

Testing of chemicals for classification according to REACH and GHS

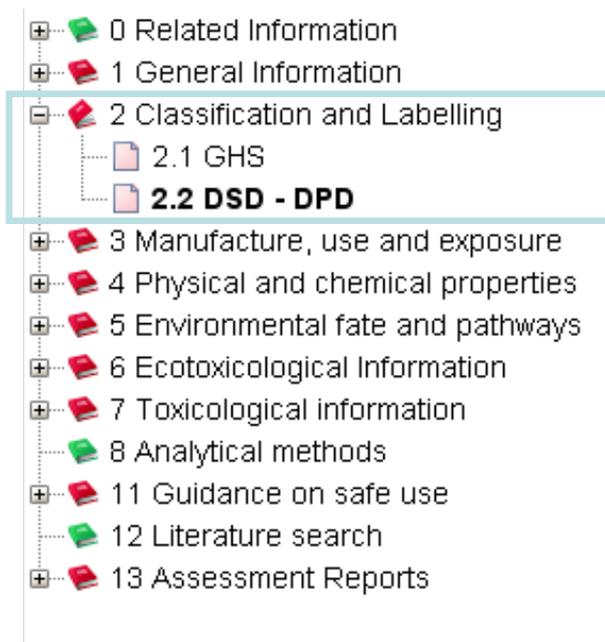
Norbert Bornatowicz,
Head Toxicology
Seibersdorf Labor GmbH
2444 Seibersdorf, AUSTRIA

Overview on the presentation

- Classification: IUCLID requirements
- Matching DSD with GHS
- Tests to fulfil both DSD and GHS classification requirements

Classification: IUCLID requirements

IUCLID section tree, classification



GHS:

Classification according to the Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures

DSD-DPD:

Classification according to Directives 67/548/EWG ("Dangerous Substances Directive", DSD) and 1999/45/EG ("Dangerous Preparations Directive", DPD)

IUCLID classification GHS

Classification

Physical hazards

	Hazard statement	Reason for no classification
Explosives		conclusive but not sufficient for classification
Flammable gases		conclusive but not sufficient for classification
Flammable aerosols		conclusive but not sufficient for classification
Oxidising gases		conclusive but not sufficient for classification
Gases under pressure		conclusive but not sufficient for classification
Flammable liquids	Flam. Liquid 3	H226: Flammable liquid and vapour.
Flammable solids		conclusive but not sufficient for classification
Self-reactive substances and mixtures		
Pyrophoric liquids		
Pyrophoric solids		
Self-heating substances and mixtures		
Substances and mixtures which in contact with water emit flammable gases		
Oxidising liquids		
Oxidising solids		
Organic peroxides		
Corrosive to metals		conclusive but not sufficient for classification

Pick list

- data lacking
- inconclusive
- conclusive but not sufficient for classification

OK Cancel

IUCLID classification DSD-DPD

Classification		Reason for no classification
Explosiveness	<input type="text"/>	conclusive but not sufficient for classification
Oxidising properties	<input type="text"/>	conclusive but not sufficient for classification
Flammability	<input type="text"/>	conclusive but not sufficient for classification
Thermal stability	<input type="text"/>	conclusive but not sufficient for classification
Acute toxicity	<input type="text"/>	conclusive but not sufficient for classification
Acute toxicity - irreversible damage after single exposure	▼ Xn, R68/21/22 Harmful; Harmful: possible risk of irreversible effects in contact with skin and if swallowed	<input type="text"/>
Repeated dose toxicity	<input type="text"/>	conclusive but not sufficient for classification
Irritation / Corrosion	<input type="text"/>	conclusive but not sufficient for classification
Sensitisation	<input type="text"/>	conclusive but not sufficient for classification
Carcinogenicity	<input type="text"/>	conclusive but not sufficient for classification
Mutagenicity - Genetic Toxicity	<input type="text"/>	conclusive but not sufficient for classification
Toxicity to reproduction - fertility	<input type="text"/>	conclusive but not sufficient for classification
Toxicity to reproduction - development	<input type="text"/>	data lacking
Toxicity to reproduction - breastfed babies	<input type="text"/>	data lacking
Environment	<input type="text"/>	conclusive but not sufficient for classification

Labelling

Information

Basis for classification according to DSD-DPD

Explosiveness
Oxidising properties
Flammability
Thermal stability
Acute toxicity
Acute toxicity - irreversible damage after single exposure
Repeated toxicity
Irritation/Corrosion
Sensitisation
Carcinogenicity
Mutagenicity - genetic toxicity
Toxicity to reproduction-development
Toxicity to reproduction-breastfed babies
Environment

Basis for classification according to GHS

Explosives	Acute toxicity - oral
Flammable gases	Acute toxicity - dermal
Flammable aerosols	Acute toxicity - inhalation
Oxidising gases	Skin corrosion / irritation
Gases under pressure	Serious eye damage / eye irritation
Flammable liquids	Respiratory sensitisation
Flammable solids	Skin sensitisation
Self-reactive substances and mixtures	Aspiration hazards
Pyrophoric liquids	Reproductive toxicity
Pyrophoric solids	Effects on or via lactation
Self-heating substances and mixtures	Germ cell mutagenicity
Substances and mixtures which in contact with water emit flammable gases	Carcinogenicity
Oxidising liquids	Specific organ toxicity - single
Oxidising solids	Specific organ toxicity - repeated
Organic peroxides	Hazardous to the aquatic environment
Corrosive to metals	Hazardous to the atmospheric environment

Matching DSD with GHS

Classification on the basis of physicochemical properties (1)

DSD-DPD

Explosiveness

Oxidising properties

Flammability

GHS

Explosives

Oxidising gases
Oxidising liquids
Oxidising solids
Organic peroxides

Flammable gases
Flammable aerosols
Flammable liquids
Flammable solids
Substances and mixtures which in contact with water emit flammable gases
Pyrophoric liquids
Pyrophoric solids
Self-heating substances and mixtures

Classification on the basis of physicochemical properties (2)

DSD-DPD

Thermal stability

-

-

GHS

Self-reactive substances and mixtures

Gases under pressure

Corrosive to metals

Classification on the basis of toxicological properties

DSD-DPD

Acute toxicity

Acute toxicity - irreversible damage after single exposure

Repeated toxicity

Irritation/Corrosion

Sensitisation

GHS

Acute toxicity - oral

Acute toxicity - dermal

Acute toxicity - inhalation

Aspiration hazards

Specific organ toxicity - single

Specific organ toxicity - repeated

Skin corrosion / irritation

Serious eye damage / eye irritation

Respiratory sensitisation

Skin sensitisation

Classification on the basis of specific effects to human health

DSD-DPD

Carcinogenicity

Mutagenicity - genetic toxicity

Toxicity to reproduction-development

Toxicity to reproduction-breastfed babies

GHS

Carcinogenicity

Germ cell mutagenicity

Reproductive toxicity

Effects on or via lactation

Classification on the basis of environmental effects

DSD-DPD

Environment

GHS

Hazardous to the aquatic environment

Hazardous to the atmospheric environment

Tests to fulfil both DSD and GHS classification requirements

Data Analysis

Collection and compilation of existing data

- Own data (clarification of data ownership)
- Data sources, databases
See Guidance on information requirements and chemical safety assessment, Chapter R.3: Information gathering
- Data from SIEF participants
- Data from chemically related substances (grouping, read-across)

Requires **expertise** to interpret the data.

For studies not in the public domain there is the requirement to demonstrate **legal title** to the information in order to protect intellectual property rights of the data owner.

Data Reliability, examples

Values for **physico-chemical properties** taken from **MSDS's** and all other company technical data can only be assigned a reliability rating of "4", unless detailed information is available. a)

Values obtained from "**peer reviewed**" data: reliability score = "2" a)

The maximum reliability score for **read-across** is "2". b)

a) ECHA Practical Guide 2: How to report weight of evidence

b) ECHA Practical Guide 6: How to report read-across and categories

Guidelines

Good Laboratory Practice (GLP)

mandatory for toxicological and ecotoxicological testing,
not mandatory for physico-chemical testing

=> not compliant with other regulations or with non-EU member states

Council regulation (EC) No 440/2008 from 30 May 2008

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:142:0001:0739:EN:PDF>

OECD methods (Section 4: Health effects) may be used in some cases

http://titania.sourceoecd.org/vl=14974079/cl=11/nw=1/rpsv/periodical/p15_about.htm?jnlissn=1607310x

UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria

Physicochemical properties (1)

Classification criteria (GHS)	Test methods	Endpoint REACH Annex VII
Explosives	DSC, Test Series 1	7.11
Oxidising gases	ISO 10156	7.13
Oxidising liquids	A.21, UN-O.2	7.13
Oxidising solids	UN-O.1	7.13
Organic peroxides	chemical structure UN methods, Part II, Sect. 28	-
Flammable gases	flammable range with air at 20 °C	7.9, 7.10
Flammable aerosols	contains flammable liquids, gases or solids	7.9, 7.10
Flammable liquids	A.9, A.12/A.13	7.9, 7.10
Flammable solids	A.10, A.12/A.13	7.9, 7.10
Substances and mixtures which in contact with water emit flammable gases	A.12, N.5	7.9, 7.10

Physicochemical properties (2)

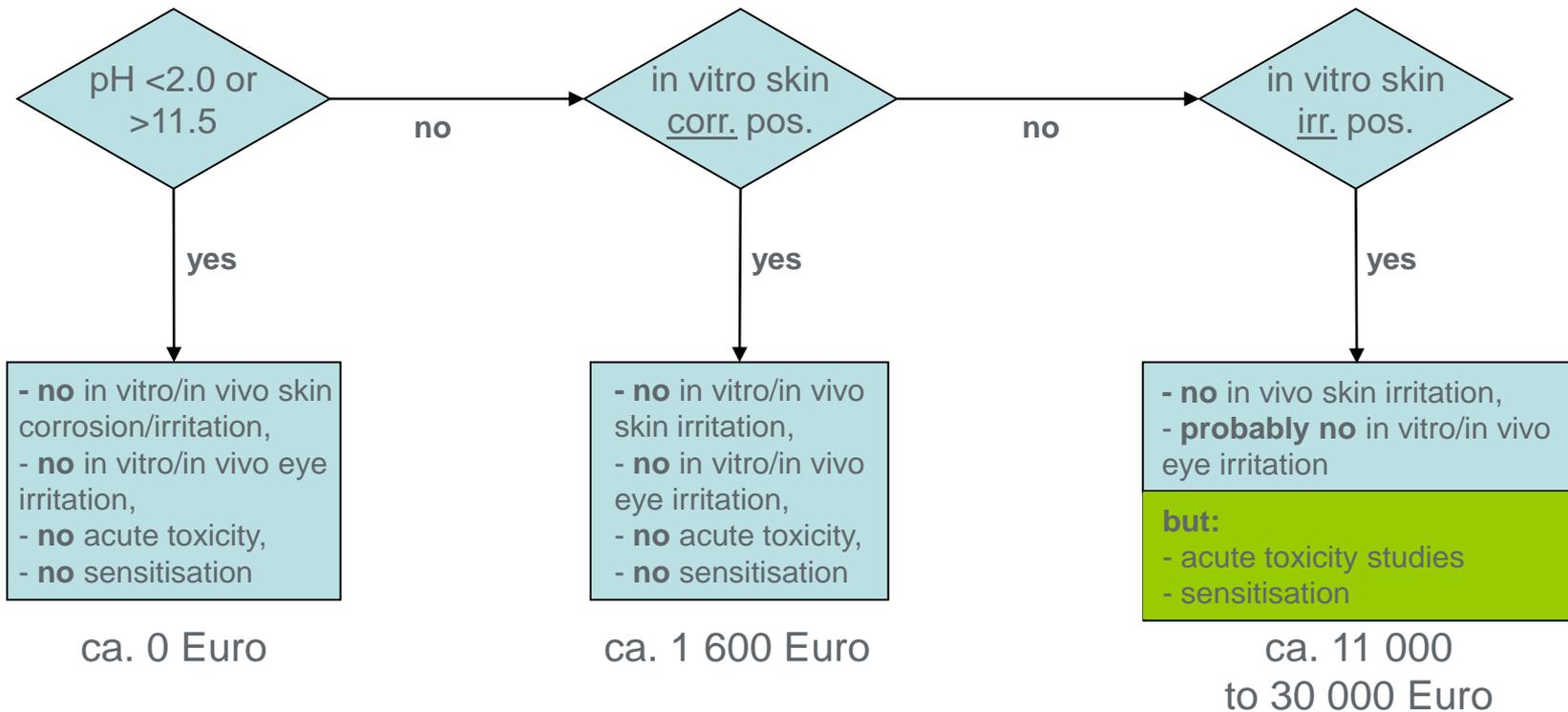
Classification criteria (GHS)	Test methods	Endpoint REACH Annex VII
Pyrophoric liquids	A.13, N.3	7.12
Pyrophoric solids	A.13, N.2	7.12
Self-heating substances and mixtures	N.4	~ 7.12
Self-reactive substances and mixtures	UN methods, Part II, Sect. 28	-
Gases under pressure	>200 kPa or liquefied pure gases: see UN Recommendations on the Transport of Dangerous Goods, Model Regulations	-
Corrosive to metals	C.1	-

Toxicological properties (1)

Classification criteria (GHS)	Test methods: OECD, EU	Endpoint REACH (Annex ..., No.)
Acute toxicity - oral	Acute toxicity,	VII, 8.5.1
Acute toxicity - dermal	Viscosity	VIII, 8.5.2, 8.5.3
Acute toxicity - inhalation		IX, 7.17
Aspiration hazards		
Specific organ toxicity - single	Acute toxicity	VII, 8.5.1 VIII, 8.5.2, 8.5.3
Specific organ toxicity - repeated	Repeated dose toxicity	VIII, 8.6.1 IX, 8.6.2 X, 8.6.3/4
Skin corrosion / irritation	In vitro and in vivo studies	VII / VIII, 8.1
Serious eye damage / eye irritation	In vitro and in vivo studies	VII / VIII, 8.2
Respiratory sensitisation	-	-
Skin sensitisation	Skin sensitisation studies	VII, 8.3

Test dependencies

example for toxicological properties



Toxicological properties (2)

Classification criteria (GHS)	Test methods: OECD, EU	Endpoint REACH (Annex ..., No.)
Carcinogenicity	Mutagenicity studies, Carcinogenicity studies	VII, 8.4.1 VIII, 8.4.2, 8.4.3 IX, 8.4 X, 8.9.1
Germ cell mutagenicity	Mutagenicity studies, (Developmental toxicity)	VII, 8.4.1 VIII, 8.4.2, 8.4.3 IX, 8.4 X, 8.9.1 (IX, 8.7.2)
Reproductive toxicity	Screening tests, Developmental toxicity, Reproduction toxicity	VIII, 8.7.1 IX / X, 8.7.2, 8.7.3
Effects on or via lactation	(Screening tests) Reproduction toxicity	(VIII, 8.7.1) IX / X, 8.7.3

Ecotoxicological properties

Classification criteria (GHS)	Test methods: OECD, EU	Endpoint REACH (Annex ..., No.)
Hazardous to the aquatic environment	Acute toxicity tests on aquatic organisms Long-term studies on aquatic organisms Surface tension Partition coefficient n-octanol/water Dissociation constant Water solubility Biodegradability Adsorption/desorption studies Bioaccumulation studies	VII, 7.6, 7.7, 7.8, 9.1.1, 9.1.2, 9.2.1.1 VIII, 9.1.3, 9.1.4. 9.2.2.1, 9.3.1 IX, 7.16, 9.2.1.2, 9.3.2
Hazardous to the atmospheric environment	-	-



Seibersdorf Labor GmbH

Vienna is very near – and so are we

Seibersdorf Labor GmbH
Toxicology
2444 Seibersdorf
AUSTRIA

phone: +43 50 550 3501 (secretary)
fax: +43 50 550 3653
email: toxikologie@seibersdorf-laboratories.at
web: www.seibersdorf-laboratories.at/toxicology

Reliability of data (Klimisch et al.)

1 = reliable without restrictions: “studies or data...generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline...or in which all parameters described are closely related/comparable to a guideline method.”

2 = reliable with restrictions: “studies or data...(mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable.”

3 = not reliable: “studies or data...in which there were interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g., unphysiologic pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgment.”

4 = not assignable: “studies or data....which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.).”