Observations: UN Global List Pilot Project versus Published GHS Classifications

Darlene Susa-Anderson

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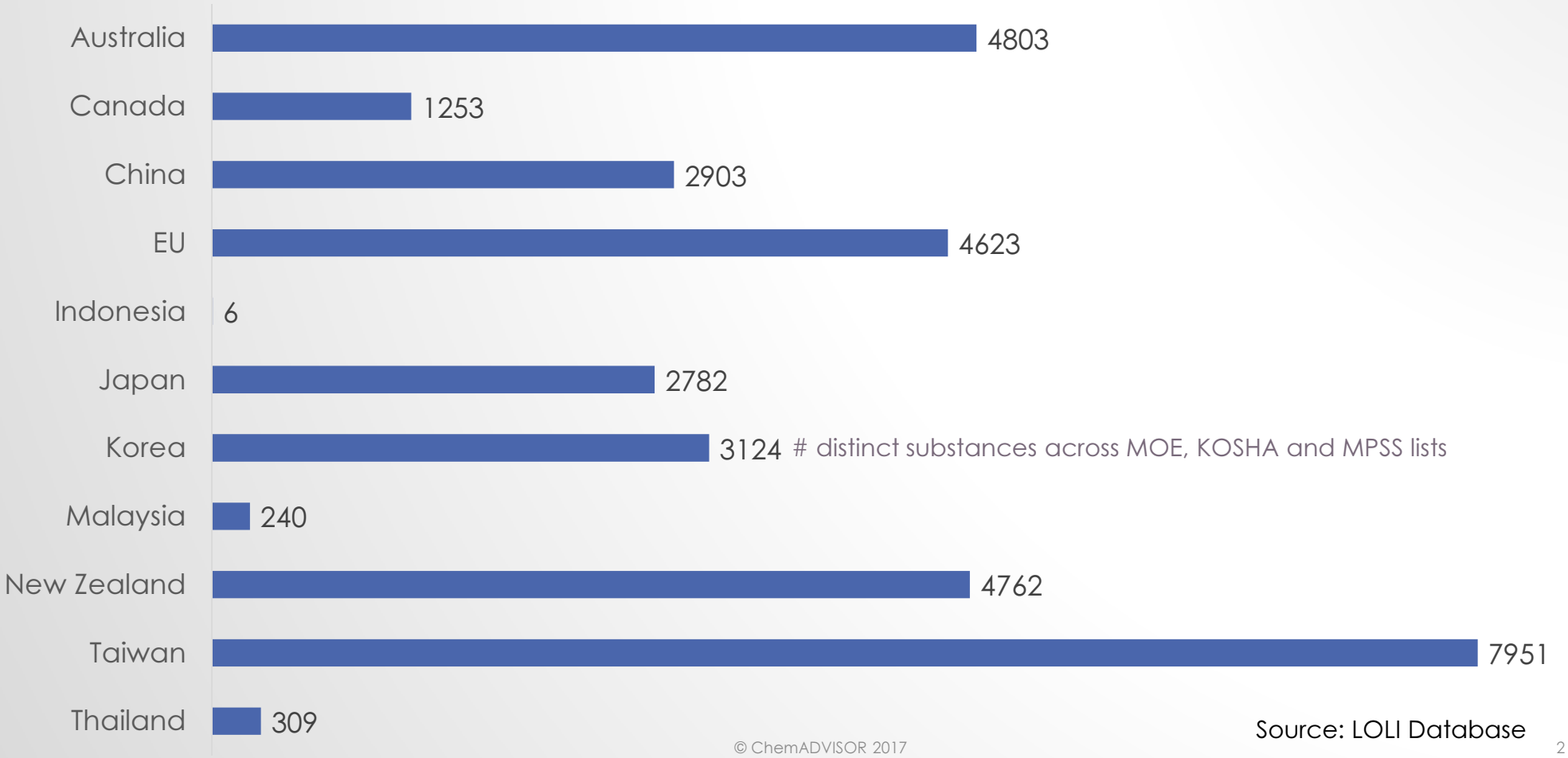
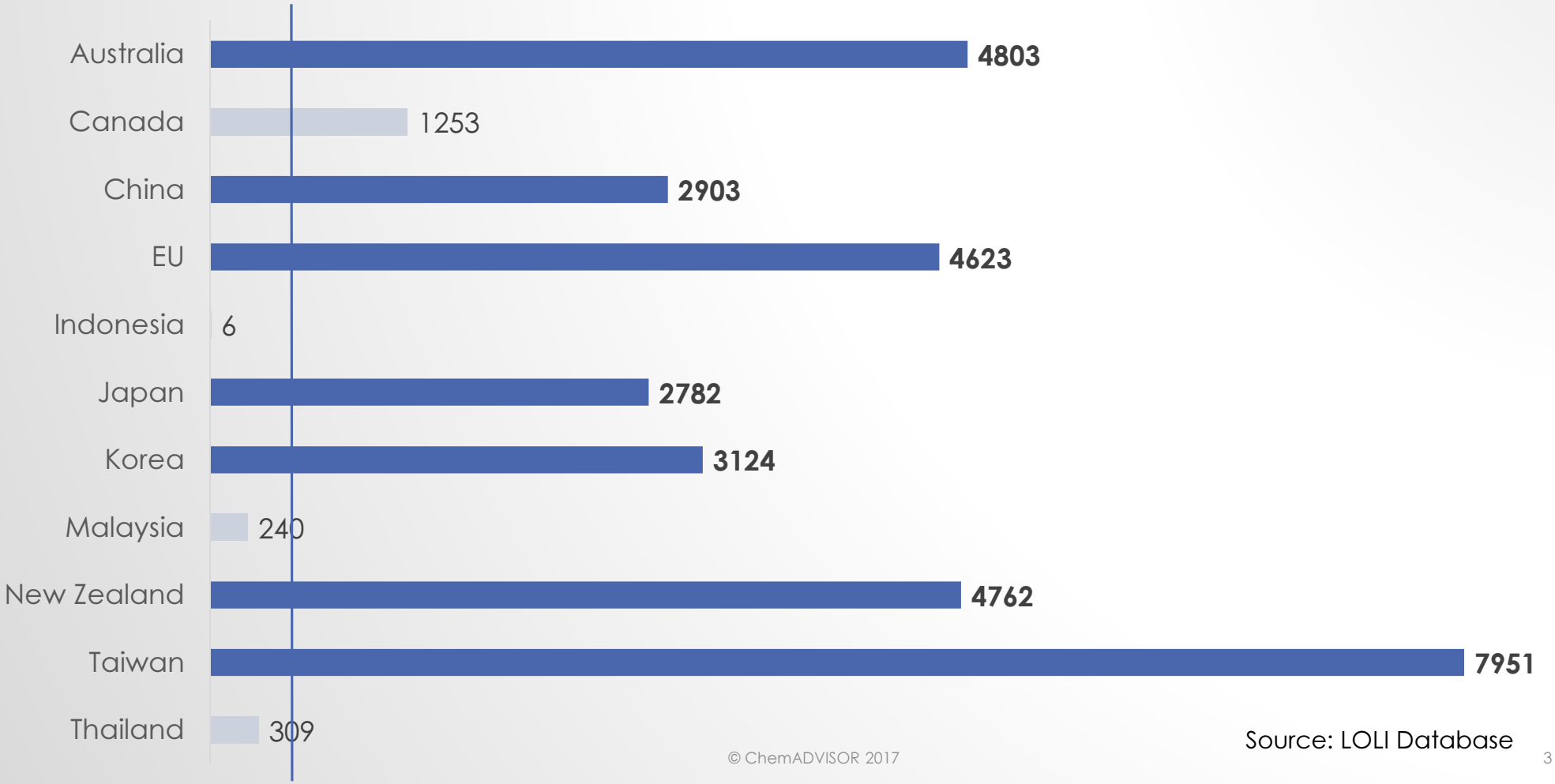
Published GHS Classifications



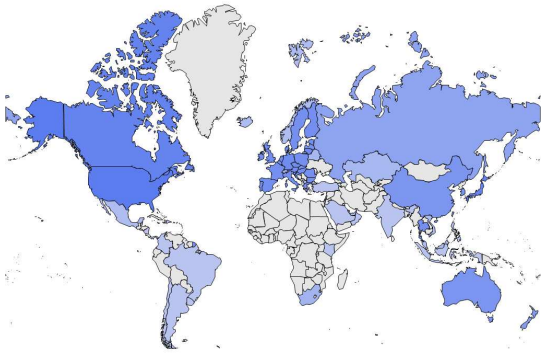
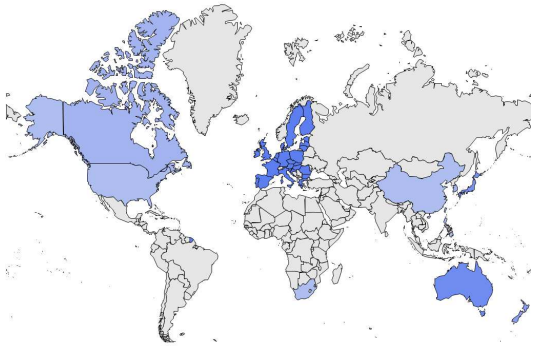
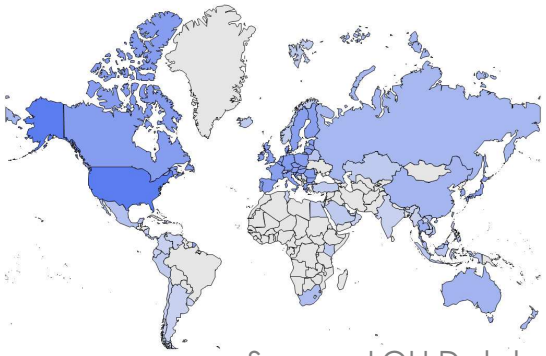
Source: LOLI Database

Published GHS Classifications



Source: LOLI Database

Pilot Project: Chemical Selection

Dicyclopentadiene	Dimethyltin dichloride	Di-n-butyl phthalate
77-73-6	753-73-1	84-74-2
 Source: LOLI Database	 Source: LOLI Database	 Source: LOLI Database
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

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
Flammable solids							**1**							**1**	**1**
Acute Toxicity - Dermal							**5**					**5**		**5**	**5**
Acute Toxicity - Inhalation	4	2			4							3	2	2	2
Acute Toxicity - Oral	4	4			4		4		4			3	4	4	3
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	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
Aspiration hazard							**1**		**1**					**1**	**1**
Hazardous to aquatic environment - acute hazard				**2**			**2**							**2**	**2**
Hazardous to aquatic environment - chronic hazard	2			2	2		2		2			2,3	2	2	2
Acute Toxicity - Inhalation - Vapour							**2**		**2**						**2**
Terrestrial vertebrate ecotoxicity												**2**			**2**

Source: LOLI Compare

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	Slide 8
Flammable Solid					1				1		
Acute Toxicity - Dermal					5		5		5	5	
Acute Toxicity - Inhalation	4	2		4			3	2	2	2	Slide 10
Acute Toxicity - Inhalation - Vapor					2	2					
Acute Toxicity - Oral	4	4		4	4	4	3	4	4	3	Slide 10
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		Slide 11
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	Slide 13
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 7

Dicyclopentadiene – a Flammable ..?

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

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°C ≤ (23°C ÷ 41°C) ≤ 60°C.

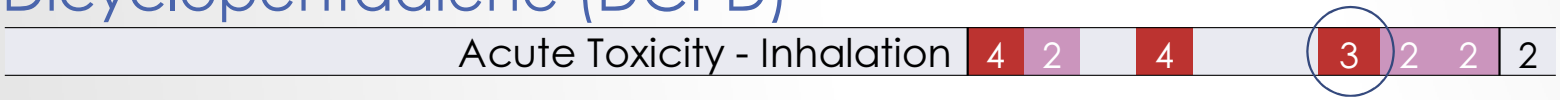
Conclusion on classification and labelling for flammable liquids

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)



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

- Japan used a rat LD_{50} 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 (but non-GLP) to classify as an *Acute toxicity oral category 3*. NZ used the same data to classify as *Acute toxicity oral category 3* as well.

Dicyclopentadiene (DCPD)

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

- New Zealand used an anonymous source which stated 'irritating' to classify as *Serious eye damage/eye irritation category 2.*

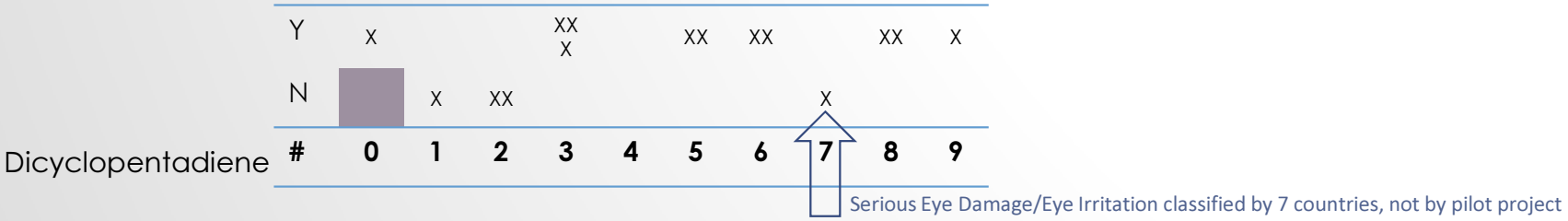
- Japan used rabbit data of 'mild' and an EU classification of R36 to conclude a classification of *Serious eye damage/eye irritation category 2B*.

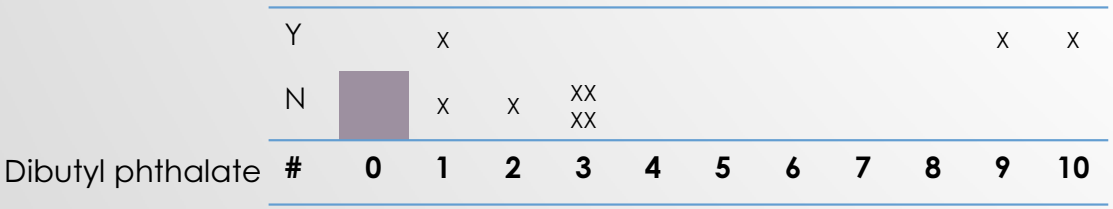
- The pilot project reviewed numerous rabbit and human data points.
- The data points mostly covered very mild, confined, and temporary (<24h) irritating effects. The human data which pointed to irritation did not have primary sources available.
- The pilot project decided not to classify this substance for this endpoint.

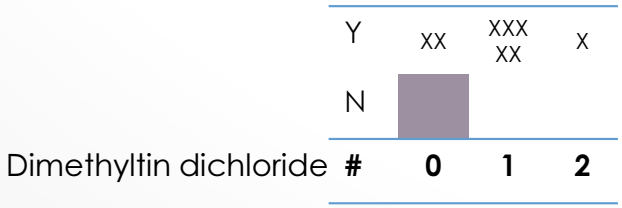
Dicyclopentadiene (DCPD)

Serious Eye Damage/Eye Irritation	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).

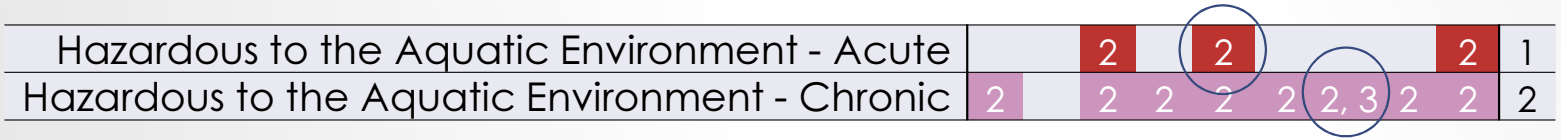






Source: ChemADVISOR compiled

Dicyclopentadiene (DCPD)

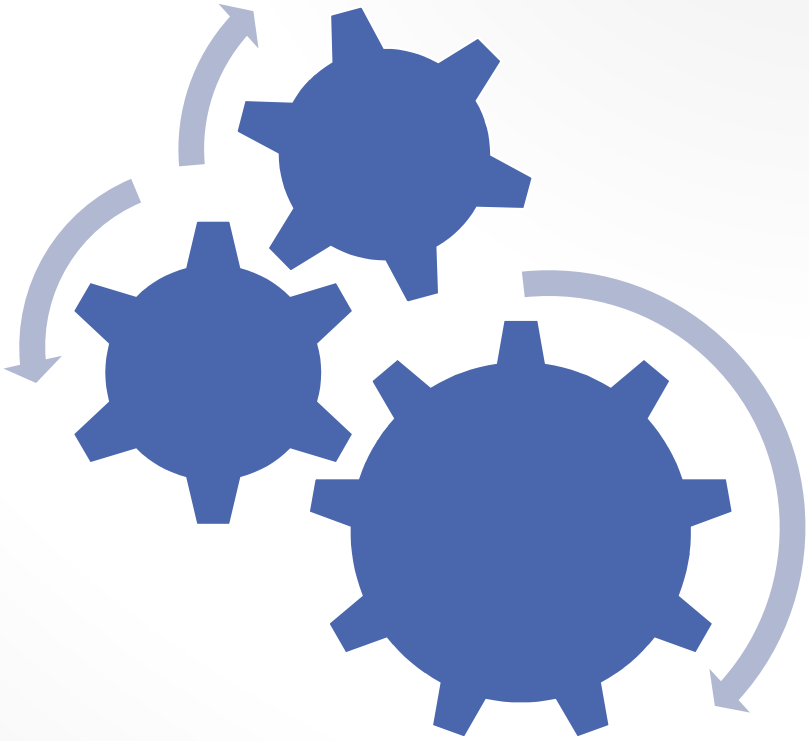


- Japan used a 96 hour LC_{50} value of 4.3 mg/L (Oryzias latipes) to classify this substance as *Hazardous to the aquatic environment acute category 2.* The pilot project had numerous data for all trophic levels (including this value) but concluded that water flea was the most sensitive species thus 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 2 or 3* while the pilot project classified as *Hazardous to the aquatic environment chronic category 2* using the surrogate approach with QSAR estimation.

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
Acute Toxicity - Dermal	3				3										3
Acute Toxicity - Inhalation	2				2										2
Acute Toxicity - Oral	3				3										3
Skin corrosion/irritation	1B				1B							2			1B
Serious eye damage/eye irritation												2			2
Reproductive toxicity	2				2										2
Specific target organ toxicity - Repeated exposure	1				1										1

Source: LOLI Compare

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

Slide 17

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.
- Note: 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

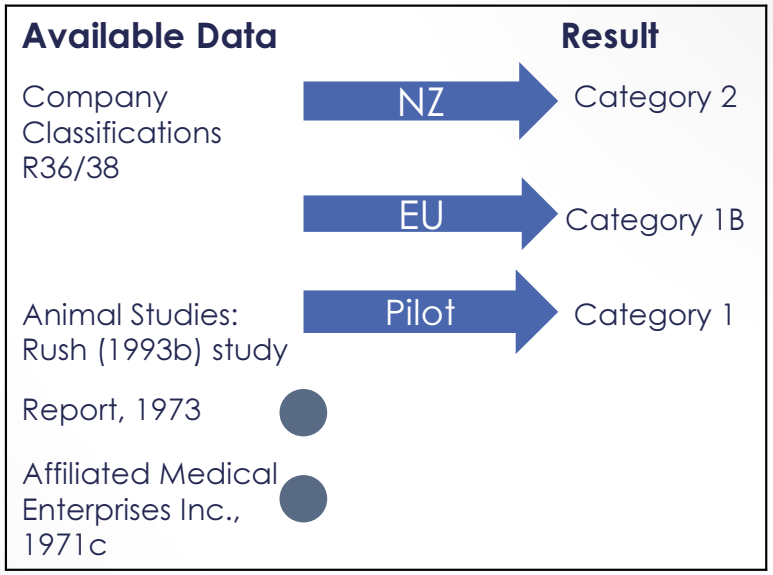
Classification Data	
6.3A	R PHRASE: R 38 [Company Data]
6.4A	R PHRASE: R 36 [Company Data]

Source: HSNO CCID

Dimethyltin dichloride: Pilot Project Classifications

Skin Corrosion/Irritation 1B 2 1

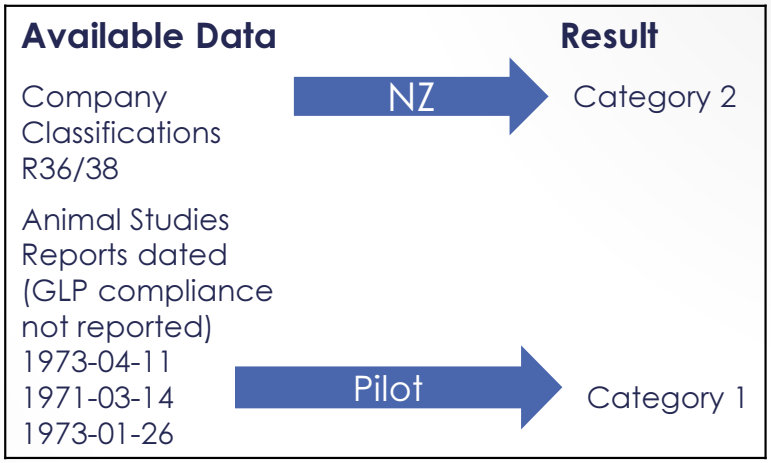
- The pilot project used animal test data.
- For skin corrosion, the data presented was from studies in 1970s and 1990s. The 1993b Rush study (GLP) was chosen as the primary source.
- The pilot project did not find sufficient information on how exposure time effects corrosivity to be able to distinguish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



Dimethyltin dichloride: Pilot Project Classifications

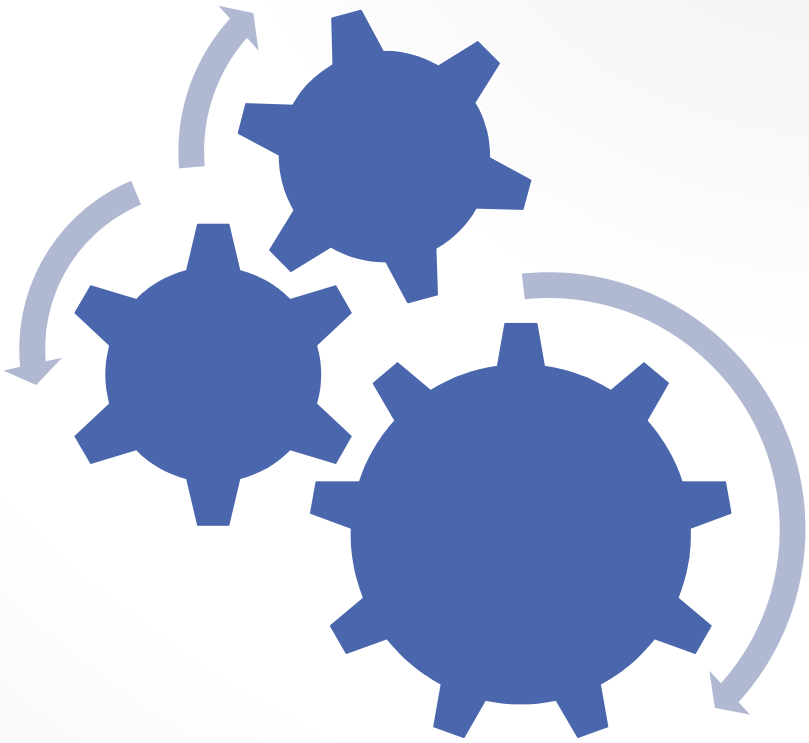
Serious Eye Damage/Eye Irritation	2	1

- 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 classification to support this classification.



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
Acute Toxicity - Oral												**5**		**5**	**5**
Skin corrosion/irritation														**3**	**3**
Serious eye damage/eye irritation									2A			2		2B	2A
Skin sensitizers							**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	2	1
Specific target organ toxicity - Repeated exposure							1		1,2					1,2	1,2
Hazardous to aquatic environment - acute hazard	**1**				**1**		**1**	**1**	**1**		**1**	**1**	**1**		**1**
Hazardous to aquatic environment - chronic hazard							**2**								**2**

Source: LOLI Compare

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		Slide 23
Skin Corrosion/Irritation									3		
Serious Eye Damage/Eye Irritation					2A		2		2B		Slide 24
Skin Sensitizer				1	1				1		
Reproductive Toxicity	1B	1	1B	1B	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	
Hazardous to the Aquatic Environment - Chronic				2						1	Slide 25

Source: ChemADVISOR compiled

Di-n-butyl phthalate (DNBP)

Acute Toxicity - Oral							5		5		

- A mouse LD_{50} 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 Cat 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_{60} in rats at 200 mg/kg after 7 hours observation time but no LD_{50} was found (Sajiki et al, 1979). Other studies cited in HSDB and NIOSH indicated a LD_{50} to range between 4.8-10 g/kg in various species (rat, mouse, guinea pig) (Lefaux, 1968; Antanyuk, 1963; Timofeevskaia 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_{50} 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
Hazardous to the Aquatic Environment - Chronic				2							1

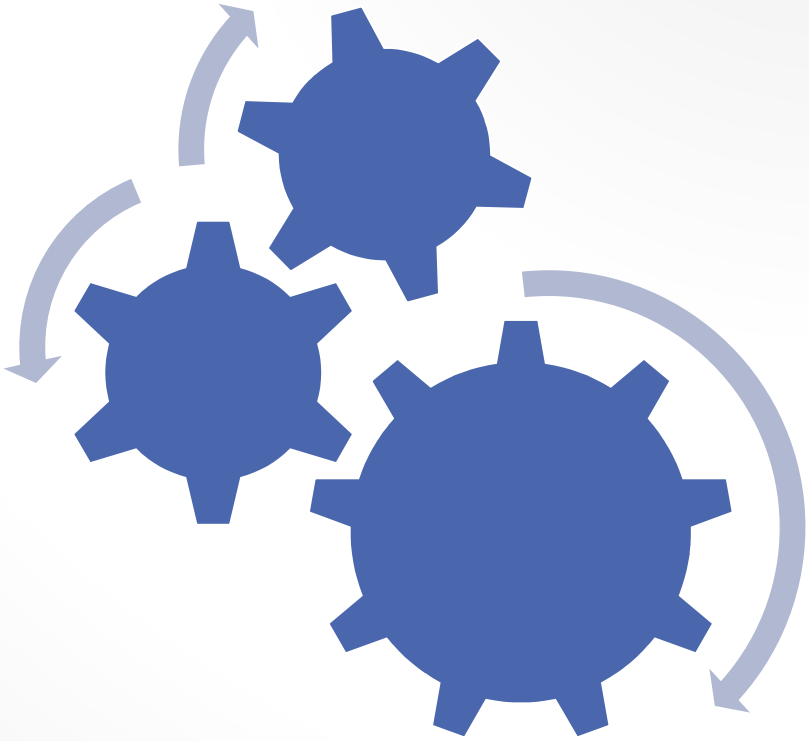
- The classification for *Hazardous to the aquatic environment chronic* was 2 in Japan and 1 by the pilot project. Unfortunately, the Japanese source for this CAS number provided no rationale for the classification in English but ChemADVISOR located the Japanese version which states:

  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 Murray rainbow fish (non standard species) as the most sensitive trophic group thus resulting in a classification of *Hazardous to the aquatic environment chronic category 1.*

Reflections

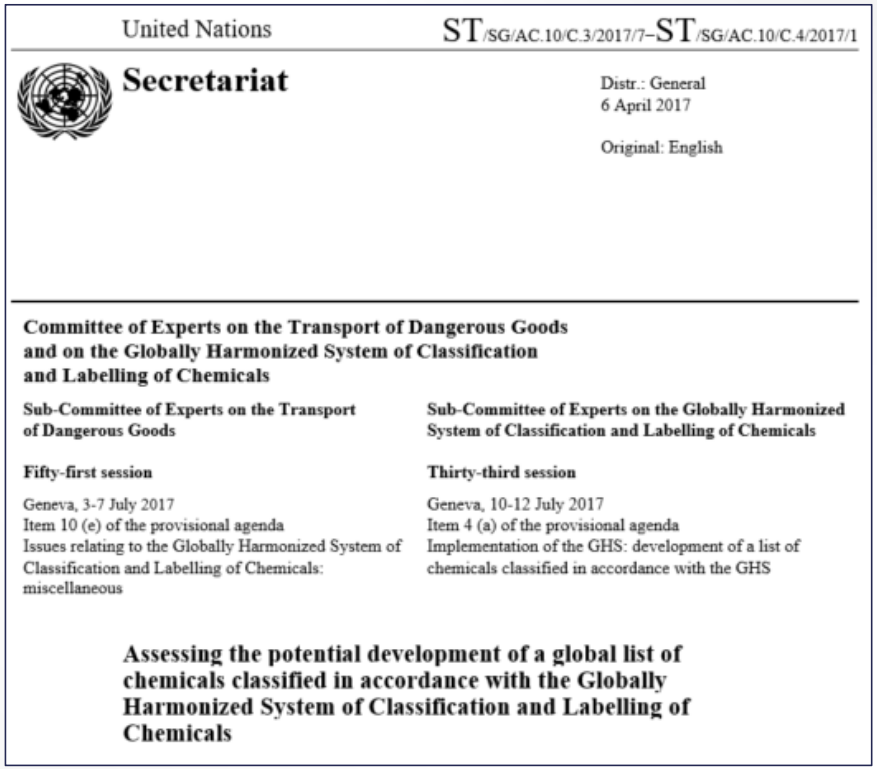
- Inconsistent application of Purple Book building blocks: include all or exclude some.
- Some existing human data not used versus animal data.



Summary of Next Steps of the GHS Sub-Committee

- "The GHS Sub-Committee has not yet decided to develop a global classification list, and has **not adopted** the classifications arrived at through the OECD process."
- "Concerns have been raised in the GHS Sub-Committee that classifications it reaches **may impact other bodies** that develop regulations and/or guidance involving hazardous chemicals… [IMO, TDG]"
- Seeking **input from affected bodies and suggestions for improvement.**

Working Document: ST/SG/AC.10/C.4/2017/1



United Nations ST/SG/AC.10/C.3/2017/7–ST/SG/AC.10/C.4/2017/1

Secretariat

Distr.: General
6 April 2017

Original: English

Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Transport of Dangerous Goods

Fifty-first session

Geneva, 3-7 July 2017
Item 10 (e) of the provisional agenda
Issues relating to the Globally Harmonized System of Classification and Labelling of Chemicals: miscellaneous

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals

Thirty-third session

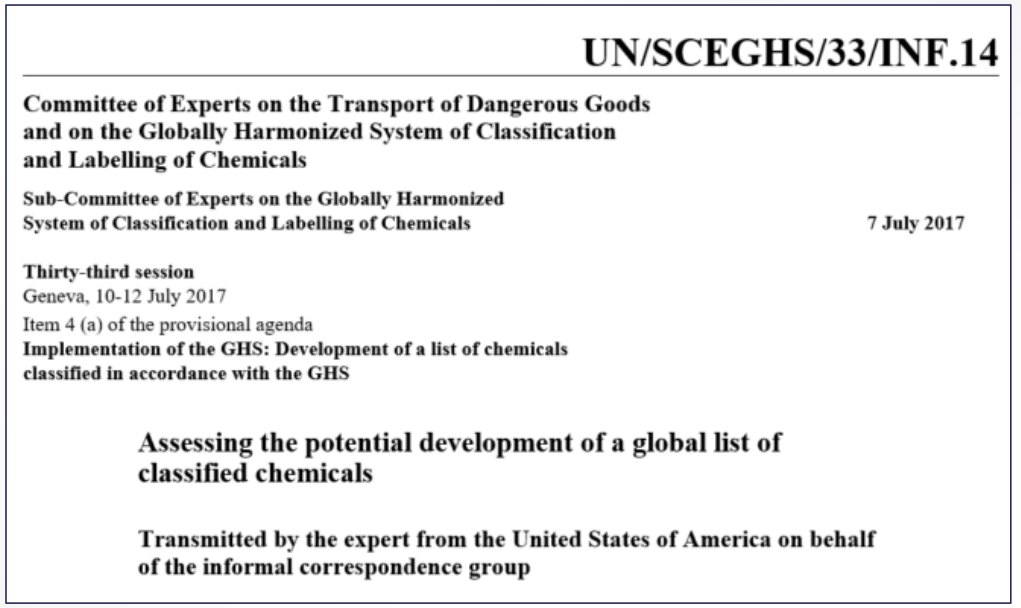
Geneva, 10-12 July 2017
Item 4 (a) of the provisional agenda
Implementation of the GHS: development of a list of chemicals classified in accordance with the GHS

Assessing the potential development of a global list of chemicals classified in accordance with the Globally Harmonized System of Classification and Labelling of Chemicals

Summary of Next Steps of the GHS Sub-Committee

- "further work on a list comparison would be useful in discovering reasons for divergences. In particular it might be helpful to identify **ambiguities in GHS criteria that could be clarified**, or situations where the divergences appear to be based on the use of different data sets."
- "… seemed unlikely at this point that a comparison list could lead directly to a harmonized global list … [the EC] voiced cautiousness in setting up a global process in parallel to the well installed and transparent European classification system."

Informal document INF.14



UN/SCEGHS/33/INF.14

Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals — **7 July 2017**

Thirty-third session
Geneva, 10-12 July 2017
Item 4 (a) of the provisional agenda
Implementation of the GHS: Development of a list of chemicals classified in accordance with the GHS

Assessing the potential development of a global list of classified chemicals

Transmitted by the expert from the United States of America on behalf of the informal correspondence group

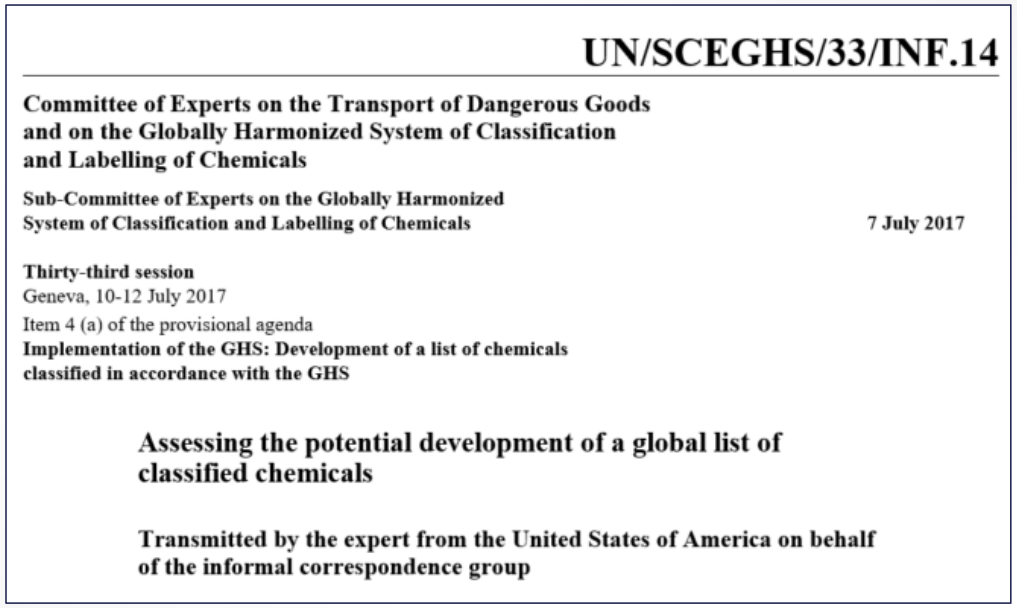
Summary of Next Steps of the GHS Sub-Committee

"As next steps, the committee agreed to:

(a) A comparison of chemicals between the ECHA RAC and Japanese lists for which a classification had been done for all endpoints. ECHA agreed to identify all RAC opinions that classified **all endpoints.**

(b) A comparison of lists for one endpoint. Germany agreed to examine the **carcinogenicity classifications in the EU-Japan comparison** already compiled to see what could be learned about the reasons for differences and what conclusions could be drawn from them."

Informal document INF.14



UN/SCEGHS/33/INF.14

Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals **7 July 2017**

Thirty-third session
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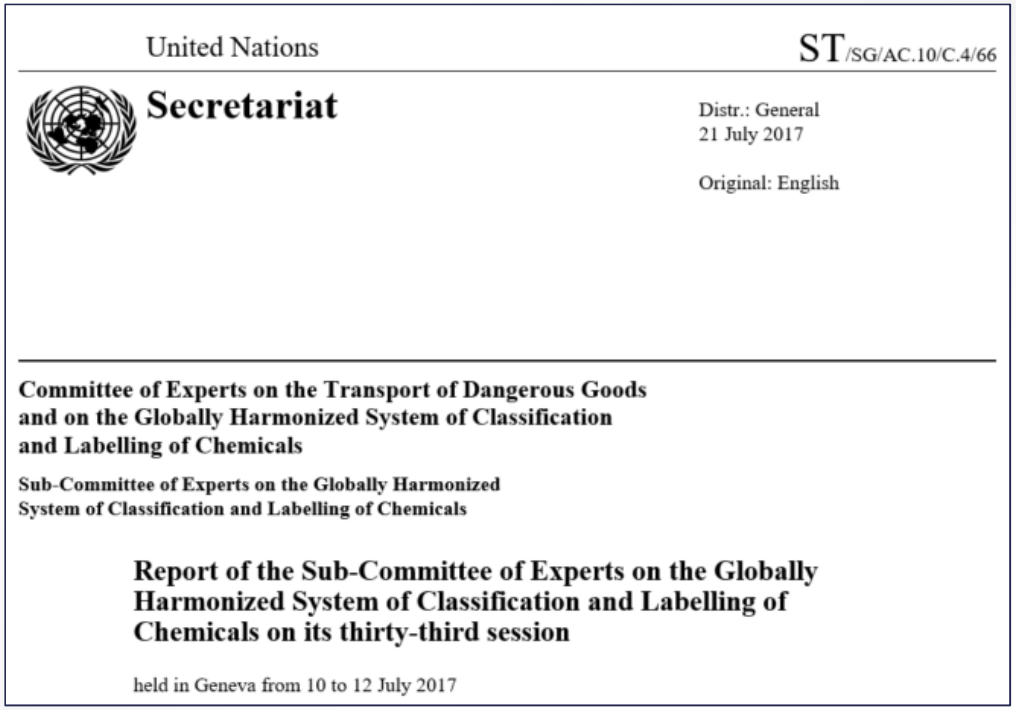
Summary of Next Steps of the GHS Sub-Committee

"While many experts felt it was time to begin work on adopting harmonized classifications for a non-binding list, others expressed concerns about potential duplication of ongoing work on the development and updating of classification lists by competent authorities and the impact that a list developed at Sub-Committee level might have on the legal obligations in their jurisdictions.

The correspondence group would submit a working document to the next session outlining its discussions for further deliberation in the Sub-Committee about a way forward."



United Nations ST/SG/AC.10/C.4/66

Secretariat

Distr.: General
21 July 2017

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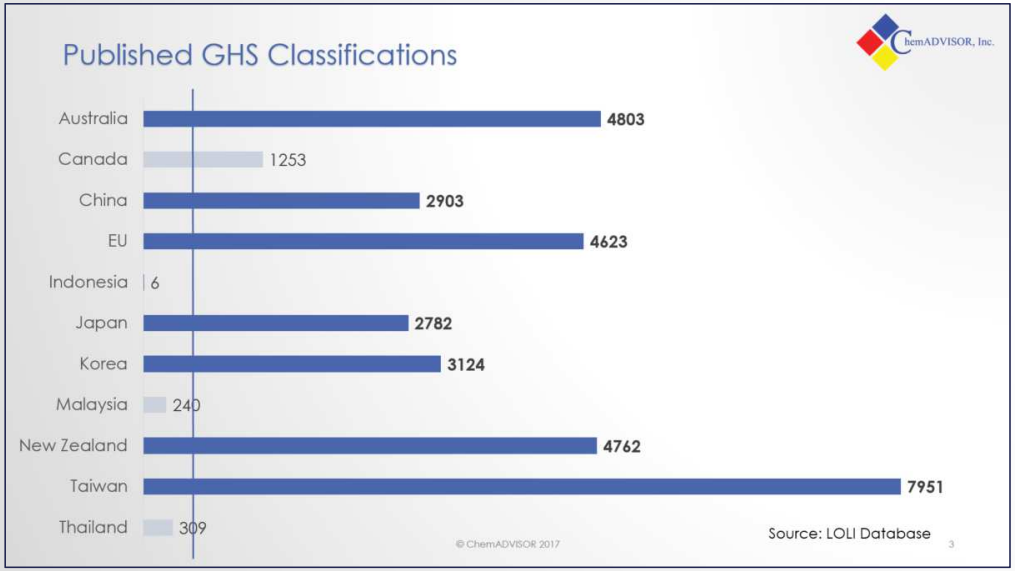
Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals

Report of the Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals on its thirty-third session

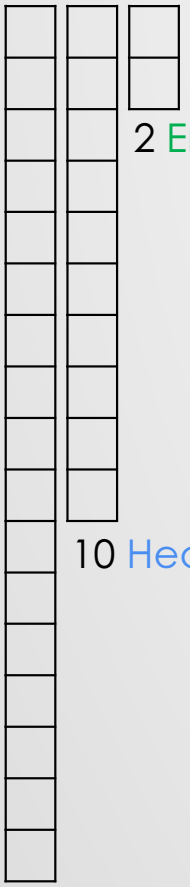
held in Geneva from 10 to 12 July 2017

“All endpoints”/ “All countries”



We used this metric of countries with more than 2000 substances on their lists because there are 0 substances which all countries have classified.

"All endpoints"



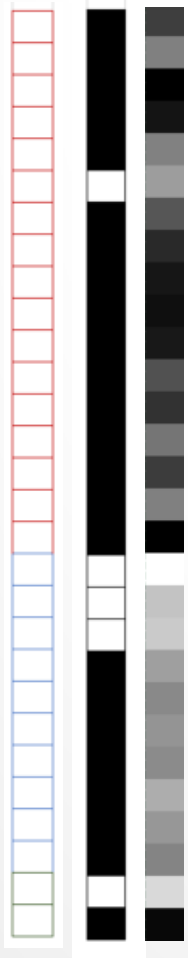
2 Environmental Hazards

10 Health Hazards

17 Physical Hazards

A single substance with 5 classifications

All substances and all classifications, overlaid

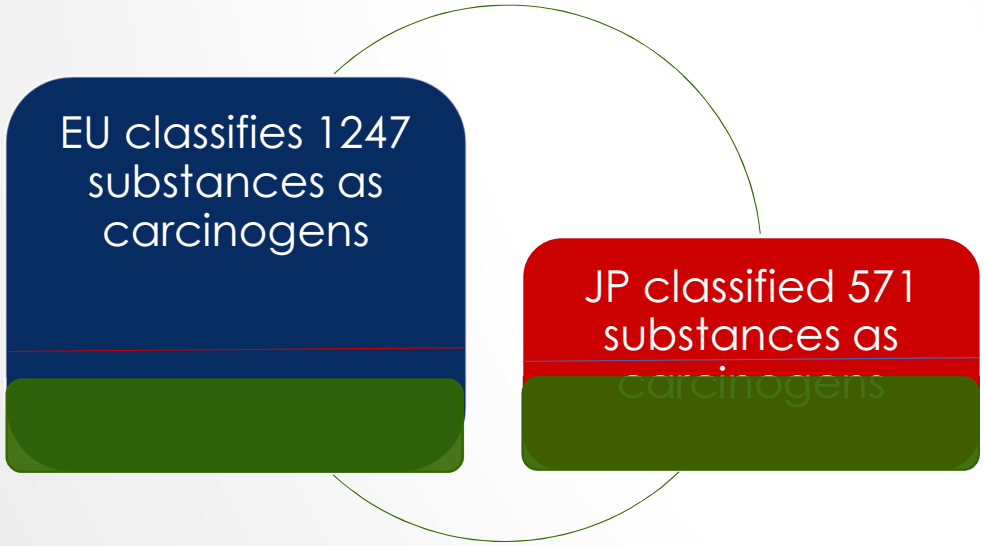


Health and Aquatic classifications applied most often. These would be a good focus for examining criteria compared to Physical, particularly as Physical hazards have received much attention from the international transportation groups.

Source: ChemADVISOR; inspired by "*What is Data Analytics?*"

Japan and EU Carcinogenicity Classifications

Of the 1007 the EU classified that Japan did not classify for carcinogenicity, Japan provided *other* GHS classifications for 75.



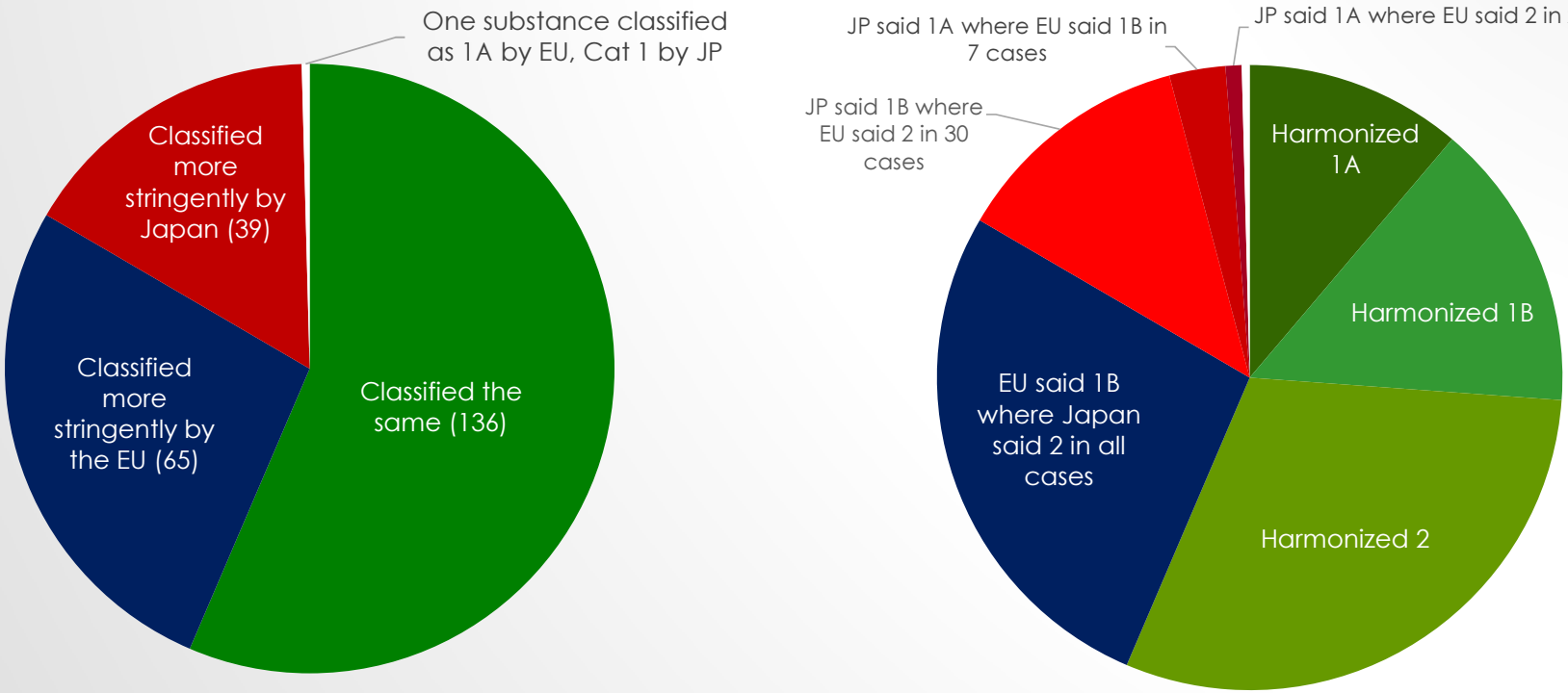
Of the 331 Japan classified that the EU did not classify for carcinogenicity, the EU provided *other* GHS classifications for 60.

240 substances classified by both groups;
these classifications are compared on the next slide

Source: ChemADVISOR compiled

Japan and EU Carcinogenicity Classifications

Visualization of the 24 substances classified by both groups, comparing the classification categories



Source: ChemADVISOR analysis of LOLI Database

Most commonly *different* classification was Cat1B v Cat2

3.6.1 Definitions

The term *carcinogen* denotes a substance or a mixture which induces cancer or increases its incidence. Substances and mixtures which have induced benign and malignant tumours in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans.

Classification of a substance or mixture as posing a carcinogenic hazard is based on its inherent properties and does not provide information on the level of the human cancer risk which the use of the substance or mixture may represent.

Category 1B

Presumed to have carcinogenic potential for humans; the placing of a substance is largely based on animal evidence.

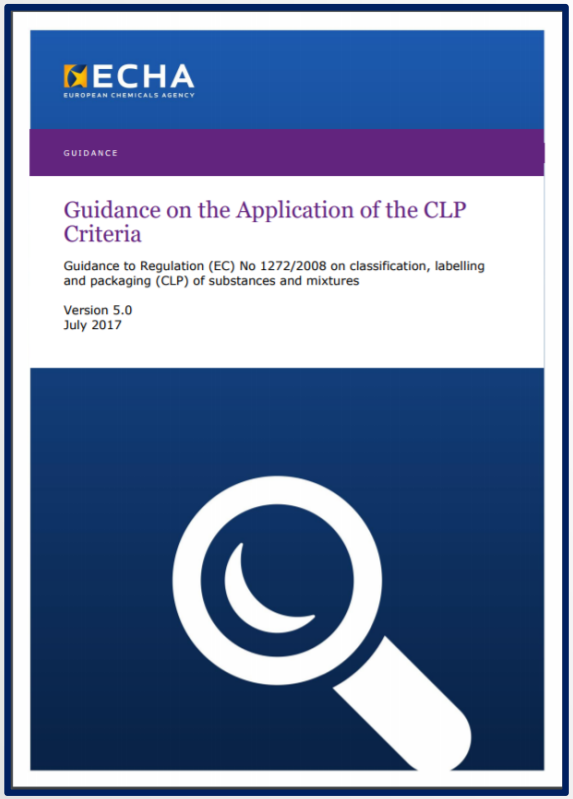
Based on strength of evidence together with additional considerations, such evidence may be derived from human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen). Alternatively, evidence may be derived from animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen). In addition, on a case by case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.

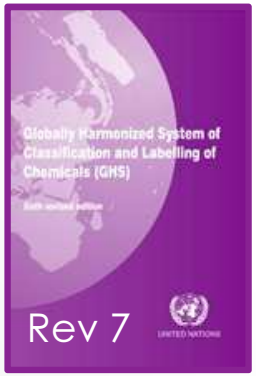
Category 2

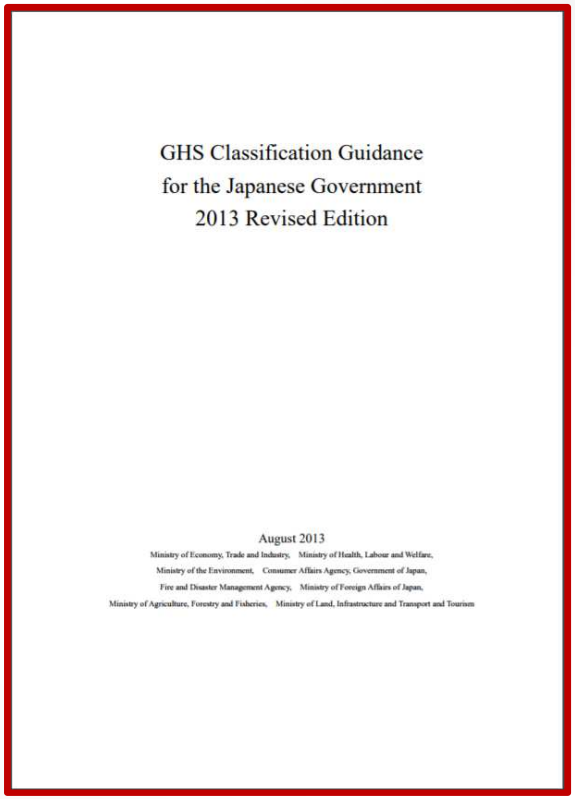
Suspected human carcinogens

The placing of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1. Based on strength of evidence together with additional considerations, such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Variations in government guidance from Purple Book?







Japanese guidance on classification

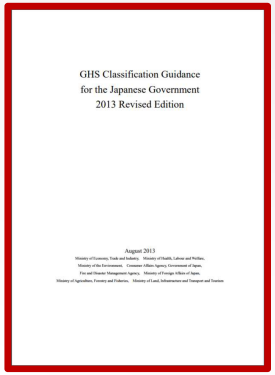
Definitions of Carcinogenicity in UN GHS are as follows, and they are adopted in this guidance.

【GHS 4th revised edition】(3.6.1)

The term *carcinogen* denotes a substance or a mixture of chemical substances which induce cancer or increase its incidence. Substances and mixtures which have induced benign and malignant tumors in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans.

Classification of a substance or mixture as posing a carcinogenic hazard is based on the inherent properties of the substance and does not provide information on the level of the human cancer risk which the use of the substance or mixture may represent.

Same as Purple Book Rev 7


GHS Classification Guidance
for the Japanese Government
2013 Revised Edition

August 2013

Category 1B

Category 1B: Presumed to have carcinogenic potential for humans; the placing of a chemical is largely based on animal evidence.

Based on strength of evidence and additional considerations (weight of evidence), such evidence may be derived from human studies that establish a causal relationship between human exposure to a chemical and the development of cancer (known human carcinogen). Alternatively, evidence may be derived from animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen). In addition, on a case by case basis, scientific judgment may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.

Same as Purple Book Rev 7

Category 2

Category 2: Suspected human carcinogens

The placing of a chemical in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the chemical in Category 1. Based on strength of evidence together with additional considerations, such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Classification: Carcinogen Category 2 Carcinogen

Same as Purple Book Rev 7

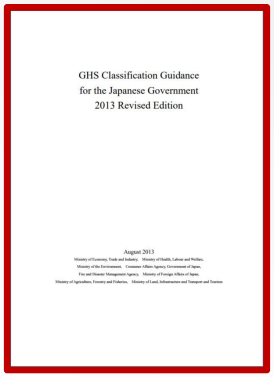
Japanese guidance on classification

Table 3-2-6-2: Correspondence table between GHS classification and classifications by other organizations (Carcinogenicity)

GHS	IARC	JSOH	ACGIH	EPA 1986	EPA 1996	EPA 2005	NTP	EU
1A	1	1	A1	A	K/L	CaH	K	1
1B	2A	2A	A2	B1, B2		L	R	2
2	2B	2B	A3	C		S		3
Classification not possible	3		A4	D	CBD	I		
Not classified	4		A5	E	NL	NL		

* When Carcinogenicity classification is performed according to the above table, data need not to be input into other items such as toxicity information or epidemiological/ occupational exposure. When EU classification alone is available, however, toxicity information is needed.

(Note 1) Since EU classification does not provide the basic hazard information for its classification decisions, review other information sources and confirm their validity. If EU classification alone is available, classify the substance as "Classification not possible".


GHS Classification Guidance
for the Japanese Government
2013 Revised Edition

August 2013

B) Substance for which GHS classification is possible without expert's judgment

For substances classified in accordance with the following procedures, the GHS classification can be adopted without an expert's judgment.

1) GHS classification of substances which have been already evaluated by the following organizations shall be performed in accordance with Table 3-2-6-2 Correspondence table of GHS classification and classifications of other organizations (Carcinogenicity). The evaluation results of IARC take precedence. If multiple assessment documents classified a substance in different categories, the substance is classified in accordance with the latest document in principle. If the latest documents (for example, EPA and NTP) classified the substance in different categories and if GHS classification is not possible, classification shall be properly carried out by referring to previous assessment documents (expert judgment shall be used on an as needed basis).

European Union guidance on classification

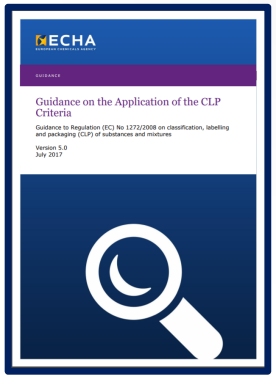
Annex I: *3.6.1.1.* *Carcinogen means a substance or a mixture of substances which induce cancer or increase its incidence. Substances which have induced benign and malignant tumours in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans.*

More explicitly, chemicals are defined as carcinogenic if they induce tumours, increase tumour incidence and/or malignancy or shorten the time to tumour occurrence. Benign tumours that are considered to have the potential to progress to malignant tumours are generally considered along with malignant tumours. Chemicals can potentially induce cancer by any route of exposure (e.g. when inhaled, ingested, applied to the skin or injected), but carcinogenic potential and potency may depend on the conditions of exposure (e.g., route, level, pattern and duration of exposure).

Carcinogenic chemicals have conventionally been divided according to the presumed mode of action; genotoxic or non-genotoxic, see Section 3.6.2.3.2.(k) of this Guidance.

Classification of a substance as a carcinogen is based on consideration of the strength of the evidence of available data for classification with considerations of all other relevant information (weight of evidence) being taken into account as appropriate. Strength of evidence involves the enumeration of tumours in human and animal studies and determination of their level of statistical significance. A number of other factors need to be considered that influence the overall likelihood that a substance poses a carcinogenic hazard in humans (weight of evidence determination). The list of factors for additional consideration is long and requires the most up-to-date scientific knowledge. It is recognised that, in most cases, expert judgement is necessary to be able to determine the most appropriate category for classification for carcinogenicity.

Same as Purple Book Rev 7



Category 1B

Category 1B, presumed to have carcinogenic potential for humans, classification is largely based on animal evidence.

The classification in Category 1A and 1B is based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived from:

- *human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or*
- *animal experiments for which there is sufficient ([1]) evidence to demonstrate animal carcinogenicity (presumed human carcinogen).*

In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.

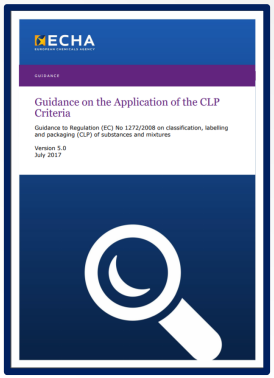
Same as Purple Book Rev 7

Category 2

The placing of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1A or 1B, based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived either from limited([1]) evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

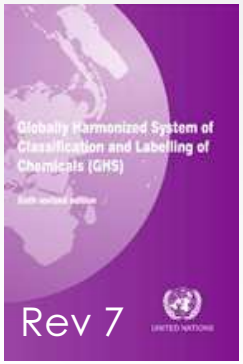
Same as Purple Book Rev 7

European Union guidance on classification



There is a strong link between CLP and the IARC classification criteria. The definitions for sufficient and limited evidence as defined by IARC are part of the criteria (CLP Annex I, 3.6.2.2.3). IARC, however, understands the criteria of 'sufficient' and 'limited' as follows: 'It is recognized that the criteria for these evaluations, described below, cannot encompass all of the factors that may be relevant to an evaluation of carcinogenicity. In considering all of the relevant scientific data, the Working Group may assign the agent to a higher or lower category than a strict interpretation of these criteria would indicate.' (IARC 2006 preamble Section 6, Evaluation and rationale). This sentence emphasises that in certain circumstances expert judgement may overrule the strict interpretation of the IARC criteria for 'sufficient' and 'limited'. These same limitations apply with the current criteria in that expert judgement is necessary and can override the strict interpretation of the definitions.

How could one group classify as 1A and the other as 2?

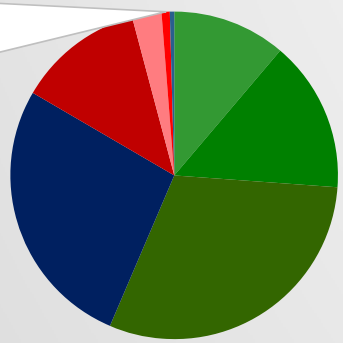


Category 1A

The placing of a substance in Category 1 is done on the basis of epidemiological and/or animal data. An individual substance may be further distinguished:

Known to have carcinogenic potential for humans; the placing of a substance is largely based on human evidence.

JP said 1A where EU said 2 in 2 cases



Category 2

Suspected human carcinogens

The placing of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1. Based on strength of evidence together with additional considerations, such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Cadmium cyanide

Nickel carbonyl

SAFE NITE Classification Rationales

For 13463-39-3 (nickel carbonyl):
http://www.safe.nite.go.jp/english/ghs/06-imcg-0049e.html

Due to the fact that the substance is classified as Group 1 (as nickel compounds) by IARC(1990)and Category K by NTP (2005).

For 542-83-6 (cadmium cyanide):
http://www.safe.nite.go.jp/english/ghs/06-imcg-1023e.html

The classification (Group 1, respectively Known to be human carcinogens, 1) as a cadmium compounds of IARC53 (1993), NTP RoC (11th, 2005), and industrial hygene academic recommendation (2004) (Group 1, respectively Known to be human carcinogens, 1) is equivalent to Category 1A, the classification of IRIS (1992) and ACGIH-TLV (2004) as cadmium compounds corresponds (B1, A2 respectively) is Category 1B. Since the newness of the source of both Category etc. was almost equivalent. So it was considered as Category 1A-1B. [view] It is more desirable to be considered as 1A from a viewpoint of safety, when subdivision was needed.

General Observations + Recommendations

- For pilot project substance classifications:
  - 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.
- For clarifying classification criteria:
  - Health and Aquatic classifications are used far more frequently by countries publishing lists than physical hazards, so these could be a productive focus for improvement.
  - Consider how classification guidance from countries may add to discrepancies.