, mouse, cattle) and even had human data. However, they ultimately used mouse data to classify as an *Acute toxicity oral category 3*.

## Dicyclopentadiene (DCPD)

Serious Eye Damage/Eye Irritation	2	2	2	2B	2	2A	2B
-----------------------------------	---	---	---	----	---	----	----

- Japan used rabbit data of 'mild' and an EU classification of R36 to conclude a classification of *Serious eye damage/eye irritation category 2B*.
- The pilot project reviewed numerous rabbit and human data points.
- The data points mostly covered very mild, confined, and temporary (<24h) irritating effects. The human data which pointed to irritation did not have primary sources available.
- The pilot project decided not to classify this substance for this endpoint.

# Dicyclopentadiene (DCPD)

2	2	2	2B	2	2A	2B
---	---	---	----	---	----	----

- This was the only instance in which more than 50% of classifying countries provided a classification for a certain endpoint, and the pilot project did not classify at all. In all other cases, whenever most existing published classifications pointed towards a classification, one was applied (even if not the same *category*).
- The below tables show the number of countries (#) that classified for any given endpoint and whether the pilot group classified for that endpoint (Y/N).

Y	x			XX X		XX	XX		XX	X
N		x	XX					X		
Dicyclopentadiene #	0	1	2	3	4	5	6	7	8	9

↑ Serious Eye Damage/Eye Irritation classified by 7 countries, not by pilot project

Y		x								x	x
N		x	x	XX XX							
Dibutyl phthalate #	0	1	2	3	4	5	6	7	8	9	10

Y	XX	XXX XX	x
N			
Dimethyltin dichloride #	0	1	2

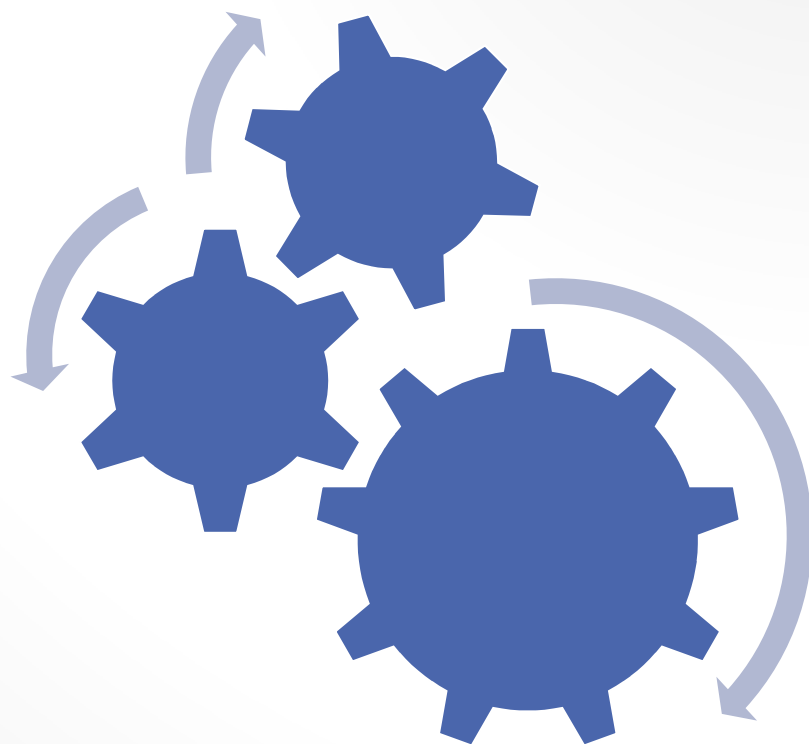
## Dicyclopentadiene (DCPD)

Hazardous to the Aquatic Environment - Acute		2		2			2	1
Hazardous to the Aquatic Environment - Chronic	2		2	2	2	2,3	2	2

- Japan used a 96 hour LC<sub>50</sub> value of 4.3 mg/L (*Oryzias latipes*) to classify this substance as *Hazardous to the aquatic environment acute category 2*. The pilot project had numerous data for all trophic levels (including this value) but concluded that water flea was the most sensitive species thus warranting a classification of *Hazardous to the aquatic environment acute category 1*.
- Japan, NZ and the pilot project all agree that Cyclopentadiene is not bioaccumulative and not rapidly degradable but NZ used fathead minnow and algae data to conclude a classification of *Hazardous to the aquatic environment chronic category 3* while the pilot project classified as *Hazardous to the aquatic environment chronic category 2*.

## Reflections

- State of matter played a role in differences.
- Different data points used.
- Data interpreted differently after extensive review of sources.



# Dimethyltin dichloride (DMTC)



	Australia	Canada	Canada HPR	China	European Union	Indonesia	Japan	Korea MOE	Korea MOEL	Korea MPSS	Malaysia	New Zealand	Taiwan	Thailand	Worst Case
<b>Acute Toxicity - Dermal</b>	<b>3</b>				<b>3</b>										<b>3</b>
<b>Acute Toxicity - Inhalation</b>	<b>2</b>				<b>2</b>										<b>2</b>
<b>Acute Toxicity - Oral</b>	<b>3</b>				<b>3</b>										<b>3</b>
Skin corrosion/irritation	1B				1B							2			1B
<b>Serious eye damage/eye irritation</b>												2			2
<b>Reproductive toxicity</b>	<b>2</b>				<b>2</b>										<b>2</b>
<b>Specific target organ toxicity - Repeated exposure</b>	<b>1</b>				<b>1</b>										<b>1</b>

# Dimethyltin dichloride (DMTC)



Hazard Class	European Union	New Zealand	Joint Pilot Project
Acute Toxicity - Dermal	3		3
Acute Toxicity - Inhalation	2		2
Acute Toxicity - Oral	3		3
Skin Corrosion/Irritation	1B	2	1
Serious Eye Damage/Eye Irritation		2	1
Reproductive Toxicity	2		2
Specific Target Organ Toxicity - Repeated Exposure	1		1
Hazardous to the Aquatic Environment - Acute			3
Hazardous to the Aquatic Environment - Chronic			3





## Dimethyltin dichloride: Published Classifications

Skin Corrosion/Irritation	1B	2	1
Serious Eye Damage/Eye Irritation		2	1

- New Zealand sourced their classifications from a company classification R38 + R36 (company was not specified).
- These EU DSD classifications convert to GHS *Category 2* for both endpoints using the HSNO Code of Practice Annex G translation table.
- The EU classification for 753-73-1 as R34 or Skin corrosion/irritation Category 1B was added in 2014 to Annex VI of the CLP.

### Dimethyltin dichloride

Cas Number: 753-73-1  
 Synonyms:  
 Molecular Weight:  
 Relative Density:  
 Water Solubility (mg/l):  
 Approval Number: HSR006086  
 UN Class:  
 UN Number:

#### Classification

6.3A	Irritating to the skin
6.4A	Irritating to the eye

#### Classification Data

6.3A	R PHRASE: R 38 [Company Data]
6.4A	R PHRASE: R 36 [Company Data]

Source: HSNO CCID

## Dimethyltin dichloride: Pilot Project Classifications

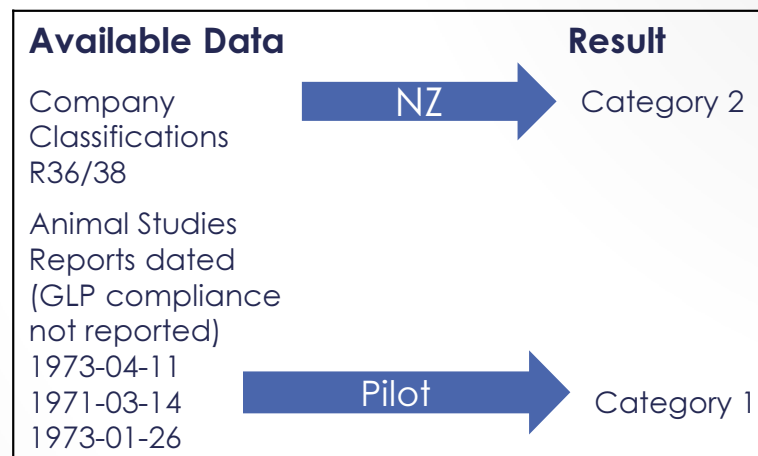
- The pilot project used animal test data.
- For skin corrosion, the data presented was from studies in 1970s and 1990s. The 1993b Rush study (GLP) was chosen as the primary source.
- The pilot project did not find sufficient information on how exposure time effects corrosivity to be able to distinguish between subcategories A/B/C.

Available Data		Result
Company Classifications R36/38	NZ →	Category 2
	EU →	Category 1B
Animal Studies: Rush (1993b) study	Pilot →	Category 1
Report, 1973	●	
Affiliated Medical Enterprises Inc., 1971c	●	

## Dimethyltin dichloride: Pilot Project Classifications

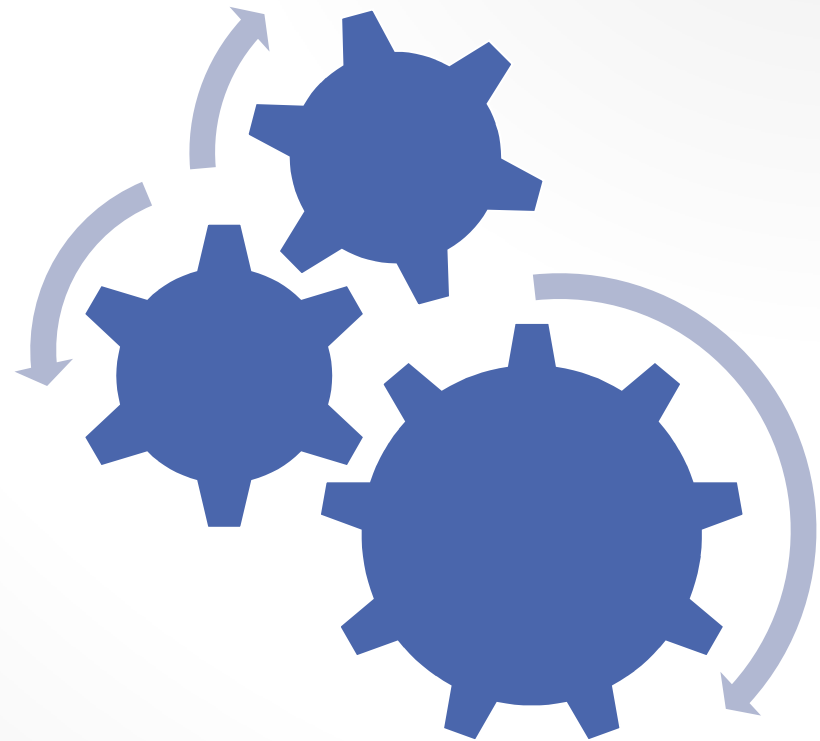
Serious Eye Damage/Eye Irritation **2** 1

- The pilot project used animal test data.
- For serious eye damage, the data presented was from studies in 1970s.
- In addition, the summary references the skin corrosivity identified.



## Reflections

- Primary reason for the difference with NZ is the use of company provided classifications versus actual data.
- We do not know if ECHA looked at different studies for the 2014 addition of Category 1B to Annex VI of the CLP, versus the pilot project led by ECHA arriving at Category 1.



# Di-n-butyl phthalate (DNBP)



	Australia	Canada	Canada HPR	China	European Union	Indonesia	Japan	Korea MOE	Korea MOEL	Korea MPSS	Malaysia	New Zealand	Taiwan	Thailand	Worst Case
<b>Acute Toxicity - Oral</b>												5		5	5
<b>Skin corrosion/irritation</b>														3	3
Serious eye damage/eye irritation									2A			2		2B	2A
<b>Skin sensitizers</b>							1	1						1	1
Specific target organ toxicity - Single exposure							3	1,3						1,3	1,3
Reproductive toxicity	1B	1			1B	1B	1	2		1B	1	1	1	2	1
Specific target organ toxicity - Repeated exposure							1	1,2						1,2	1,2
<b>Hazardous to aquatic environment - acute hazard</b>	1				1	1	1	1		1	1	1			1
<b>Hazardous to aquatic environment - chronic hazard</b>							2								2

# Di-n-butyl phthalate (DNBP)



Hazard Class	Australia	Canada	EU	Japan Korea MOE	Korea MOEL	Malaysia	NZ	Taiwan	Thailand	Joint	
Acute Toxicity - Oral							5		5		
Skin Corrosion/Irritation									3		
Serious Eye Damage/Eye Irritation					2A		2		2B		
Skin Sensitizer				1	1				1		
Reproductive Toxicity	1B	1	1B	1B	1	2	1B	1	1	2	1B
Specific Target Organ Toxicity - Single Exposure				3		1, 3			1, 3		
Specific Target Organ Toxicity - Repeated Exposure				1		1, 2			1, 2		
Hazardous to the Aquatic Environment - Acute	1		1	1	1	1	1	1	1		1
Hazardous to the Aquatic Environment - Chronic				2							1

[Slide 23](#)

[Slide 24](#)

[Slide 25](#)

Source: ChemADVISOR compiled

## Di-n-butyl phthalate (DNBP)

Acute Toxicity - Oral

5

5

- A mouse LD<sub>50</sub> value of 4840 mg/kg was used by NZ to classify as Category 5.
- Interestingly, the pilot project included this data point (as well as numerous other rat test data) in its evaluation but concluded that this substance is not classifiable since "the GHS criterion indicates that the Category 4 cutoff is 2 g/kg".
- The US was the lead country for this substance's evaluation and it appears that the US GHS Category 5 exclusion was inadvertently used rather than the Purple Book.

### *Short summary and overall relevance of the provided information on acute oral toxicity*

Review of the existing information obtained from HSDB indicated that DBP orally administered in rats caused LD<sub>60</sub> in rats at 200 mg/kg after 7 hours observation time but no LD<sub>50</sub> was found (Sajiki et al, 1979). Other studies cited in HSDB and NIOSH indicated a LD<sub>50</sub> to range between 4.8-10 g/kg in various species (rat, mouse, guinea pig) (Lefaux, 1968; Antanyuk, 1963; Timofeevskaja et al 1980; Sine, 1993; BIBRA, 1987; BASF, 1961; Smith 1953)). None of these studies could be independently analyzed for reliability.

### *Comparison with the GHS criteria*

The range of doses for LD<sub>50</sub> was 4.8 to 10 g/kg after oral administration of DBP. The GHS criterion indicates that Category 4 cutoff is 2 g/kg. Therefore DBP is not classifiable for acute oral toxicity.

### *Conclusion on classification and labelling for acute oral toxicity*

No classification

Source: REPORT ON THE PROPOSAL FOR CLASSIFICATION AND LABELLING (C&L) OF DIBUTYL PHTHALATE

## Di-n-butyl phthalate (DNBP)

Serious Eye Damage/Eye Irritation

2A

2

2B

- A human data point of 'irritating' was used by NZ to classify as Category 2.
- The pilot project did not include human data, used animal data but concluded 'no classification due to insufficient data'.

SPECIES: Human

RESULT: Irritating

REFERENCE SOURCE: BASF AG Ludwigshafen BASF AG Ludwigshafen Huels AG Marl (294) BIBRA: Toxicity Profile on Dibutyl Phthalate (DBP), Maerz 1987. (IUCLID 2000).

Source: HSNO CCID

### *Short summary and overall relevance of the provided information on serious eye damage/eye irritation*

Two studies were found that indicate mild reversible eye reaction, both studies are found to be reliable due to use of OECD and FDA test guidelines under GLP conditions. Irritation index was listed as 0.11/110.

### *Comparison with the GHS criteria*

Data from the 2 identified studies indicate the effects observed were completely reversed by 72 hours. However, because scoring information was either not given or was not given as a standardized index no classification can be determined.

### *Conclusion on classification and labelling for serious eye damage/eye irritation*

No classification due to insufficient data

Source: REPORT ON THE PROPOSAL FOR CLASSIFICATION AND LABELLING (C&L) OF DIBUTYL PHTHALATE



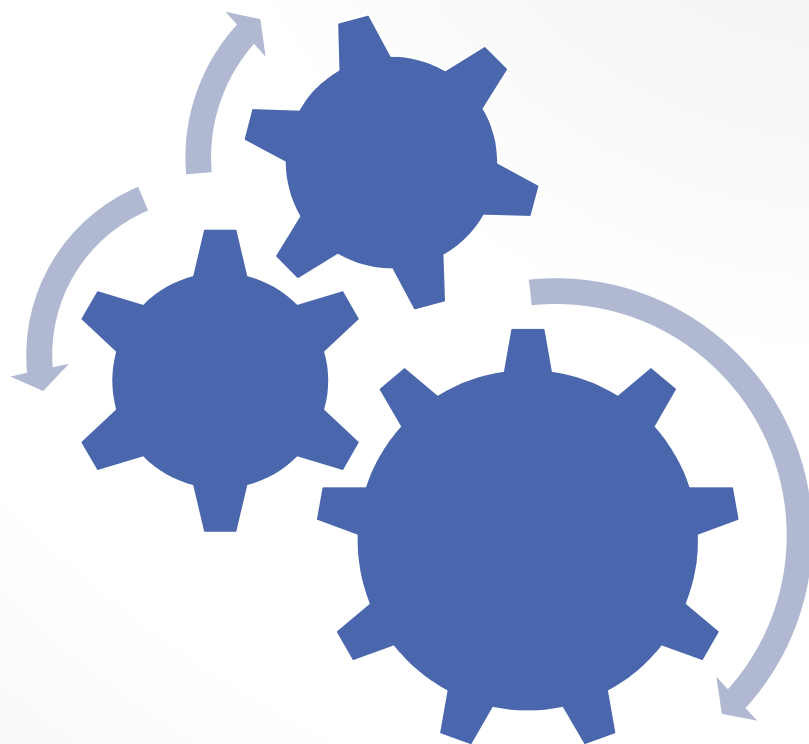
## Di-n-butyl phthalate (DNBP)

Hazardous to the Aquatic Environment - Acute	1		1	1	1	1	1	1	1	1	1		1
Hazardous to the Aquatic Environment - Chronic				2									1

- The classification for *Hazardous to the aquatic environment chronic* was 2 in Japan and 1 by the pilot project. Unfortunately, the Japanese source for this CAS number provided no rationale for the classification in English but ChemADVISOR located the Japanese version which states:  
 It has rapid degradability (the decomposition by BOD (28 days) = 69% (Existing Chemical Safety Inspections Data, 1975), BOD5: COD=0.63 (EU-RAR, 2003); 10 days NOEC of crustacean (Gammaridae) = 0.10 mg/L (NITE initial risk assessment, 2005); 99 days NOEC of fish (Rainbow trout) = 0.10 mg/L (NITE initial risk assessment, 2005); thus, it is classified as Category 2.
- The pilot project relied on an NOEC value for fish as the most sensitive trophic group thus resulting in a classification of *Hazardous to the aquatic environment chronic category 1*.

## Reflections

- Inconsistent application of Purple Book building blocks: include all or exclude some.
- Some existing human data not used versus animal data.



## General Observations + Recommendations

- Much interest in this topic; we hope the project will continue!
- Standardizing a minimum set of sources to review would ensure any discrepancies with existing classification are due to *additional* information not just different information.
- Review for all GHS Building Blocks, or declare a subset to be reviewed.
- Consider existing efforts to classify substances in addition to data sources, including but not limited to published country classifications.