



Bundesanstalt für Arbeitsschutz und Arbeitsmedizin

CLP: human health hazards

Classification criteria

for substances & mixtures & changes

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CLP: human health hazards

ACUTE TOXICITY

SKIN CORROSION/IRRITATION

SERIOUS EYE DAMAGE /EYE IRRITATION

RESPIRATORY OR SKIN SENSITISATION

GERM CELL MUTAGENICITY

CARCINOGENICITY

REPRODUCTIVE TOXICITY

SPECIFIC TARGET ORGAN TOXICITY – SINGLE EXPO

SPECIFIC TARGET ORGAN TOXICITY – REP'T EXPO

ASPIRATION HAZARD

CLP regulation

including EU “left-overs” not covered by GHS

i) Criteria remain the same e.g.

EUH029 *Contact with water liberates toxic gas.*

EUH066 *Repeated exposure may cause skin
dryness/cracking.*

[EUH070 *Toxic by eye contact.]*

Changes in
Substance classification
criteria:
Health hazards

CLP vs DSD: differences in C&L criteria

e. g.: Acute oral toxicity – LD₅₀ [mg/kg]

**67/548/EEC
(DSD)**

		
Very toxic < 25	toxic > 25 - 200	harmful > 200 - 2000

200 - 300

**EC No. 1272/2008
(CLP)**

Category 1 < 5	Category 2 > 5 - < 50	Category 3 > 50 - < 300	Category 4 > 300 - < 2,000
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EU GHS regulation CLP: changes

Acute toxicity: CLP  (Cat. 3) vs DSD Xn 

LD₅₀ in the range

200-300 mg/kg (oral),

400-1000 mg/kg (dermal)

2-10 mg/l (vapour)

also: gases, not: aerosols

2. analogous changes

Target organ toxicity – single exposure

EU GHS regulation CLP: changes

Annex I 67/548/EEC (n=3366 entries, 29. ATP)

Xn R22		LD ₅₀ 200-2000 mg/kg	n=527
thereof GHS		LD ₅₀ 200-300 mg/kg	n=29 0.9%
Xn R21		LD ₅₀ 400-2000 mg/kg	
thereof GHS		LD ₅₀ 400-1000 mg/kg	1.8%

New substances n=4001

Xn R22	GHS		0.55%
Xn R21	GHS		0.8%

EU R64 and R67 “other toxicological property”
GHS: ‘full’ hazard

[4. carcinogenicity (GHS: IARC-criteria).
Cat. 1B, valid study m&f positive]

[5. fertility impairment:
1x in vivo study positive: Cat 1B]

Aspiration hazard: changes in criteria

CLP:

Hydrocarbons with kinematic viscosity ≤ 20.5 mm²/s, 40°C

DSD:

- kinematic viscosity ≤ 7 mm²/s, 40°C
- Flow time less than 30 s in 3 mm ISO cup (ISO 2431)
- exclusion criterion: surface tension > 33 mN/m, 25°C

Similar: classify mixture $\geq 10\%$

EU GHS regulation CLP: changes: summary

criteria identical (difference restricted to single cases)

CMR, sensitisation, lactation, corrosion/irritation

criteria nearly identical

target organ toxicity / repeated exposure

criteria different

acute toxicity, target organ toxicity / single exposure

example: glutardialdehyde classification

acute toxicity oral Cat. 3	acute toxicity inhal. Cat. 1	skin corrosion / irritation Cat. 1C	Sensitisation (respiratory)	Sensitisation (skin)	hazardous to the aquatic environment acute Cat. 1
					
Danger	Danger	Danger	Danger	Warning	Warning
Toxic if swallowed	Fatal if inhaled	Causes severe skin burns and eye damage	May cause allergic or asthmatic symptoms or breathing difficulties if inhaled	May cause an allergic skin reaction	Very toxic to aquatic life

example: glutardialdehyde labelling



Danger

H301 Toxic if swallowed

H330 Fatal if inhaled

H314 Causes severe skin burns and eye damage

H334 May cause allergic or asthmatic symptoms or breathing difficulties if inhaled

H317 May cause allergic skin reaction

H400 Very toxic to aquatic life

Changes in
Mixture classification
criteria:
Health hazards

CLP: Classification criteria for mixtures & changes?

Mixture classification generally:

Increase in the margin of evaluation:

Deviation from classification criteria as a consequence of expert judgment allowed

- in case criteria cannot be directly applied

CLP: Classification criteria for mixtures & changes?

bridging principles *tested to untested mixtures*

- **dilution** added substance less/similarly hazardous
- **batching** *CLP Annex I 1.1.3.2 und 1.1.3.6*
- **concentration** mixture in Cat. 1; increase Cat. 1 substance
- **interpolation** mixture 1 + 2 similar cat., 3 conc. inbetween
- **substantially similar**
 mixtures A+B, C+B, A =C in % & classification

CLP: Classification criteria for mixtures & changes?

Conventional methods:

additivity principle for

acute toxicity

skin/eye corrosion/irritation

fixed concentration limits

Sensitisation

sTOT

CMR

Aspiration *(including kinematic viscosity)*

CLP novelty: specific concentration limit setting for classification

- *supplier may set lower or higher SCL
in case proven by data*
- *generally possible for all health hazards*
- *guidance to be made available by ECHA
(autumn 2009)*

CLP Novelty: setting of specific concentration limits for classification

SCL setting: CLP guidance contents

e.g.

carcinogenicity T25 concept Sanner et al. 1997

skin sensitisation Basketter et al. 2005

reproductive toxicity



acute toxicity ,automatic' SCL setting

aspiration ,automatic' SCL setting

SCL setting: CLP guidance contents

Hazard class	Cat.	Lower SCL	Higher SCLs
Acute toxicity	all	not applicable	not applicable
Skin corrosion/irritation	all	yes	yes
Serious eye damage/eye irritation	all	yes	yes
Respiratory sensitisation	1	yes	no
Skin sensitisation	1	yes	yes
Germ cell mutagenicity	all	no	no
Carcinogenicity	all	yes	yes
Reproductive toxicity	all	under discussion	under discussion
Target Organ Toxicity-single	1/2/3	yes / no / yes	no / no / yes
Target Organ Toxicity-rep't	1/2	yes / no	no / no
Aspiration hazard	1	not applicable	not applicable

CLP: Classification criteria for mixtures & changes?

acute toxicity:

- route: mainly oral **problem in case of no data!**
 - calculation formula using ATEs: generally LD/LC_{50}
 - portions substances with unknown toxicity > 10 %:
exclusion
- ⇒ communication of LD_{50}/ATE in the supply chain!
- ⇒ *Mainly method different; overall consequences low*

Skin/eye corrosion/irritation: mixtures

2 general approaches: additivity vs non-additivity

Eye: partly skin irritation included in calculation; UN GHS criteria partly wrong or at least unclear

Concentration limits decrease (next slide)

Skin & eye irritation/corrosion: mixtures

substance classified as (>%)	DSD	CLP
corrosive R35	10 5 R34 1 R38	5 1 H315
corrosive R34	10 5 R38	5 1 H315
irritant (skin)	20	10
irritant (eye, severe)	10 5 R36	3 1 H319
irritant (eye)	20	10

CLP: Classification criteria for mixtures & changes?

1 fixed concentration limit for classification - examples

substance classification	CLP	DSD	change?
CM (Cats. 1 & 2)	0.1	0.1	no
R (Cats.1 & 2)	0.3	0.5	irrelevant
CM (Cat. 3)	1	1	no
R (Cat. 3)	3	5	irrelevant
Sensitisation (R42 & R43)	1	1	no
sTOT repeated (T vs GHS Cat. 1)	1	1	no
sTOT repeated (Xn vs GHS Cat. 2)	10	10	no

Summary: changes to be expected:
substance & mixtures classification

- 1) Total number of classified substances similar
- 2) Acute toxicity: few substances: ,Xn' change to ,T'
- 3) Total number of classified mixtures may increase