General Introduction to GHS, CLP and downstream consequences

PRISME2 Workshop

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Why do we need GHS?

Substance – oral toxicity LD_{50} = 257 mg/kg

GHS	**Danger (Skull & Crossbones)**
Transport	**liquid: slightly toxic/ solid: not classified**
EU	**Harmful (St Andrew's Cross)**
US	**Toxic**
CAN	**Toxic**
Australia	**Harmful**
India	**Non-toxic**
Japan	**Toxic**
Malaysia	**Harmful**
Thailand	**Harmful**
New Zealand	**Hazardous**
China	**Not Dangerous**
Korea	**Toxic**

GHS – A global system!

A long way from Rio, 1992...till today

GHS is not legally binding but countries are encouraged to implement

GHS provides common basis for classification and hazard communication for transport and supply and use

GHS includes a "building block" approach to facilitate implementation ➔ freedom to take up hazard classes and/or categories but NO change of criteria for classes/categories taken up

GHS will not be completely "harmonised" at first

GHS and "old" EU system have many similarities

GHS & the European legislative process

- Regulation on **C**lassification, **L**abelling and **P**ackaging of substances and mixtures (CLP) adopts the GHS in Europe
- Formally adopted by EU Parliament and the Council on Dec 16 2008
  - Publication in Official Journal 31 Dec. 2008, Regulation (EC) 1272/2008, OJ L 353
- Entry into force 20 January 2009
- Regulatory instrument: Regulation based in Art.95 of the EU Treaty (harmonisation of the internal market)
- Scope: substances and mixtures, including C&L of Plant Protection Products and Biocides.

CLP Regulation - Principles

- Applies general **principles** of GHS
- Introduces the **GHS criteria** for data interpretation, classification and labelling
- Uses the GHS '**building block**' approach and a few other 'optionalities' to **adapt** the system to the EU needs
- Keeps the **scope as close as possible** to the old system
- Ensures **consistency** with transport rules
- Stays as close as possible to the GHS format and terminology, e.g.
  - "Mixtures" not "Preparations"
  - "Hazardous" not "Dangerous"

Respecting the principles

- Takes up all GHS Hazard Classes
- Uses 'building block' approach to omit categories not in the old EU system (Flammable liquids cat. 4; Acute Toxiciy Cat. 5; Skin corrosion/irritation Cat. 3; Aspiration hazard Cat. 2; Acute aquatic toxicity Cat. 2 & 3).
- Maintains current level of protection by including EU "left-overs" not yet covered by GHS (Ozone depletion, Annex I Part 5 – Additional labelling requirements in Annex II, e.g. EUH014 [R14] "Reacts violently with water", EUH066 [R66] "Repeated exposure may cause skin dryness or cracking"
- Avoids changing the scope of REACH and downstream legislation
- Takes over Annex I of Dir. 67/548/EEC (harmonised classification, repealed)
- Takes over Title XI (Classification and labelling inventory) from REACH

CLP Regulation - Overview

Legal text containing principles and general rules

- TITLE I - General Issues
- TITLE II – Hazard Classification

  Chapter 1 Identification and Examination of Information

  Chapter 2 Evaluation of Hazard Information and Decision on Classification
- TITLE III – Hazard Communication in Form of Labelling

  Chapter 1 Content of the Label

  Chapter 2 Application of Labels
- TITLE IV - Packaging
- TITLE V – Harmonisation of C&L of Substances and the C&L Inventory

  Chapter 1 Establishing Harmonised Classification and Labelling of Substances

  Chapter 2 Classification and Labelling Inventory
- TITLE VI – Competent Authorities and Enforcement
- TITLE VII – Common and Final Provisions

CLP Regulation - Overview

Annexes on technical details

- Annex I: Classification and labelling requirements for hazardous substances and mixtures
- Annex II: Special rules for labelling and packaging
- Annex III: List of Hazard Statements
- Annex IV: List of Precautionary Statements
- Annex V: Pictograms
- Annex VI: Harmonised List of Hazardous Substances
- Annex VII: Translation Table for classification

CLP : Translation Tables - examples

EU R-Phrase	GHS code	GHS hazard
R42	H334	Respiratory Sensitiser
R43	H317	Skin Sensitiser
Carc.Cat.2; R45	H350	Carcinogen Cat. 1B
Repr.Cat.2; R60	H360	Reproductive toxicant Cat. 1 B (“May damage fertility”) (“May damage unborn child”)
Repr.Cat.2; R61	H360	

Supplier's main roles and obligations

- **Classify**
  - **Before placing on the market**
  - **If REACH requires classification, e.g. on-site isolated intermediates**
- **Respect harmonised classification (Annex VI) or self-classify**
- **Ensure appropriate Labelling and Packaging before placing on the market**
  - For purposes of C+L+P
    - Downstream users may use classification from supplier, provided no change of composition
    - Distributors: no obligation to classify; for purposes of L+P, may use classification from supplier
- **Cooperate with others in the supply chain for meeting requirements.**

Self classification - duties

- **Identify and examine available information from many sources**
  - No obligation to test, except for physico-chemical properties
  - May generate new info through testing, but animal testing only last resort
- **Evaluate information**
  - Apply Annex I criteria, including expert judgment/weight of evidence
  - For mixtures: bridging principles – calculation method

Hazard communication: Labelling (Title III)

- **Content of the label**
  - **Labelling elements:**
    - Product ID, Hazard pictograms, signal words, hazard and precuationary statements, supplemental infor (supplier ID, quantity)
  - **Use of languages**
  - **Derogations; use of alternative name for substances in mixtures**
  - **Updating information on the label**

Hazard communication: Safety Data Sheet

- **Safety Data Sheet** requirements specified in **Annex II of REACH**
- General format (order of sections) already reflects the UN GHS
- Annex II under revision for more detailed adaptation to UN GHS and CLP

C&L Harmonisation and the C&L inventory (Title V)

- **Replaces REACH Title XI**

•Chapter 1 – establishing harmonised classification and labelling of substances

  - •For specific hazard categories *(Cfr. REACH: CMRs, respiratory sensitisers, other case by case if justified; specific active substances)*
  - •Procedure to include a substance in Annex VI – started by authorities or industry actor, decision by European Commission

- Chapter 2 – Classification and Labelling inventory
  - •Scope unchanged (replaces Title XI of REACH)
  - •Obligation to notify ECHA
  - •Agreed entries
  - •C&L inventory will be publicly available from ECHA website

Notification to the C&L inventory (Title V)

- **<u>What:</u> substances** placed on the market **on their own or in a mixture**
  - either meet the criteria for classification as hazardous
  - or subject to REACH registration
  - if not already submitted as part of the registration dossier or already notified by that notifier
- **<u>By whom:</u>** Manufacturer(**M**) or Importer(**I**), or **group of M or I** (*not by exporter to the EU*!)
- **<u>When:</u>** within **one month** after the substance is placed on the market

Examples:

1. *Substance supplied before and again on Dec 1, 2010 ➔ deadline 1 Jan 2011 (in practice 3/1/2011)*
2. *Substance supplied on 8 Nov, 2009 and only again on 1 Feb 2011 ➔ deadline 1 March 2011*
3. *Substance supplied for the first time 20 Aug 2012 ➔ deadline 20 Sept 2012*

Transitional Period

REACH

3.5 y. HPV etc. | 2.5 y. > 100 t/a | 5 y. > 1 t/a

1 Dec 2010 — 1 June 2015

CLP

3.5 y. Substances | 4.5 y. Mixtures

For substances and mixtures:
Exist. system: binding
CLP: optional;
Label: CLP if use option

For substances:
CLP: obligatory*
SDS must contain exist. and CLP classification
For mixtures: EU-System: binding
CLP: optional; Label: CLP if use option

After the entire transition period:
For substances & mixtures:
CLP: obligatory*
Exist. system: loses its legal status

*derogation for already placed on the market:
- substances until 1.12.2012
- mixtures until 1.6.2017

Transitional Period and Guidance

- **Entry into force: 20 Jan 2009**
- **Transitional period** staggered:
  - *Substances: 1 Dec 2010*
  - *Notification to C&L inventory within 1 month after placing on the market*
  - *Mixtures: 1 June 2015*
- Repeal old Directives (67/548/EEC and 1999/45/EC) by June 2015
- **Guidance to CLP →**
  http://echa.europa.eu/clp/clp_help_en.asp
  - "*Introductory guidance on CLP regulation*" describes basic obligations and procedures
  - "*Guidance on the application of the CLP criteria*" describes the general principles of C&L under CLP and provides detailed guidance on the criteria for classification of substances and mixtures
  - Questions and Answers documents.

Downstream Legislation

"Downstream" Legislation

- Obligations in the EU Community legislation referring to C&L (workers safety, Seveso II, consumer products, etc.), more than 20 pieces of EU downstream legislation impacted
  - careful analysis of possible effects by Commission services
  - Study demonstrates that effects are mostly minimal or can be minimised through appropriate consequential changes
  - Two legal acts adopted to amend downstream legislation:
    - Regulation 1336/2008, OJ L 354 to amend Regulation 648/2004 (detergents)
    - Directive 2008/112/EC, OJ L 345 to amend Directives 75/768 (cosmetics), 88/378/ (toys), 1999/13 (VOC), 2000/53 (ELV), 2002/96 (WEEE) and 2004/42 (VOC due to paints and varnishes)
  - Type of amendments: changes of references to CLP regulation, conversion of categories and risk/safety phrases, alignment with GHS terminology.
  - REACH is directly amended by the CLP regulation

Occupational safety & health directives

- Five OSH downstream directives make reference to the EU C&L system
    - To define aspects of the scope of application
- **Directives:**
    - Chemical Agents Directive 98/24/EC
    - Carcinogens and Mutagens Directive 2004/37/EC
    - Safety Signs Directive 92/58/EEC
    - Pregnant Workers Directive 92/85/EEC
    - Young People at Work Directive 94/33/EEC

DG EMPL prepares proposal to adapt
Intention: change of scope should be avoided

Hazardous Waste: Dir. 2008/98/EC, 91/689/EEC and Decision 2000/532/EC

Reference to C&L:

- Hazardous Waste Directive includes 14 „H-characteristics": H4-H8, H10-H11 reflects the classifications *Very Toxic, Toxic, Harmful, Corrosive, Irritant and CMR* as defined in Directive 67/548/EEC; generic concentration limits from Directive 1999/45/EC apply
- The new Waste Framework Directive includes 15 „H-characteristics" (new H13: Substances and preparations capable by any means, after disposal, of yielding another haz. substance)
- But: Waste is excluded from the scope of C&L legislation!
- Test methods in Annex V to Directive 67/548/EEC are repealed →transferred to Test Method Regulation (EC) No 440/2008

Hazardous Waste: Dir. 2008/98/EC, 91/689/EEC and Decision 2000/532/EC

- **Alignment of Waste Legislation to CLP is intended** to ensure consistency & simplification *(hazardousness of chemicals that become waste can be easily assessed)*
- If CLP applied directly – potential additional classification: *wastes containing e.g. corrosive and irritant ingredients resulting in non hazardous entries in the EWL becoming hazardous waste*
- Periodical revision of EU List of Waste (Low) foreseen in order to:
    - *Take into account scientific progress*
    - *Assess possible benefits of changes in structure*
    - *Simplification: addition of new entries and deletion of entries*
    - *Alignment with CLP*
- Study conducted by Ökopol – Review of EU LoW

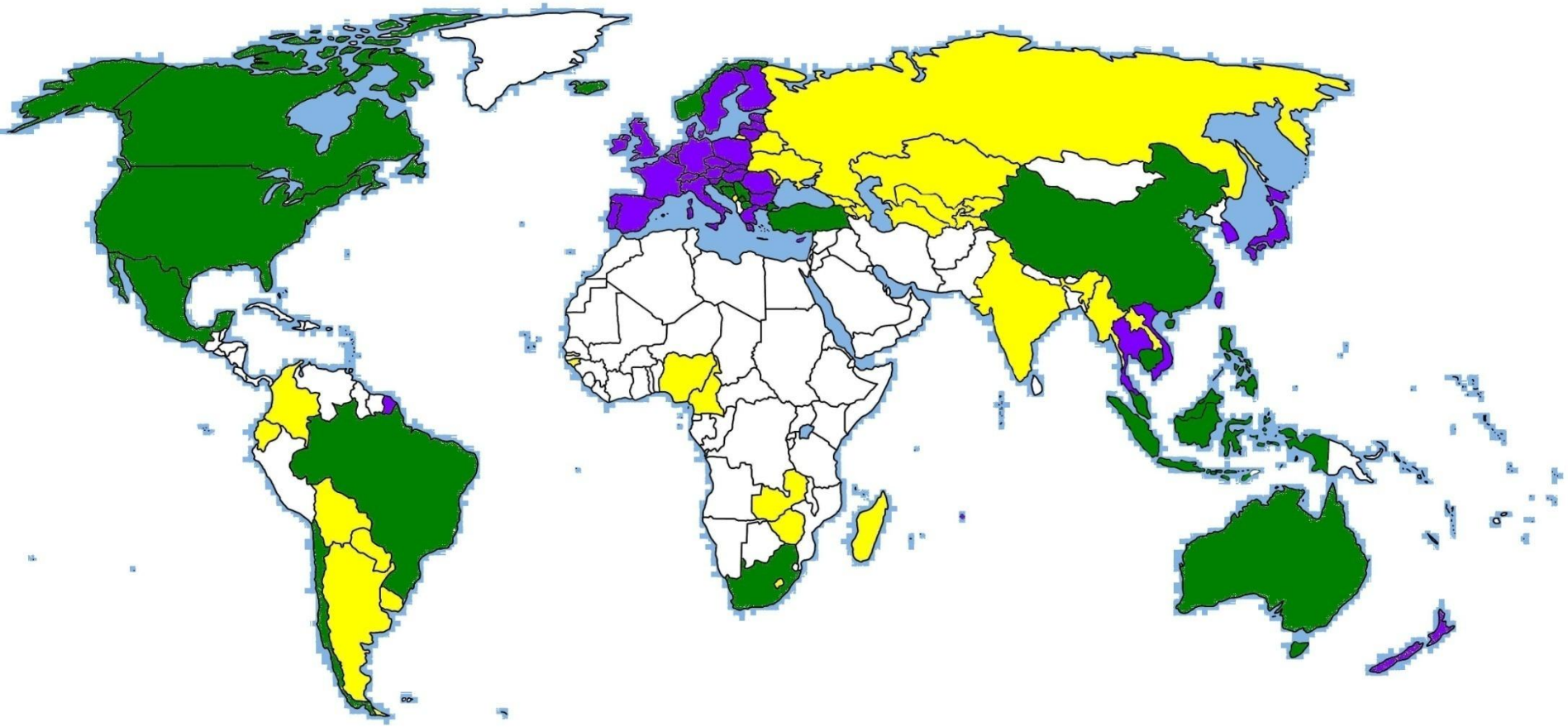
http://ec.europa.eu/environment/waste/pdf/low_review_oekopol.pdf

- Different options considered
- Change in scope should be avoided
- No major change in structure expected

Hazardous Waste: Dir. 2008/98/EC, 91/689/EEC and Decision 2000/532/EC

- Expert WG (MS CAs) set up to discuss options of alignment
- Result of WG will be presented at Technical Adaptation Committee (TAC) for adoption
- Timeline: discussion with WG will go on in 2010
- Modification of LoW in 2011

GHS Status Worldwide – early 2009



activities

preparation

Implementation

CLP – General Principles for Classification

Information – sources and testing
Evaluation of data
Evaluation of mixtures
Specific concentration limits, M-factors and generic cut-off values
Special cases

Other key issues to consider

Information – sources and testing

- The information shall relate to the forms or physical states in which the substance or mixture is placed on the market and in which it can reasonably be expected to be used
- For Health and Environmental effects new data can be generated for substances if all other alternatives cannot provide 'adequate reliability and quality of data'
- Testing of mixtures not allowed for 'germ cell mutagenicity', 'carcinogenicity' and 'reproductive toxicity' (CMRs)
- Where mixture data demonstrates such effects which have not been identified from the information on the individual substances, those data shall also be taken into account – *implies that negative data on a mixture does not count*

Information – sources and testing

Tests on non-human primates and humans are prohibited for the purposes of the CLP Regulation, however human data from other sources, such as clinical studies can be used

For the evaluation of mixtures relation to the 'biodegradation and bioaccumulation' in 'hazardous to the aquatic environment', *only data on the substances in the mixture can be used*

For physical hazards *complaint* tests are required unless there is adequate and reliable information is already available. New tests have to be carried out at the latest from 1 January 2014, in compliance with a relevant recognised quality system or by laboratories complying with a relevant recognised standard

Evaluation of data

Role and application of expert judgement and weight of evidence determination

***Weight of evidence* determination using expert judgment can be used where the criteria cannot be applied directly to available identified information**

- ***Weight of evidence* determination means that all available information positive and negative is considered together and the data weighted appropriately (quality and consistency) in a single weight of evidence determination**
- ***Expert judgement* for classifying mixtures so as to cover as many mixtures as possible**
- ***Expert judgment* may be required for substances, especially where weight of evidence determinations are needed – this is more likely for chronic health endpoints**

Evaluation of data

Normally hazardous effects seen in appropriate animal studies or from human experience consistent with the criteria shall normally justify classification

- **Generally, adequate, reliable and representative data on humans shall have precedence over other data**
- **However, positive results from animal studies are not necessarily negated by the lack of positive human experience**

Mechanistic information & metabolism studies are considered relevant.

- **When such data raises doubt about relevance in humans, a lower classification may be warranted**
- **When there is scientific evidence that the mechanism or mode of action is not relevant to humans, the substance or mixture should not be classified**

Evaluation of Mixtures

TIERED APPROACH

Use test data for the mixture, when available (not for CMRs)

↓

Use Bridging Principles, when data available on some constituents

↓

Calculation when data available on all constituents

- **Additivity (Acute Toxicity)**
- **Summation (Skin and Eye Irritation, Aquatic)**
- **Specific or Generic Concentration Limits (Sensitisation, CMRs, STOT)**

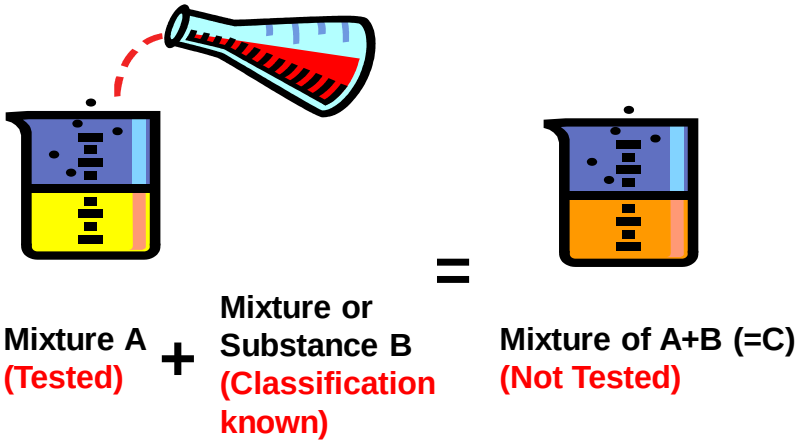
Evaluation of Mixtures

Bridging Principle Provides for the situation in which the mixture has not been tested, but a *similar mixture has been tested*. 'Similar' can be defined in terms of:

- Dilution
- Batching
- Concentration of Acute Components
- Interpolation
- Substantially similar mixtures

Acute Toxicity – Bridging example

Dilution



If 'B' is water or is *non-toxic then classification of 'C' can be calculated**

- **e.g. if LD_{50} of 'A' is 50 mg/kg (Acute Cat 2), and it is diluted 2x with water, then toxicity of 'C' is estimated to be 100 mg/kg (Acute Cat 3)**

* > LD_{50} 5000 mg/kg

Acute Toxicity – ATEs

Conversion of Acute Oral Toxicity Data from a Range or Limited Dose study or from the Classification Category in the absence of actual data

	Classification category or experimentally obtained acute toxicity range estimate	Converted Acute Toxicity Point Estimate ATE
Oral (mg/kg bw)	0 < Category 1 ≤ 5	0.5
	5 < Category 2 ≤ 50	5
	50 < Category 3 ≤ 300	100
	300 < Category 4 ≤ 2000	500
	2000 < Category 5 ≤ 5000	2500

Concentration limits, M-factors and Cut-off values

Cut-off values indicate when the presence of a substance needs to be ***taken into account*** whether as an identified impurity, additive, or individual constituent (see Article 11).

Table 1.1 **Generic cut-off values**	
Hazard class	**Generic cut-off values to be taken into account**
Acute Toxicity: — Category 1-3 — Category 4	 0,1 % 1 %
Skin corrosion/Irritation	1 % (1)
Serious damage to eyes/eye irritation	1 % (2)
Hazardous to Aquatic Environment — Acute Category 1 — Chronic Category 1 — Chronic Category 2	 0,1 % (3) 0,1 % (3) 1 %

Concentration limits, M-factors and Cut-off values

Specific concentration limits (SCLs) and Generic concentration limits are *threshold*s at or above which the presence in another substance or in a mixture as an identified impurity, additive or individual constituent leads to the classification of the substance or mixture as hazardous - *but not always*! (Article 10)

- **Generic Concentration Limits are assigned to certain hazard classes in the Hazard Criteria**
- **Lower SCLs can be set by the manufacturer, importer or downstream user but need adequate and reliable data (?)**
- **Higher levels can be set exceptional circumstances specific, but precedents set**
- **Substance Specific SCLs may be set in Annex VI or the C&L Inventory**

Generic concentration limits - Examples

Ingredient classified as	**Generic concentration limits** triggering classification of a mixture as:	
	Category 1	Category 2
Category 1 Mutagen	≥ 0.1 %	
Category 2 Mutagen		≥ 1.0 %
Category 1 Carcinogen	> 0.1 %	
Category 2 Carcinogen		> 0.1 %* > 1.0 %
Category 1 Reproduction	**> 0.1 %** **≥ 0.3 %** **EU ≥ 0.5 %**	
Category 2 Reproduction **		**≥ 0.1 %*** **≥ 3.0 %** **EU ≥ 0.5 %**
Category 1 STOT RE	≥ 10 %	> 1.0 %
Category 2 STOT RE		≥10 % > 1.0 % *

* An SDS should be available on request
** Note there is a new Category Effects on or via Lactation

Specific concentration limits

Which cut-off applies (for each hazard class)

- For a substance with a SCL in Annex VI or the CLP Inventory, the lower figure either, the SCL or Generic cut-off applies
- For a substance with a SCL in Annex VI or the CLP Inventory but for hazard class without a Generic cut-off, the SCL applies

- For a substance with no SCL then the Generic cut-off applies
- For a substance with no SCL and with no Generic cut-off, then the Generic Concentration Limit in the Hazard Criteria applies

M-factors for environmental hazards

Acute Category 1 and Chronic Category 1 components with toxicities below 1 mg/l contribute to the toxicity of the mixture even at a low concentration and are given increased weight in applying the summation of classification approach

Instead of adding up the percentages a weighted sum is used by multiplying the concentrations of components by a multiplying factor

Multiplying Factors for Highly Toxic Components for a Mixture	
$L(E)C_{50}$ value	**Multiplying factor (M)**
$0.1 < L(E)C_{50} \leq 1$	1
$0.01 < L(E)C_{50} \leq 0.1$	10
$0.001 < L(E)C_{50} \leq 0.01$	100
$0.0001 < L(E)C_{50} \leq 0.001$	1000
$0.00001 < L(E)C_{50} \leq 0.0001$	10000
(continue in factor 10 intervals)	

Calculation – summation (acute)

All components toxicity >0.1 mg/l

Σ **Components classified as:**		**Mixture is classified as:**
Acute I	>25%	Acute I
(10 x Acute I) + Acute II	>25%	Acute II
(100 x Acute I)+(10 x Acute II)+Acute III	>25%	Acute III

Calculation – summation (acute)

All components toxicity <0.1 mg/l

Σ **Components classified as:**		**Mixture is classified as:**
Acute I x M	>25%	Acute I
(M x 10 x Acute I) + Acute II	>25%	Acute II
(M x 100 x Acute I)+(10 x Acute II)+Acute III	>25%	Acute III

Specific cases requiring further evaluation (art.12)

Certain properties can be taken in into account for the purposes of classification:

- adequate and reliable information demonstrates that in practice the physical hazards of a substance or a mixture differ from those shown by tests

- conclusive scientific experimental data show that the substance or mixture is not *biologically available* and those data have been ascertained to be adequate and reliable

- adequate and reliable scientific information demonstrates the potential occurrence of synergistic or antagonistic effects among the substances in a mixture for which the evaluation was decided on the basis of the information for the substances in the mixture

Some key differences from the old DSD EU system

- Acute Toxicity Category Cut-Offs changed, plus extra Category
- Conversion to an estimated Acute Toxicity point Estimate
- Mixtures classification process changed for Acute Effects- no Specific Concentration Limits

- Corrosive Cat 1 divided in to Cat 1A/1B/1C
- Criteria Differences for skin and eye irritation – mild eye irritation
- CMR Category Numbering Changes
- Significant Changes to Reproductive Toxicity
- Possibility of Route Specific Labelling for CMRs
- Cut-offs for communication on SDS for CMRs and STOT

Other key issues

- Read Across Tables (Annex VII)
- Minimum classifications in Annex VI (marked by *) mainly Acute Toxicity & STOT
- Requirement to more do a more severe classification if data available (1.2.1 Annex VI)
- Need to go back to original data

Acute Oral Toxicity – Translation Issues

EC No 1272/2008 (CLP)			67/549/EEC (DSD)		
Hazard Category	LD_{50} mg/kg		Risk Phrase	LD_{50} mg/kg	
	Lower	Upper		Lower	Upper
1		≤ 5			
2	> 5	≤ 50	R28 T+		≤ 25
3	> 50	≤ 300	R25 T	> 25	≤ 200
4	> 300	≤ 2000	R22 Xn	> 200	≤ 2000
5	> 2000	≤ 5000*			

Substance LD50 275 mg/kg

- **67/548/EEC = Xn R22**
- **CLP Annex VI = Acute Tox 4**

Actual CLP should be Acute Tox 3 and should be applied according to Annex VI 1.2.1

"the manufacturer or importer has access to data or other information as specified in Part 1 of Annex I that lead to classification in a more severe category compared to the minimum classification. Classification in the more severe category must then be applied."

THANK YOU!

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