

Guidance on the Application of the CLP Criteria

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

Draft Version 5.0
January 2017



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Guidance on the Application of CLP Criteria

Reference: ECHA-xx-x-xx-EN

Cat.Number:

ISBN: xxx-xx-xxxx-xxx-x

DOI:

Publ.date: xxxx 2017

Language: EN

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1 Document History

Version	Comment	Date
n.a.	First edition	August 2009
n.a.	Please note that change between the version published in August 2009 and that of April 2011 are not recorded in this document history.	April 2011
Version 2.0	<p>Revision of the Guidance addressing content in relation to the environmental criteria chapters and Annexes following the 2nd Adaptation to Technical Progress to the CLP Regulation (Commission Regulation (EU) No 286/2011). The ECHA Secretariat revised the Guidance <i>Part 4 – Environmental hazards</i> and <i>Annexes</i> of the guidance document referring to the revised criteria for the long-term aquatic hazard for substances and mixtures and added new <i>Part 4 – Additional hazards</i> referring to the hazard class 'hazardous to the ozone layer'. As well, a number of examples have been included in the respective Parts and Annexes to illustrate the revisions performed. Further to this, a range of editorial corrections were proposed for <i>Part 1- General principles for classification and labelling</i>.</p> <p>The update includes the following:</p> <ul style="list-style-type: none"> • Revision of Part 1, by eliminating and amending out of date information and restructuring the text in order to reflect the Guidance update. • All green boxes in Part 4 that are impacted by the 2nd ATP were updated. As the CLP legal text uses commas instead of dots to define numbers smaller than 1, the green boxes now show commas as well. • Revision of Part 4, by providing guidance on the application of the new long-term aquatic hazard criteria for substances and mixtures. • Section 4.1.3 Classification of substances hazardous to the aquatic environment and section 4.1.4 Classification of mixtures hazardous to the aquatic environment were substantially revised, for example by addition of new references, as well as the new/ revised examples to illustrate relevant topics in the Part 4. • New Part 5 - Additional hazards was added (please note that Part 5: Labelling was deleted from the Guidance in previous non recorded versions and covered via a new Guidance on Labelling and Packaging in accordance with Regulation (EC) No 1272/2008 published in April 2011). • Most of the I.3 sub-sections in Annex I – Aquatic toxicity were revised. 	April 2012

	<ul style="list-style-type: none"> • In Annex II – Rapid degradation the terminology was modified. • Most of the Annex IV – Metals and Inorganic Metal Compounds was substantially modified and revised, as well as in sub-section IV.7 new examples were added. 	
Version 3.0	<p>Revision of Guidance Part 3 Health Hazards, relating to specific concentration limits (SCLs) for 4 hazard classes and the inclusion of a new Annex.</p> <p>The update includes the following:</p> <ul style="list-style-type: none"> • Revision of Part 3, by providing guidance on the setting of lower and higher SCLs for 4 health hazard classes in section 3.2.2.5 Skin Corrosion/Irritation; section 3.3.2.5 Serious Eye Damage/Eye Irritation; section 3.7.2.5 Reproductive Toxicity and section 3.8.2.6 STOT-SE, in accordance with CLP Article 10(7); • Inclusion of a new Annex (Annex VI) providing guidance on setting SCLs for the reproductive toxicity hazard class based on potency considerations. 	November 2012
Version 4.0	<p>(i) Revision of the CLP Guidance addressing content in relation to the Part 2: Physical hazards, Part 3: Health hazards and Annex VI following the 2nd and the 4th Adaptation to Technical Progress to the CLP Regulation (Commission Regulation (EU) No 286/2011 of 10 March 2011 and Commission Regulation (EU) No 487/2013 of 8 May 2013).</p> <p>The revision includes:</p> <ul style="list-style-type: none"> • Numbering of chapters within CLP Guidance, Parts 2 & 3 were synchronised with corresponding chapter numbering of CLP, Annex I. • Changes in the legal text due the 2nd and 4th ATPs. • Changes in the legal text due to the 4th ATP were highlighted in orange within all relevant green boxes. All changes are preceded by a note highlighting the changes. (To note: a corrigendum will change the colour of relative legal text boxes from orange to green when the 4th ATP applies). <p>In addition, the revisions to Part 2: Physical hazards include the following:</p> <ul style="list-style-type: none"> • Chapters 'Pyrophoric liquids and solids' and 'Oxidising liquids and solids' were divided into four chapters: 'Pyrophoric liquids', 'Pyrophoric solids', 'Oxidising liquids' and 'Oxidising solids' respectively. • Based on the 4th ATP the CLP Guidance Chapter 2.2 Flammable gases was extended to take into account the scope of CLP, Annex I, section 2.2 to include chemically unstable gases. 	November 2013

- Further, the 4th ATP amended the criteria in CLP Annex I, Section 2.3 Flammable aerosols and renamed it into 2.3 Aerosols. Hence, the CLP Guidance was amended accordingly.
- All chapters were rechecked and redundant and/or outdated information were deleted, reorganised and/or revised. For example, 'Introduction' chapters were significantly shortened, however several "examples" sections (i.e. 'Example for classification...') were further elaborated.
- Where missing, a new sub-chapter 'Relation to other physical hazards' was added.
- Sub-chapter 2.0.4 'Physical state' was extended with additional information about substance/mixture form and some examples.
- In sub-chapter 2.1.5.2 'Additional labelling provisions' within chapter 2.1 'Explosives' further guidance about hazard communication was provided.
- In sub-chapter 2.5.6.1 a new recommendation for shot hazard codes to identify the classification of gasses under pressure was added.
- Footnotes with references to endorsed or on-going revisions of the GHS which have not yet been implemented into the CLP via a respective ATP were included in relevant sub-chapters of this guidance for information only.

In addition, the major revisions to Part 3: Health hazards include the following:

- All sections: revisions to legal text for the 4th ATP, including revisions to Precautionary Statements in the Tables with labelling information
- Section 3.1: the introduction of new guidance for the 4th ATP in section 3.1.4.1
- Sections 3.2.2.5 and 3.3.2.5: clarification to the recently published text (Version 3.0) for the setting of SCLs.
- Section 3.4 (sensitisation) has been significantly re-organised to present all the information on respiratory sensitisation together, followed by the information on skin sensitisation. This is in line with how the sections are presented in the CLP Regulation and in GHS documents.
- Section 3.4: integration of subcategories for respiratory and skin sensitisation based on potency of a substance; clarification of semi-quantitative terms like 'low to moderate sensitisation rate' and 'high or low exposure';

	<p>elaboration of evaluation of human data for skin sensitisation and the addition of new examples.</p> <ul style="list-style-type: none"> • Section 3.7 the introduction of new guidance for the 4th ATP in section 3.7.4.1 and section 3.7.5.1. <p>(ii) Corrigendum of Part 1: General principles for classification and labelling and Part 4: Environmental hazards and its related Annexes I-V.</p> <p>The corrigendum includes the following:</p> <ul style="list-style-type: none"> • The list of abbreviations was updated. • Update or deletion of outdated references to Guidance on information requirements and chemical safety assessment, Endpoint specific guidance (Chapter R.7a) within Annexes I-V. • A footnote informing the reader that with effect from 1 September 2013, Directive 98/8/EC had been repealed by Biocidal Products Regulation (EU) No 528/2012 was added. • In Part 1, Part 4 and Annexes modal verbs 'shall' were replaced with 'must' where appropriate. • A footnote related to respiratory sensitisation and skin sensitisation in Table 1.5.1-a was removed. • A correction to Example D, sub-chapter 4.1.4.7.5 was applied, namely a reference to CLP, Annex I, point (b) (ii) of Table 4.1.0 was introduced. In addition the result of a summation method calculation was corrected. 	
Version 4.1	<p>Corrigendum to take account of the end of the transition period of the 4th ATP (as foreseen in version 4.0 above):</p> <ul style="list-style-type: none"> • change the colour of relative legal text boxes from orange to green; • in Part 2, to delete section 2.2.1 Flammable gases and section 2.3.1 Flammable Aerosols (outdated text) and renumber sections 2.2.2 Flammable gases (including chemically unstable gases) and 2.3.2 Aerosols accordingly; • in Part 3, to delete the "outdated text" in sections 3.7.4.1 and 3.7.5.1 in Reproductive Toxicity. <p>In addition, minor editorial errors were corrected and minor reformatting was made.</p>	June 2015
Version 5.0	<p>Partial revision of the Guidance to update the content mainly following the 8th Adaptation to Technical Progress to the CLP Regulation (Commission Regulation (EU) No 286/2011). Revision of few specific additional topics.</p>	Xxxx 2017

The update includes the following:

(i) Throughout the document:

- Revision of legal references and legal text quotations.
- Renumbering of some sections.
- Deletion of sections regarding the reclassification of substances and mixtures previously classified in accordance with the DSD or DPD.

(ii) Revision of Part 1:

- Deletion of reference to pre-CLP legislation and transitional period.
- Addition of reference to read-across and grouping in the context of bioavailability.
- Removal of quotation of Article 31(3) of REACH.
- Clarification about applicability of additivity principle.
- Clarification about the application of mixture rules to substances with CMR constituents.
- Reduction of section 1.2.3.1 on physical hazards to avoid redundancy with section 2.0.4.
- Revision of section 1.7 and removal of unnecessary information. Table on additional information using transport classification moved to a new Annex VII.

(iii) Revision of the following sections of Part 2:

- 2.1 (Explosives): replacement of new figure 2.1.3; Update of label elements; addition new note 2 to table 2.1.2 on requirement for SDSs.
- 2.3 (Aerosols): update text on classification criteria; update of decision logic 2.3.1-a. Update of section 2.3.6 on the relation to transport classification.
- 2.14 (Oxidising solids): addition of criteria using test 0.3; update of labelling elements.

(iv) Minor changes to the following sections in Part 2:

- 2.8 (Self-reactive): Update of label elements.
- 2.12 (Emitting flammable gases): Update of label elements.
- 2.15 (Organic peroxides): Update of decision logic 2.15.1. Update of label elements.

(v) Revision of following sections in Part 3:

- 3.1 (Acute toxicity): Reference to new *in-vitro* test. Indication that harmonised ATE values will be included in Annex VI to CLP. Deletion of reference to the concept of relating the conditions of an acute inhalation test to real life. Indication that not-classified components may influence ATE and, in general, clarification about

components to be considered for mixture classification according to the case. Indication to avoid under classification for oral toxicity. Addition of new examples 13a and 13b on the application of additivity methods for mixtures with components in different physical forms.

- 3.2 (Skin corrosion): subsection on non-testing methods updated and clarified the need to assess the relevance. Update of classification criteria. Inclusion of new figure illustrating the tiered evaluation approach. Inclusion of a new figure illustrating the relative weight of different available pieces of information to be considered when weight of Evidence (WoE) is applied. Replacement of the decision logic chart with separate decision logics for substances and mixtures, based on the chart from GHS. Clarification about classification of mixture as Category 1 without subcategory.
- 3.3 (Serious eye damage/irritation): clarification of the need for further data when considerations about alkaline/acid reserve suggest no risk added. Interpretation of non-testing methods results enhanced. Mentioned the use of LVET data. Inclusion of new figure illustrating the tiered evaluation approach. Inclusion of reference to new figure on hierarchy of information added in section 3.2. Replacement of the decision logic chart with separate decision logics for substances and mixtures, based on the chart from GHS.
- 3.4 (Respiratory or skin sensitisation): Deletion of the relationship between skin and respiratory sensitisation potential. Identification of non-human data brought in line with REACH guidance. Introduction of available non-testing systems. Clarification of the test sample to be used in human diagnostic patch testing.
- 3.5 (Germ cell mutagenicity): Reference to OECD TG 488 added. New section on classification of substances containing CMR constituents, additives or impurities included.

(iv) Minor changes to the following sections in Part 3:

- 3.6 (Carcinogenicity): removal of reference to supporting evidence for classification under DSD. Update of label elements. New section included on classification of substances containing CMR constituents, additives or impurities.
- 3.7 (Reproductive toxicity): New section included on classification of substances containing CMR constituents, additives or impurities.
- 3.8 (STOT-SE): Editorial corrections to the examples.

(vi) Minor changes to Part 4 to update the terminology when referring to short-term (acute) and long-term (chronic) studies.

1

2 Preface

3 This document is the Guidance on the Application of the CLP Criteria. It is a comprehensive
4 technical and scientific document on the application of Regulation (EC) No 1272/2008 on the
5 classification, labelling and packaging of substances and mixtures (CLP), which replaced the
6 Dangerous Substances Directive 67/548/EEC (DSD) and the Dangerous Preparations Directive
7 1999/45/EC (DPD) in a staggered way. CLP is based on the Globally Harmonised System of
8 Classification and Labelling of Chemicals (GHS) and is implementing the provisions of the GHS
9 within the EU. The objective of this document is to provide detailed guidance on the application
10 of the CLP criteria for physical, health and environmental hazards. The guidance is developed to
11 primarily assist manufacturers, importers and downstream users in applying the classification
12 and labelling criteria, and it also includes practical examples. It is also assumed to be the
13 guidance on classification and labelling for Competent Authorities in the Member States (MS
14 CA), for the Commission services and the European Chemicals Agency (ECHA).

15 In certain chapters, like for example the ones on carcinogenicity, mutagenicity and reproductive
16 toxicity, the guidance includes to a larger extent scientific advice on how to interpret different
17 data used for classification. This additional guidance is based on experience gained within the
18 EU during the application of the classification criteria under Directive 67/548/EEC, and is written
19 for the experts within the respective fields.

20 This guidance document was developed as a REACH Implementation Project (RIP 3.6) at the
21 Institute for Health and Consumer Products (IHCP) of the Joint Research Centre in Ispra, with
22 support from working groups consisting of experts on classification and labelling from EU
23 Member States and Industry. The project started in September 2007 and the different working
24 groups had meetings and continuous discussions to discuss and develop the guidance text until
25 spring 2009. Finally all texts were consolidated and edited at the IHCP. RIP 3.6 was financially
26 supported with an administrative arrangement made with Directorate-General Enterprise and
27 Industry (currently DG Growth). The guidance was handed over to ECHA in summer 2009.

28 After that the guidance has been revised twice – version 2.0 in April 2012 on the long-term
29 aquatic hazard and version 3.0 in November 2012 in relation to the guidance chapters on
30 setting of specific concentration limits (SCLs) for health hazards.

31 During 2012/2013, further drafting work was done in close collaboration with European experts,
32 to take account of a range of guidance aspects (for example further guidance on the criteria for
33 respiratory and skin sensitisation, and other health related points, as well as guidance on the
34 criteria for chemically unstable gases and aerosols and other physical hazards related changes)
35 following the 2nd and/or the 4th Adaptation to Technical Progress (ATP) to the CLP (Commission
36 Regulation (EU) No 286/2011 and No 487/2013¹). This work resulted in publication of version
37 4.0 in November 2013 and the subsequent corrigendum version 4.1 June 2015 to update the
38 text following the transitional period for the 4th ATP.

39 In relation to labelling and packaging, a new stand-alone guidance document was prepared
40 (*Guidance on Labelling and Packaging in accordance with Regulation (EC) No 1272/2008*),
41 warranting the deletion of Part 5 and of Annex V of the Guidance on the Application of the CLP
42 Criteria. The Guidance on Labelling and Packaging in accordance with Regulation (EC) No
43 1272/2008 is published on ECHA's guidance website, under
44 http://guidance.echa.europa.eu/guidance_en.htm.

¹ Commission Regulation (EU) No 286/2011 of 10 March 2011 and Commission Regulation (EU) No 487/2013 of 8 May 2013 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures.

1 Both guidance documents were further updated in 2016 to address the changes due to the 8th
2 ATP (e.g. new alternative methods to classify oxidising solids, changes in the classification for
3 skin corrosion/irritation, serious eye damage/irritation and aerosols, as well as changes in
4 precautionary statements).

5 Therefore, the current version of the Guidance reflects the changes made by the 8th ATP
6 (Regulation 2016/918) in Annex I to CLP. These changes apply from 1 February 2018.

7 However:

- 8 - The 8th ATP may already be applied on a voluntary basis before that date.
- 9 - Substances and mixtures placed on the market before 1 February 2018 shall not be
10 required to be relabelled and repackaged in accordance with the 8th ATP during a
11 period of two years, i.e. before 1 February 2020.

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1 List of Abbreviations

Standard term / Abbreviation	Explanation
ADD	Directive 75/324/EEC on aerosol dispensers ²
ADN	European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways (Accord européen relatif au transport international des marchandises dangereuses par voie de navigation intérieure) ³
ADR	European Agreement concerning the International Carriage of Dangerous Goods by Road (Accord européen relatif au transport international des marchandises dangereuses par route) ⁴
ANE	Ammonium Nitrate Emulsion
ASTM	American Society for the Testing of Materials
ATE	Acute Toxicity Estimate
ATP	Adaptation to Technical Progress (ATP) to the CLP Regulation
BAM	Bundesanstalt für Materialforschung und -prüfung (Federal Institute for Materials Research and Testing)
BCF	Bioconcentration Factor
BCOP	Bovine Corneal Opacity and Permeability test
BfR	German Federal Institute for Risk Assessment
BfR DSS	Decision support system by the German Federal Institute for Risk Assessment
BMF	Biomagnification factor
BOD	Biological Oxygen Demand
BP	Boiling point
bw	Body weight

² Directive (75/324/EEC) of the Council on the approximation of the laws of the Member States relating to aerosol dispensers [OJ L 147, 9.6.1975, p.40]. Directive as last amended by Commission Directive 2013/10/EU [OJ L 77, 20.03.2013, p.20].

³ European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways, concluded at Geneva on 26 May 2000, as amended.

⁴ European Agreement concerning the International Carriage of Dangerous Goods by Road, concluded at Geneva on 30 September 1957, as amended.

Standard term / Abbreviation	Explanation
C&L	Classification and Labelling
CA	Competent Authority
cATpE	Converted Acute Toxicity point Estimate
CLP	Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures ⁵
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSA	Chemical Safety Assessment
CSR	Chemical Safety Report
DIN	Deutsches Institut für Normung (German Institute for Standardisation)
DNA	Deoxyribonucleic Acid
DOC	Dissolved Organic Carbon
DPD	Directive 1999/45/EC on the classification and labelling of Dangerous Preparations ⁶
DSD	Directive 67/548/EEC on the classification and labelling of Dangerous Substances ⁷
EC3	Effective Concentration inducing a stimulation index of 3 in the LLNA test
ECHA	European Chemicals Agency, Helsinki (http://echa.europa.eu/home_en.asp)
ECVAM	European Centre for the Validation of Alternative Methods (http://ihcp.jrc.ec.europa.eu/our_labs/eurl-ecvam)

⁵ Regulation (EC) No 1272/2008 of the European Parliament and Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC and amending Regulation (EC) No 1907/2006 [OJ L 353, 31.12.2008, p. 1].

⁶ Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations [OJ L 200, 30.7.1999, p. 1].

⁷ Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances [OJ 196, 16.8.1967, p. 1].

Standard term / Abbreviation	Explanation
ED	Effective Dose
EN	A European Standard
ERV	Ecotoxicity Reference Value
ESAC	ECVAM Scientific Advisory Committee (see ECVAM website https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam)
EUH	The hazard statements carried through from DSD and DPD, which are not yet included in the GHS are codified as 'EUH'
f/F	Female
FP	Flash point
GCL	General Concentration Limits
GHS	Globally Harmonised System of Classification and Labelling of Chemicals ⁸
GJIC	Gap junction intercellular communication
GLP	Good Laboratory Practice
GnRH	Gonadotropin-releasing hormone
GPMT	Guinea Pig Maximisation Test
GV	Guidance Value
Hb	Haemoglobin
HET-CAM	Hen's Egg Test on Chorio-allantoic Membrane
HS (or H statement)	Hazard statement
HSM	Human skin model
Ht	Hematocrit
IARC	International Agency for Research on Cancer (http://www.iarc.fr/)
IATA DGR	International Air Transport Association , Dangerous Goods Regulations Manual

⁸ Globally Harmonised System of Classification and Labelling of Chemicals (GHS), Fifth revised edition, United Nations, New York and Geneva, 2013.

Standard term / Abbreviation	Explanation
IBC	Intermediate Bulk Container
ICAO TI	International Civil Aviation Organization (Technical Instructions for the Safe Transport of Dangerous Goods by Air)
ICE	Isolated Chicken Eye
IEC	International Electrotechnical Commission (http://www.iec.ch/)
IMDG Code	International Maritime Dangerous Goods Code
IMO	International maritime Organisation
IPCS	International Programme on Chemical Safety (joint programme of WHO, ILO and UNEP)
IR/CSA	Guidance on Information Requirements and Chemical Safety Assessment, ECHA (http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm)
IRE	Isolated Rabbit Eye
ISO	International Organisation for Standardization
ITDG	Directive 2008/68 on the Inland Transport of Dangerous Goods ⁹
ITS	Integrated Testing Strategy
K _{ow}	the n-octanol/water partition coefficient
LEL	Lower Explosion Limit
LD ₅₀ /LC ₅₀	Median (50%) lethal dose/concentration
LFL	Lower Flammability Limit
LLNA	Local Lymph Node Assay
LO (A) EL/C	Lowest Observed (Adverse) Effect Level/Concentration
LVET	Low Volume Eye Test
m/M	Male

⁹ Directive 2008/68/EC of the European Parliament and of the Council of 24 September 2008 on the inland transport of dangerous goods, implementing the European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR), the Regulations concerning the International Carriage of Dangerous Goods by Rail (RID) and the European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways (ADN) [OJ L 260, 30.9.2008, p. 13].

Standard term / Abbreviation	Explanation
MetHB	Methaemoglobinaemia
MetHb	Methaemoglobin
M-factor	Multiplying factor
MP	Melting Point
MSCA	Member State Competent Authority
MTD	Maximal Tolerated Dose
MW	Molecular weight
n.a.	Not available
NC	No Classification
NE	Narcotic effect(s)
NO(A)EC	No Observed (Adverse) Effect Concentration
NO(A)EL	No Observed (Adverse) Effect Level
ODS	Ozone Depleting Substances
ODP	Ozone Depleting Potential
OECD	Organisation for Economic Co-operation and Development
OECD TG	OECD Test Guideline All Test Guidelines are available at the OECD homepage: http://www.oecd.org/document/40/0,3343,en_2649_34377_37051_368_1_1_1_1,00.html
OP	Oxidising Power
P statement (or PS)	Precautionary statement
PB/PK	Physiologically-based pharmacokinetic
PPAR α	Peroxisome proliferator-activated receptor-alpha
PS (or P statement)	Precautionary statement
(Q)SAR	(Quantitative) Structure Activity Relationship

Standard term / Abbreviation	Explanation
REACH	Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals ¹⁰
RID	Règlement concernant le transport international ferroviaire de marchandises dangereuses (Regulations concerning the International Carriage of Dangerous Goods by Rail) ¹¹
RIP	REACH Implementation Project
RTI	Respiratory tract irritation
SADT	Self-Accelerating Decomposition Temperature
SCL	Specific Concentration Limit
SDS	Safety Data Sheet
SIFT	Skin integrity function test
SSD	Species Sensitivity Distribution
STOT-SE	Specific Target Organ Toxicity - Single Exposure
STOT-RE	Specific Target Organ Toxicity - Repeated Exposure
SVC	Saturated Vapour Concentration
T25	The daily dose (in mg/kg bodyweight/day) inducing a tumour incidence of 25 % upon lifetime exposure
T95	Inhalation chamber equilibrium (attained at the time t95)
T/D	Transformation/Dissolution
T/Dp	Transformation/Dissolution Protocol
TER	Transcutaneous electrical resistance

¹⁰ Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and omission of Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. [OJ L 396, 30.12.2006 p.1.] [Corrigendum: OJ L 136, 29.5.2007 p.3].

¹¹ Regulations concerning the International Carriage of Dangerous Goods by Rail, appearing as Appendix C to the Convention concerning International Carriage by Rail (COTIF) concluded at Vilnius on 3 June 1999, as amended.

Standard term / Abbreviation	Explanation
TG	Test Guideline
TGD	Technical Guidance Document
TM	Test Method as listed in the Test Methods Regulation
Test Methods Regulation	Regulation (EC) No 440/2008 laying down test methods pursuant to the REACH Regulation ¹²
TOPKAT	Mathematical (Q)SAR model for prediction of skin corrosion/irritation
UDP	Uridine 5'-diphosphate
UDPG	Uridine diphosphate glucuronyl
UEL	Upper Explosion Limit
UFL	Upper Flammability Limit
UGT	UDP-glucuronyltransferase
UN	United Nations
UN-MTC	The UN Manual of Tests and Criteria contains criteria, test methods and procedures to be used for classification of dangerous goods according to the provisions of Parts 2 and 3 of the United Nations Recommendations on the Transport of Dangerous Goods, Model Regulations, as well as of chemicals presenting physical hazards according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). More information and the latest revision are available at: http://www.unece.org/trans/danger/publi/manual/manual_e.html .
UN RTDG Model Regulations	UN Recommendations on the Transport of Dangerous Goods - Model Regulations. It covers all modal transport regulations (ADR, RID, ADN, IMDG and ITDG). It is regularly updated and amended every two years. More information and the latest revision are available at: http://www.unece.org/trans/danger/publi/unrec/rev13/13nature_e.html
UNSCEGHS (or SCEGHS)	United Nations SubCommittee of Experts on the Globally Harmonised System (http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html)

¹² Council Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) [OJ L 142, 31.5.2008, p. 1] [Corrigendum: OJ L 143, 3.6.2008, p. 55].

Standard term / Abbreviation	Explanation
UNSCETDG (or SCETDG)	United Nations SubCommittee of Experts on the Transport of Dangerous Goods (http://www.unece.org/trans/danger/danger.htm)
US-FHSA	United States Federal Hazardous Substance Act - 40 Code of Federal Regulations 1500.41
UVCB	Substances of unknown or variable composition, complex reaction products or biological materials
VDI	Verein Deutscher Ingenieure (The Association of German Engineers)
VP	Vapour Pressure
WAF	Water Accommodated Fraction
WoE	Weight of Evidence
WSF	Water soluble fraction

1



NOTEs to the reader:

In this document, text cited from Regulation (EC) No 1272/2008 is indicated in green boxes in *italic* font.

This symbol highlights text to be noted.

1. PART 1: GENERAL PRINCIPLES FOR CLASSIFICATION AND LABELLING

1.1. INTRODUCTION

1.1.1. The objective of the guidance document

This document is a comprehensive technical and scientific guidance on the application of Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures¹³, hereafter referred to as CLP.

CLP amended the Dangerous Substance Directive 67/548/EEC¹⁴ (DSD), the Dangerous Preparations Directive 1999/45/EC¹⁵ (DPD) and Regulation (EC) No 1907/2006¹⁶ (REACH), and repealed DSD and DPD from 1 June 2015 (CLP Article 61). CLP was implemented based on the United Nations' Globally Harmonised System of Classification and Labelling of Chemicals (UN GHS) without lowering the protection of human health and the environment, compared to the classification, labelling and packaging system in DSD and DPD. The implementation of GHS into CLP followed various declarations made by the Community to confirm its intention to contribute to GHS development and to implement GHS into EU law.

A core principle of CLP is self-classification of a substance or mixture by the manufacturer, importer or downstream user (CLP Article 4(3) and Recital 17), which involves identification of the hazards of the substance or mixture followed by classification as a result of the comparison of the hazard information with the criteria in CLP. This guidance will enable industry to self-classify chemicals and to provide appropriate hazard communication information to the target populations potentially handling the substance or mixture or exposed to it. For substances of particular concern (carcinogens, mutagens, substances toxic for reproduction (CMRs) and respiratory sensitisers) or for other substances where EU-wide action is needed, CLP sets out a system for formal harmonisation of classifications at EU level.

Given that many provisions under REACH are linked to classification, the implementation of REACH and CLP is interlinked and should be planned and applied in tandem. General advice on the implementation of CLP is available in the ECHA's *Introductory Guidance on the CLP Regulation*, available at ECHA website (<http://echa.europa.eu/web/guest/guidance-documents/guidance-on-clp>).

The objective of this document is to provide detailed guidance on the application of the CLP criteria for physical, health and environmental hazards.

¹³ Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 [OJ L 353, 31.12.2008, p. 1]

¹⁴ Council Directive 67/548/EEC relating to the classification, packaging and labelling of dangerous substances, as amended [OJ 196, 16.8.1967, p. 1]

¹⁵ Directive 1999/45/EC as of 30 July 2002 of the European Parliament and of the Council relating to the classification, packaging and labelling of dangerous preparation, as amended [OJ L 200, 30.7.1999, p.1]

¹⁶ Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and omission of Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. [OJ L 396, 30.12.2006 p.1.] [Corrigendum: OJ L 136, 29.5.2007 p.3]

1 1.1.2. Background

2 The aim of classification and labelling is to identify the hazardous properties of a substance or a
3 mixture by applying specific classification criteria to the available hazard data, and then to
4 provide appropriate hazard labelling and information on safety measures.

5 The EU has had a comprehensive system for the classification and labelling of dangerous
6 substances and mixtures for over 40 years, in the past mainly DSD and DPD. In addition, the
7 Safety Data Sheet (SDS) Directive 91/155/EEC¹⁷ required suppliers to provide more detailed
8 information for professional users. These directives contributed to a single market in chemicals
9 in the EU, based on a high level of protection of human safety and health and the environment.

10 The GHS was developed worldwide to minimise differences between systems of different
11 jurisdictions for classification and labelling of substances and mixtures. The GHS aims to
12 contribute towards global efforts to provide protection from hazardous effects of chemicals and
13 to facilitate trade.

14 The GHS criteria for classifying hazardous substances and mixtures were developed taking into
15 account existing systems for hazard classification, such as the EU supply and use system, the
16 Canadian and US Pesticide systems, GESAMP¹⁸ hazard evaluation procedure, IMO¹⁹ Scheme for
17 Marine Pollutants, the UN Recommendations on the Transport of Dangerous Goods (UN/RTGD),
18 and the US Land Transport. These systems include supply and subsequent use of chemicals, the
19 sea transport of chemical substances as well as transport of chemical substances by road and
20 rail. The harmonised criteria are therefore intended to identify hazardous chemicals in a
21 common way for use throughout all these systems.

22 The GHS provides a basis for an internationally uniform information system on hazardous
23 substances and mixtures. It provides harmonised criteria for classification and hazard
24 communication measures for different target audiences, including consumers, workers and
25 emergency responders, and in transport. It follows a 'building block' approach to enable
26 jurisdictions to adopt the system according to the needs of their law and the various target
27 audiences. However, although the final aim of GHS is to have a fully harmonised classification
28 and labelling system worldwide, it is recognised that differences may persist between sectors (
29 e.g. transport, supply and use), but should not occur within a sector globally (section 1.1.3.1.5,
30 UNSCEGHS, 6th revision).

31 The GHS was agreed by the UN Committee of Experts on the Transport of Dangerous Goods and
32 the Globally Harmonized System of Classification and Labelling of Chemicals (CETDG/GHS). It
33 was formally approved by the UN Economic and Social Council (UN ECOSOC) in July 2003 and
34 published further in 2003 after a decade of negotiations. It is updated biannually. The changes
35 in GHS are not automatically reflected in the CLP Regulation. The latter is adapted and
36 updated by the Commission via Adaptations to Technical Progress (ATPs - see Article 53(1) of
37 CLP).

38 1.1.3. Hazard classification

39 Hazard classification is a process involving the identification of information on the physical,
40 health, environmental or other hazards of a substance or a mixture as set out in Annex I to CLP.
41 This is followed by the comparison of the hazard information (including the *severity of hazard*)
42 with defined criteria, in order to determine the *classification* of the substance or mixture. Thus,

¹⁷ Council Directive 91/155/EEC relating to defining and laying down the detailed arrangements for the system of specific information relating to dangerous preparations and dangerous substances, as amended [OJ L 076, 22.03.1991, p. 35], repealed and replaced by Regulation (EC) No 1907/2006 as of 1 June 2007.

¹⁸ Group of Experts on the Scientific Aspects of Marine Environmental Protection.

¹⁹ International Maritime Organisation.

1 under CLP, a manufacturer, importer or downstream user will apply the following steps to arrive
2 at a self-classification of a substance or a mixture:

- 3 • identification of relevant available information regarding the potential hazards (including
4 *severity of hazard*) of a substance or mixture;
- 5 • examination of the information gathered to assess whether it is relevant, reliable and
6 sufficient for classification purposes;
- 7 • evaluation of the information (data) by applying the classification criteria in Annex I, CLP
8 for each hazard class and differentiation; and
- 9 • decision on whether the hazard information for the substance or mixture meets the
10 criteria for one or more hazard classes or differentiations and therefore decision on the
11 classification of the substance or mixture as hazardous in relation to these hazard
12 classes or differentiations (assignment of hazard categories, SCL(s), M-factor(s) and
13 hazard statement(s) according to the provisions in Annex I, CLP).

14 Preliminary information on identification of relevant data is provided in section 1.1.6 of this
15 guidance document, while guidance on available test methods is provided in Part B of the ECHA
16 *Guidance document on Information Requirements and Chemical Safety Assessment* (Chapters
17 R.2 to R.4, IR/CSA), available on the ECHA Website
18 ([http://echa.europa.eu/web/guest/guidance-documents/guidance-on-information-requirements-
19 and-chemical-safety-assessment](http://echa.europa.eu/web/guest/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment)). Chapters R.7a/b/c of the same Guidance provide more
20 detailed information and endpoint-specific guidance.

21 Classification according to CLP is based on *intrinsic* hazards, i.e. the basic properties of a
22 substance or mixture as determined in standard tests or by other means designed to identify
23 hazards. It should be noted that for some hazard classes the intrinsic properties of a substance
24 or mixture are not always the only aspects relevant for classification, e.g. explosives or aerosols
25 for which classification is also package dependent, or aspiration hazard which may not be
26 relevant for certain package types. As CLP is hazard-based, it does not take exposure into
27 consideration in arriving at a classification. It should further be noted that classification of
28 substances and mixtures may be required even when placed on the market in forms that are
29 not hazardous. E.g. metals in massive form, alloys, mixtures containing polymers or
30 elastomers, should be classified according to the criteria for e.g. toxic effects by inhalation but
31 may not need to be labelled.

32 **1.1.4. Who is responsible for the hazard classification**

33 CLP and REACH place the responsibility for hazard classification and related provisions such as
34 packaging, hazard communication and SDS on the suppliers of substances and mixtures. Both
35 *substances and mixtures* must be classified, labelled and packaged in accordance with CLP
36 before placing them on the market.

37 **1.1.5. Which substances and mixtures should be classified**

38 Substances and mixtures placed on the market fall within the scope of classification under CLP
39 and should be evaluated in order to reach a decision as to whether or not the criteria are met
40 and therefore if they should be classified. Substances are also subject to classification where
41 they are subject to registration or notification under REACH, even if they are not placed on the
42 market.

43 However, a number of substances and mixtures are exempted from the requirements of the CLP
44 Regulation as a whole (CLP Article 1):

- 1 • radioactive substances and mixtures (Directive 96/29/Euratom²⁰);
- 2 • substances and mixtures which are subject to customs supervision, provided that they
- 3 do not undergo any treatment or processing, and which are in temporary storage, or in a
- 4 free zone or free warehouse with a view to re-exportation, or in transit;
- 5 • non-isolated intermediates;
- 6 • substances and mixtures used in scientific experimentation, analysis or chemical
- 7 research, provided they are not placed on the market and they are used under controlled
- 8 conditions in accordance with EU workplace and environmental legislation;
- 9 • waste, as defined in Directive 2006/12/EC²¹; and
- 10 • certain substances or mixtures in the finished state, intended for the final user:
 - 11 • medicinal products, as defined in Directive 2001/83/EC²²,
 - 12 • veterinary medicinal products, as defined in Directive 2001/82/EC²³,
 - 13 • cosmetic products, as defined in Directive 76/768/EEC²⁴,
 - 14 • medical devices as defined in Directive 90/385/EEC²⁵ (active implantable medical
 - 15 devices) and 93/42/EEC²⁶ (medical devices in general), which are invasive or
 - 16 used in direct physical contact with the human body, and in vitro diagnostic
 - 17 medical devices (Directive 98/79/EC²⁷), and
 - 18 • food or feeding stuffs as defined in Regulation 178/2002²⁸, including when they
 - 19 are used as food additives within the scope of Directive 89/107/EEC²⁹, as a
 - 20 flavouring in foodstuffs within the scope of Directive 88/388/EEC and Decision
 - 21 1999/217/EC³⁰, as an additive in feeding stuffs within the scope of Regulation

²⁰ Council Directive 96/29/Euratom of 13 May 1996 laying down basic safety standards for the protection of the health of workers and the general public against the dangers arising from ionizing radiation [OJ L 159, 29.6.1996, p. 1].

²¹ Directive 2006/12/EC of the European Parliament and of the Council of 5 April 2006 on waste [OJ L 114, 27.4.2006, p. 9]

²² Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use [OJ L 311, 28.11.2001, p. 67]

²³ Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products [OJ L 311, 28.11.2001, p. 1]

²⁴ Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products [OJ L 262, 27.9.1976, p. 169]

²⁵ Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices [OJ L 189, 20.7.1990, p. 17]

²⁶ Council Directive 93/42/EEC of 14 June 1993 concerning medical devices [OJ L 169, 12.7.1993, p. 1]

²⁷ Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices [OJ L 331, 7.12.1998, p. 1]

²⁸ Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety [OJ L 31, 1.2.2002, p. 1]

²⁹ Council Directive 89/107/EEC of 21 December 1988 on the approximation of the laws of the Member States concerning food additives authorized for use in foodstuffs intended for human consumption [OJ L 40, 11.2.1989, p. 27]

³⁰ 1999/217/EC: Commission Decision of 23 February 1999 adopting a register of flavouring substances used in or on foodstuffs drawn up in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council of 28 October 1996 [OJ L 84, 27.3.1999, p. 1]

1 (EC) 1831/2003³¹, and in animal nutrition within the scope of Directive
2 82/471/EEC³².

3 In addition, Member States may exempt certain substances or mixtures in specific cases where
4 necessary for the purpose of national defence.

5 Although CLP does not apply to the transport of dangerous goods by air, sea, road, rail or inland
6 waterways (CLP Article 1(6)), the criteria for classification are normally intended to be the same
7 in the two systems. Thus, a substance or mixture classified in a hazard class which is common
8 to both CLP and the transport legislation will normally be classified the same in both systems.
9 However, the transport classifications do not include all of the GHS categories, so the absence
10 of a transport classification does not mean the substance or mixture should not be classified
11 under CLP.

12 **1.1.6. What information is needed for classification**

13 **1.1.6.1. Information for the classification of substances**

14 The classification of a substance is based on the relevant information available on its hazardous
15 properties. This information can include experimental data generated in tests for physical
16 hazards, toxicological and ecotoxicological tests, historical human data such as accident records
17 or epidemiological studies, or information generated in *in vitro* tests, (Quantitative) Structure
18 Activity Relationships ((Q)SAR), 'read across', or grouping approaches.

19 CLP does not require new testing for the purpose of classification for health or environmental
20 hazards; testing for physical hazards is required unless adequate and reliable information is
21 already available (CLP Article 8(2)). However, a substance placed on the market for research
22 and development (R&D) purposes may have been manufactured or imported in quantities that
23 are too small to perform physical hazard testing. In these cases it would not be proportionate to
24 request the respective manufacturer, importer or downstream user to perform the tests
25 required in Part 2 of Annex I to CLP.

26 Although data may be provided through the application of REACH, it should be recognised that
27 the data set required by REACH (particularly at lower tonnages) will not necessarily enable the
28 comparison with the criteria for all hazard classes. Information may also be available from other
29 EU legislation for which there are specific requirements for test data to be generated, such as
30 legislation on plant protection products (Regulation (EC) No 1107/2009³³ and Directive
31 91/414/EEC³⁴) and on biocidal products (Regulation (EU) No 528/2012³⁵ and Directive

³¹ Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition [OJ L 268, 18.10.2003, p. 29]

³² Council Directive 82/471/EEC of 30 June 1982 concerning certain products used in animal nutrition [OJ L 213, 21.7.1982, p. 8]

³³ Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market repeals Council Directives 79/117/EEC and 91/414/EEC with effect from 14 June 2011. However Article 80 of Regulation (EC) No 1107/2009 specifies that directive 91/414/EEC shall continue to apply with respect to active substances included in Annex I to that Directive for certain transitional periods.

³⁴ Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market, as amended [OJ L 230, 19.8.91, p. 1]

³⁵ Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. It should be noted that with effect from 1 September 2013, Biocidal Products Regulation (EU) No 528/2012 repealed Directive 98/8/EC.

1 98/8/EC³⁶), or from various non-EU programmes. Finally, the supplier may decide to conduct
2 new testing in order to fill data gaps, provided that he has exhausted all other means of
3 generating information. Testing on animals must be avoided wherever possible and alternative
4 methods (including *in vitro* testing, the use of (Q)SARs, read-across and/or grouping
5 approaches) must always be considered first, provided they are scientifically validated,
6 sufficiently adequate and reliable. In the case of a substance containing impurities, additives or
7 other constituents, the classification of the substance should be, similar to mixtures, preferably
8 based on available information (including test data) on the substance as placed on the market
9 or as reasonably expected to be used, except when classifying for CMR properties or when
10 evaluating the bioaccumulation and degradation properties within the 'hazardous to the aquatic
11 environment' hazard class (referred to in sections 4.1.3.3.2 and 4.1.2.9 of Annex I to CLP). In
12 such cases it is strongly recommended that the classification of the substance, similarly to
13 mixtures (article 6(3) and 6(4), CLP), is based on information of known CMR constituent(s),
14 unless positive data on the substance are available as there is no toxicological difference
15 between a mixture and a substance containing other constituent substances³⁷ unless there is
16 adequate and reliable scientific evidence available clearly showing otherwise.

17 If, for the purpose of CLP, it is required or decided to generate new data, certain test methods
18 and quality conditions must be met. Studies must be conducted in accordance with the EU test
19 methods (Regulation (EC) 440/2008)³⁸ or other international test methods validated according
20 to international procedures such as those of the OECD. For physical hazards new tests must be
21 carried out in compliance with relevant recognised quality system or by laboratories complying
22 with a relevant recognised standard, and for health and environmental hazards in compliance
23 with the principles of Good Laboratory Practice (GLP³⁹). Animal tests must comply with the
24 Directive 86/609/EEC⁴⁰. Tests on non-human primates are prohibited for the purposes of CLP.
25 Tests on humans must not be performed for the purpose of CLP. However, existing data
26 obtained from other sources, such as accident records and epidemiological and clinical studies,
27 can be used.

28 **1.1.6.2. Information relevant for the classification of mixtures**

29 For mixtures, classification for physical hazards should normally be based on the results of tests
30 carried out on the mixtures themselves (unless, as for substances, a mixture placed on the
31 market for R&D purposes has been manufactured or imported in quantities that are too small to
32 perform physical hazard testing). New tests for physical hazards must be carried out in
33 compliance with relevant recognised quality system or by laboratories complying with a relevant
34 recognised Standard.

35 When considering health and environmental hazards, the classification should preferably be
36 based on information (including test data) on the mixture itself, if available, except when
37 classifying for e.g. CMR effects or when evaluating the bioaccumulation and degradation

³⁶ Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market, as amended [OJ L 123, 24.4.98, p. 1]

³⁷ Please note that a case is still pending before the Court of Justice on the classification of a UVCB based on information on its constituents: Case C-691/15 P.

³⁸ Council Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)[OJ L 142, 31.5.2008, p. 1].

³⁹ More information on the GLP principles and related requirements is available in the Q&As section on the ECHA website at <https://www.echa.europa.eu/web/quest/support/qas-support/qas>.

⁴⁰ Directive 86/609/EEC regarding the protection of animals used for experimental and other scientific purposes, [OJ L 358, 18.12.1986, p. 1].

1 properties within the 'hazardous to the aquatic environment' hazard class referred to in sections
2 4.1.2.8 and 4.1.2.9 of Annex I to CLP. In these cases, classification of the mixtures must be
3 based on the information on the substances.

4 New tests for the purpose of classification and labelling for health or environmental hazards
5 may only be performed when the manufacturer, importer or downstream user has exhausted all
6 other means of generating information (according to article 8, CLP). However, if no *in vivo* test
7 data are available on a mixture, such data should normally not be generated; rather, all
8 available information on the ingredients⁴¹ of the mixture should be used to derive a
9 classification.

10 Annex I to CLP specifies 'bridging principles' which enables suppliers to derive health or
11 environmental classifications of their mixtures based on available data on similar tested
12 mixtures and on the ingredient substances. Annex I also provides specific rules for the
13 classification of mixtures based on the classification of the individual substances in the mixture.

⁴¹ Note that the term "ingredient" is used in this guidance with the same meaning of "component" to indicate a substance in a mixture.

1 **1.1.7. Data evaluation and reaching a decision on classification**

2 **1.1.7.1. Classification of substances**

3 After the available information has been assembled, a systematic evaluation of this information
4 is necessary in order to derive a classification. The information must be compared with the
5 criteria for classification for each hazard class or differentiation within the hazard class.
6 Differentiation is a distinction depending on the route of exposure or the nature of the effects. A
7 decision should be made as to whether the substance meets the criteria for classification. When
8 this is the case; the classifier should assign one or more hazard categories for each relevant
9 hazard class or differentiation. The substance is then assigned the appropriate hazard
10 communication elements.

11 In some cases the classification decision may be straightforward, requiring only an evaluation of
12 whether the substance gave a positive or negative result in a specific test that can be directly
13 compared with the classification criteria. In other cases, scientific judgements must be made
14 (e.g. on dose-response relationships, equivocal results and non-standardised tests) in a weight
15 of evidence determination when applying the criteria. Expert judgement may therefore be
16 needed to decide whether the results of a particular test or the available information in a Weight
17 of evidence assessment meet the criteria laid down in Annex I.

18 **1.1.7.2. Influence of impurities, additives or individual constituents on the** 19 **classification of a substance**

20 Substances may contain impurities, additives, or other constituents while still meeting the
21 substance definition in CLP. This applies to both mono-constituent, multi-constituent (e.g.
22 reaction masses) and UVCB substances. The classification of such impurities, additives or
23 individual constituents may influence the classification of the substance, in addition to the other
24 hazardous properties. If data on the substance with its components are not available (or for
25 CMRs, see section 1.1.6.1), in principle, the same classification and labelling rules as for
26 mixtures should apply also for such substances⁴².

27 **1.1.8. Updating of hazard classifications**

28 Updating of classifications may be necessary if, for example, new information is obtained or if
29 the criteria in CLP are amended. When manufacturers, importers or downstream users become
30 aware of new information or an amendment to CLP or when a change is introduced in a
31 substance or mixture, they must reconsider the classification of the substance or mixture. Note
32 that "new" here refers to information not previously considered (or even new interpretation of
33 old data), not necessarily newly produced data. A downstream user may use the classification
34 derived in accordance with the criteria by his supplier; this does not relieve the downstream
35 user from the obligation to share new information with the supplier to allow him to meet the
36 requirements.

37 **1.1.9. The interface between hazard classification and hazard** 38 **communication**

39 CLP provides an integrated system of hazard communication elements on the label including
40 hazard pictograms, signal words, hazard statements and precautionary statements. Provision of
41 this information to the end user is obligatory, irrespective of conditions of use and risk. While
42 the Chemical Safety Assessment (CSA) on a particular substance performed for the purpose of
43 REACH may indicate 'safe use', a situation resulting in unforeseen exposure may occur, such as

⁴² Please note that a case is still pending before the Court of Justice on the classification of a UVCB based on information on its constituents: Case C-691/15 P.

1 in an accident. In such a situation, workers, managers and emergency personnel will need
2 information on the hazard profile of the substance, which will be provided by the label and the
3 SDS. These sources of information will also provide useful information to the worker on the safe
4 handling of the chemical.

5 It is recognised that the hazard communication needs of the various end users may differ.
6 Consumers are primarily dependent on the label of a substance or a mixture as a source of hazard
7 and precautionary information, while the requirement for provision of an SDS is primarily
8 applicable to professional users. Thus, the label facilitates communication of key hazard
9 information on a substance or a mixture and additional safety advice (precautionary statements)
10 to consumers, as well as to workers.

11 **1.1.10. The interface between self-classification and harmonised** 12 **classification, and the list of harmonised classifications**

13 CLP places emphasis on self-classification by industry of the substances or mixtures they
14 supply. In some cases, substances are subject to harmonised classification at EU level, while
15 mixtures must always be self-classified, except for pesticidal and biocidal products where the
16 Member State competent authorities (MSCAs) decide on the classification as part of the national
17 authorisation scheme (CLP Article 36(2)).

18 If a substance has a harmonised classification as provided in Annex VI to CLP, this classification
19 must always be used by a manufacturer, importer or downstream user, except for the minimum
20 classifications indicated with an asterisk (*) in Table 3.1. The use of the minimum classification
21 is explained in section 1.2.1 of Annex VI. For such minimum classifications, when available data
22 exists to justify a more stringent category than the given minimum, the more stringent
23 category must be used. It should be noted that where some but not all hazard classes or
24 differentiations within a hazard class have been harmonised, the remaining hazards must be
25 evaluated and self-classified to complete the classification (according to CLP Article 4(3) and
26 CLP Recital 17).

27 Under CLP, the harmonised classification and labelling of substances normally aims to cover
28 properties of the highest concern (CMR and respiratory sensitisation) but CLP also allows
29 harmonisation for other properties if there is a need for such an action at EU-level. Decisions on
30 harmonised classification are taken by the European Commission through comitology (CLP
31 Article 37(5)), following a proposal submitted to ECHA and an opinion developed by ECHA's Risk
32 Assessment Committee (RAC) on the proposal (CLP Article 37(4)). Whenever a manufacturer,
33 importer or downstream user has new information which may affect an harmonised
34 classification, he must submit a proposal for a change to the member State Competent
35 Authority where the substance is placed on the market.

36 Substances regulated under the Biocidal Products Regulation (EU) No 528/2012 or under the
37 Plant Protection Products Regulation (EC) No 1107/2009 will normally be subject to harmonised
38 classification and labelling for all hazardous properties. These proposals for harmonised
39 classification and labelling are prepared by MSCAs only (CLP Article 36(2)). However, in general
40 proposals for harmonised classification for a particular substance to be added in Annex VI to
41 CLP can be made by both MSCAs and by manufacturers, importers and downstream users (CLP
42 Article 37). Only MSCAs can propose a revision of an existing harmonised classification and
43 labelling to ECHA (CLP Article 37(6)).

44 Harmonised classification and labelling of a substance provides for a high level of protection of
45 human health and the environment, and provides legal clarity for different suppliers of the same
46 substance of high concern (i.e. manufacturers of substances, importers of substances or
47 mixtures, producers of specific articles, downstream users (including manufacturers of
48 mixtures) and distributors).

1 Part 3 of Annex VI to CLP contains the list of harmonised classifications and labellings (except
2 precautionary statements). All harmonised classifications previously adopted under DSD and
3 listed in Annex I to DSD were translated to CLP classifications and carried over to the list of
4 harmonised classifications in Annex VI to CLP also including the Notes assigned to the entries as
5 referred to in the DSD. This was done to maintain the same level of protection under CLP as
6 under DSD. The harmonisation of classification of substances is a continuous process building
7 on all efforts already done within the EU so far to evaluate hazards of substances that caused
8 concern.

9 Annex VI contains a number of entries indicated with Note B. The note relates to substances
10 (acids, bases, etc.) that are placed on the market in aqueous solutions. The required classification
11 and labelling may be different at different concentrations. These entries have a general
12 designation of the following type: 'nitric acid ... %'. These entries give the classification of the
13 substance in a water solution above the GCL or SCL. The GCLs or SCLs are applied as usual in
14 the classification of any mixture containing the substance. Thus, the concentration of the
15 undiluted substance is compared with the GCL or SCL, as appropriate. For example, when diluted
16 75% phosphoric acid is added to a mixture to make up 10% of the mixture, the final concentration
17 of phosphoric acid in the final mixture is 7.5%. As for this substance the SCL for skin and eye
18 irritation is 10%, the final mixture does not require classification for these hazard classes based
19 on phosphoric acid. The presence of Note B specifies that the supplier of an aqueous solution of
20 such a substance must state the percentage concentration of the solution on the label.

21 Note that the pure substance, i.e. not in water solution, may have different hazards. If there is
22 no entry in Annex VI covering the anhydrous form, a classification would need to be derived based
23 on available information. As the human body contains water, it is likely that the hazards of the
24 aquatic solution still apply. Additional hazards may however occur, for example, hydrogen cyanide
25 is Flam. liq.1 when it is pure but not in solution.

26

27 **1.1.11. The Classification and Labelling Inventory (C&L Inventory)**

28 Manufacturers and importers are required to notify ECHA of the classification and labelling of
29 hazardous substance(s) placed on the market as such or in a mixture (above a certain
30 concentration leading to the classification of the mixture) and of substances subject to
31 registration in accordance with the REACH Regulation. ECHA will then include the information in
32 the classification and labelling inventory in the form of a database. Substances require
33 notification within one month after their placing on the market. There is no need to notify the
34 substance if the same information has already been submitted as part of a registration under
35 REACH by the same actor, as the classification and labelling, when part of the registration
36 package, will automatically be added to the C&L Inventory (CLP Article 40(1)). Further guidance
37 on what should be included in a notification and how to do it is available on the ECHA website
38 <http://echa.europa.eu/web/guest/regulations/clp/cl-inventory/notification-to-the-cl-inventory>.

39 ECHA makes certain information from the C&L Inventory publicly available on its website,
40 including the substance name, the classification, labelling and any relevant specific
41 concentration limit or M-factor(s). It is indicated in the Inventory if there is a harmonised
42 classification for the entry, or if it is an agreed entry between manufacturers or importers.
43 Multiple notifications of the same substance can be submitted by different manufacturers or
44 importers, with potential differences in the notified classifications. Notifiers and registrants are
45 required to make every effort to come to an agreed entry.

46 The information in the C&L Inventory comes from registrants and C&L notifications. This
47 information has not been reviewed or verified by the Agency or any other authority.

1 **1.1.12. Relation of classification to other EU legislation**

2 A network of EU legislation relies on classification in one way or the other (see section 22 of the
3 *Introductory Guidance on the CLP Regulation* for a detailed list of the laws concerned). This
4 downstream legislation includes laws protecting consumers and workers, as well as rules on
5 transport, biocides, pesticides, cosmetics and waste. Therefore, apart from the important
6 hazard communication on the label and in the SDS, there are significant downstream
7 consequences of classification in that it also has a direct effect on risk management measures
8 under REACH and other legislation.

9 **1.1.12.1. REACH**

10 Classification plays a key role in REACH; it must be included in the registration dossier for a
11 substance and it triggers certain provisions such as the performance of an exposure assessment
12 and risk characterisation as part of the CSA and the obligation to provide an SDS. Classification
13 of a substance as mutagenic, carcinogenic or toxic to reproduction (CMR) may also lead to
14 restrictions and the need to apply for authorisations ((EC) No 1907/2006).

15 **1.1.12.2. Plant Protection Products and Biocides**

16 Active substances as well as any plant protection products or biocidal products containing them
17 must be classified in accordance with the CLP Regulation.

18 It should be noted that with effect from 14 June 2011, Directive 91/414/EEC has been repealed
19 by Regulation (EC) 1107/2009. This means that references to the repealed Directive must now
20 be construed as references to the new Regulation. Nevertheless, Article 80 of the new
21 Regulation specifies that Directive 91/414/EEC must continue to apply with respect to active
22 substances included in Annex I to that Directive for certain transitional periods

23 It should be noted that with effect from 1 September 2013, Directive 98/8/EC has been
24 repealed by Regulation (EU) 528/2012. This means that references to the repealed Directive
25 must now be construed as references to the new Regulation. Nevertheless, Articles 89 – 95 of
26 the new Regulation specifies the transitional measures which must continue to apply.

27 In relation to classification, the new Regulations, bring about some changes, e.g. certain
28 classifications (e.g. CMR, Cat. 1A and 1B) may now preclude approval of the respective
29 substance as an active substance, safener, or synergist in plant protection products or biocidal
30 products.

31 **1.1.12.3. Transport legislation**

32 Many of the GHS criteria (by hazard class) are already implemented through the UN Model
33 Regulations for Transport of Dangerous Goods and related legal instruments (ADR, RID, ADN,
34 IMDG Code and ICAO TI).

35 Available transport classifications can be a source of information for the classification and
36 labelling of substances and mixtures under CLP, especially for physical hazards, see also Section
37 [2](#) of this document.

38 **1.2. THE SIGNIFICANCE OF THE TERMS 'FORM OR PHYSICAL STATE' 39 AND 'REASONABLY EXPECTED USE' WITH RESPECT TO CLASSIFICATION 40 ACCORDING TO CLP**

41 **1.2.1. 'Form or physical state' and 'reasonably expected use'**

42 CLP refers to the terms 'form or physical state' and 'reasonably expected use' in the following
43 Articles:

Article 5 (1) *Manufacturers, importers and downstream users of a substance shall identify the relevant available information for the purposes of determining whether the substance entails a physical, health or environmental hazard as set out in Annex I*

[...]

The information shall relate to the forms or physical states in which the substance is placed on the market and in which it can reasonably be expected to be used.

Article 6 (1) *The information shall relate to the forms or physical states in which the mixture is placed on the market and, when relevant, in which it can reasonably be expected to be used.*

Article 8 (6) *Tests that are carried out for the purposes of this Regulation shall be carried out on the substance or on the mixture in the form(s) or physical state(s) in which the substance or mixture is placed on the market and in which it can reasonably be expected to be used.*

Article 9 (5) *When evaluating the available information for the purposes of classification, the manufacturers, importers and downstream users shall consider the forms and physical states in which the substance or mixture is placed on the market and in which it can reasonably be expected to be used.*

1 The objective of hazard classification is to identify the intrinsic physical, health and
2 environmental hazards of substances and mixtures taking into account all uses that can be
3 reasonably expected.

4 In this context, the intention of the UN GHS should be kept in mind:

5 The GHS (subsection 1.3.2.2.1) uses the term 'hazard classification' to indicate that only the
6 **intrinsic hazardous properties** of substances or mixtures are considered.

7 The following guidance is intended to clarify the references to 'reasonably expected use' and
8 'form or physical state' in this context.

9 **1.2.2. The term 'reasonably expected use' in relation to hazard** 10 **classification**

11 Hazard classification is based on the intrinsic properties of a substance or mixture and does not
12 take into account exposure. Reasonably expected use summarises all physical forms and states
13 of a substance or mixture that may occur during intended use or reasonably foreseeable
14 conditions of misuse.

15 Reasonably expected use of a substance or mixture is as follows:

- 16 • Any process, including production, handling, maintenance, storage, transport or disposal.
- 17 • All technical operations/manufacturing activities like e.g. spraying, filing, and sawing.
- 18 • Any putative consumer contact through e.g. do-it-yourself or household chemicals.
- 19 • All professional and non-professional uses including reasonably foreseeable accidental
20 exposure, but not abuse such as criminal or suicidal uses.

21 Reasonably expected use is also related to any consumer disposal or any work in which a
22 substance or mixture is used, or intended to be used irrespective of its present limited use or
23 use pattern. Thus, use should not be mixed up with usage category.

1 **1.2.3. The term 'form or physical state' in relation to hazard classification**

2 Depending on different prerequisites, form or physical state is taken into account differently in
3 the practice of testing and classification for physical, health, and environmental hazards which is
4 described in the following paragraphs.

5 It should be noted that in some cases a substance may autooxidise (in contact with air) or
6 decompose to a more hazardous form. This may warrant classification of the substance even
7 though it in itself is not or is less hazardous. A case-by-case evaluation should be done
8 considering available hazard information on humans or animals and/or the rate and extent of
9 autoxidation or decomposition. The case-by-case evaluation should also consider how the
10 substance can be reasonably expected to be used.

11 **1.2.3.1. Physical hazards**

12 Different forms or physical states of a substance or mixture may result in different physical
13 properties and hazards with possible consequences for the hazard classification of a substance
14 or mixture. Putative forms comprise properties such as crystal structure, particle size,
15 homogeneity (e.g. emulsions) and texture (e.g. viscosity or tablet form). Examples of physical
16 state factors are: surface treatment (e.g. coating), state of aggregation, moisture content,
17 residual solvent, activation or stabilisation.

18 The classification of a substance or mixture relates to the tested form and physical state. If the
19 form and / or physical state is changed it has to be evaluated whether this might affect the
20 classification and whether re-testing is necessary. For example, a hazardous phase separation
21 may occur due to a temperature change under conditions of storage, or a solid substance may
22 be molten to bring it into the liquid phase (e.g. for pumping).

23 General considerations

24 The test sample should be representative for the substance or mixture placed on the market.
25 This is especially important in case of small 'batch' production. Mixtures might for example
26 contain inert components which, if they are over-represented in the test sample, will lead to
27 incorrect hazard classification.

28 Specific requirements of certain test methods

29 Some test methods for the classification of physical hazards have specific requirements
30 regarding the form / particle size of the sample to be tested. In these cases, the specific
31 requirements of the test methods prevail. Examples of tests which have specific requirements
32 regarding the form/particle size of the sample to be tested include those used to determine the
33 classification of explosives and of substances which in contact with water emit flammable gases.

34 In other test methods, there are no specific requirements regarding the particle size but it is
35 stated explicitly that the particle size may have a significant effect on the test result. Therefore,
36 these properties should be mentioned in the test report (i.e. testing of oxidising solids).

37 Section 2.0.4 provide further details about the relevance of the physical state for testing
38 purposes.

39 **1.2.3.2. Human health hazards**

40 Also for human health, different forms (e.g. particle sizes, coating) or physical states may result
41 in different hazardous properties of a substance or mixture in use. However, due to test
42 complexity, not every form or physical state can be tested for each health hazard. In general,
43 testing should be performed on the smallest available particle size and the default approach is
44 to test for different routes of exposure (oral, dermal, inhalation). Again, due to test complexity,
45 mostly the data for only one exposure route are available.

1 In general, the assumption is made that the testing conditions of valid animal assays reflect the
2 hazards to man and these data must be used for classification. Moreover, it is assumed that
3 classification for human health hazards takes into account all the potential hazards which are
4 likely to be faced for all forms or physical states in which the substance is placed on the market
5 and can reasonably be expected to be used. It is assumed that it comprises putative accidental
6 exposures. This approach generally, but not necessarily comprehensively, covers the whole
7 range of intrinsic properties of a substance or mixture: in some cases, substances or mixtures
8 have to be transformed into specific forms not mirroring 'real-life' exposures in order that an
9 animal test can be performed. As a consequence, the results of such tests may have to be
10 evaluated taking into account any limitations due to the fact that the specific form of the tested
11 substance or mixture does not or not perfectly represent that to which human exposure may
12 occur during intended, known, or reasonably expected use. Such evaluation has to be
13 performed according to the state of the scientific and technical knowledge. The burden of proof
14 is on the person placing a substance or mixture on the market.

15 **1.2.3.3. Environmental hazards**

16 The environmental hazard classification is principally concerned with the aquatic environment
17 and the basis of the identification of hazard is the aquatic toxicity of the substance or mixture,
18 and information on the degradation and bioaccumulation behaviour.

19 The system of classification is designed to ensure that a single classification applies to a
20 substance. In general it takes no account of the specific form since this can vary and is not
21 intrinsic to the substance. The form in which the substance is placed on the market is taken into
22 account when deciding what label to apply and various derogations from labelling exist, e.g. for
23 metals in the massive form. In the massive form the hazard may not be present and the
24 substance need not be labelled. The SDS will, however, indicate the classification and intrinsic
25 hazardous properties to warn the user that subsequent transformation of the substance may
26 produce the hazardous form.

27 For aquatic hazard classification, organic substances are generally tested in the dissolved form.
28 Exceptions to this approach include complex, multi-component substances and metals and their
29 compounds. Examples of alternative approaches include the use of Water Accommodated
30 Fractions (WAF) for complex, multi-component substances where the toxicity cut-off is related
31 to the loading, and a test strategy for metals and their compounds in which the specific form
32 (i.e. particle size) used for testing is standardised and forms or physical states are not further
33 taken into account.

34 **1.3. SPECIFIC CASES REQUIRING FURTHER EVALUATION – LACK OF** 35 **BIOAVAILABILITY**

36 **1.3.1. Definition**

37 Bioavailability is the rate and extent to which a substance can be taken up by an organism and
38 is available for metabolism or interaction with biologically significant receptors. Bioavailability
39 (biological availability) involves both release from a medium (if present) and absorption by an
40 organism (IPCS 2004).

41 **1.3.2. Bioavailability**

Article 12

Specific cases requiring further evaluation

Where, as a result of the evaluation carried out pursuant to Article 9, the following properties or effects are identified, manufacturers, importers and downstream users shall take them into account for the purposes of classification:

[...]

(b) 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;

[...]

1 In general, bioavailability is not explicitly evaluated in hazard classification – the observation of
2 systemic toxicity implicitly demonstrates a degree of bioavailability. On the other hand, when no
3 toxicity is demonstrated in a test, this may be a result of either lack of intrinsic toxicity of the
4 substance or lack of bioavailability in the test system employed. Nevertheless, as indicated in
5 Article 12 (b) of CLP there may be cases where a specific evaluation of bioavailability is
6 warranted. Bioavailability may also need to be considered for grouping and read across.

7 In general terms, for a substance or mixture to have an effect on a biological or environmental
8 system, there must be some degree of bioavailability. Therefore, it follows that a substance or
9 mixture need normally not be classified when it can be shown by conclusive experimental data
10 from internationally acceptable test methods, e.g. from the Test Method Regulation (EC) No
11 440/2008, that the substance or a substance in a mixture is not biologically available (UN GHS
12 1.3.2.4.5.1). A non bioavailable substance may, however, react with e.g. other components in a
13 mixture to transform to soluble available forms. The rate and extent at which this process,
14 known as 'transformation' for the purposes of the classification guidance, takes place can vary
15 extensively between different substances, and can be an important factor in determining the
16 appropriate hazard category (see Annex IV, Section IV.1 of this document). Note that a
17 substance which is inert and insoluble may still pose a hazard requiring classification, e.g.
18 asbestos fibers. Further, it is important to note that bioavailability is not limited to systemic
19 bioavailability but also includes local bioavailability for example for local effects like irritation
20 and sensitisation.

21 When considering the non-bioavailability of a substance or a mixture, the evaluation should be
22 based on data for all relevant constituents of a substance or ingredients of the mixture. Further,
23 one should consider potential interaction of the ingredients that could influence the
24 bioavailability of the mixture as such or one of its components.

25 Bioavailability considerations are only relevant with respect to classification for health and/or
26 environmental hazards and not for physical hazards.

27 **1.3.2.1. Human health hazards**

28 The assumption is that all substances and mixtures are considered to be bioavailable to some
29 extent. However, there are a few specific cases in which bioavailability may have an influence
30 on hazard classification. For instance in the case of some metals and polymers, the nature of
31 the physical form (metals in solid form) and the molecular size (polymers are very large
32 molecules), or their physico-chemical properties may limit absorption. Where a supplier
33 proposes derogation from hazard classification on the basis of bioavailability, he has to provide
34 adequate and robust data to support the conclusion of lack of bioavailability. It is possible that a
35 substance is bioavailable by one route but not another (e.g. absorbed following inhalation but
36 not absorbed through the skin). In such cases the lack of bioavailability may derogate
37 classification for the relevant route.

38 In general, a prediction of lower bioavailability must be supported by robust evidence and a
39 weight of evidence determination using expert judgment must be applied.

1 Information on bioavailability is usually obtained from adequate, reliable, and conclusive
2 toxicokinetic studies for all relevant routes of exposure and all relevant forms or physical states
3 where the substance and/or metabolite(s) of the substance have been quantified in body fluids
4 and/or target organs. At present (2016), *in vitro* tests for bioelution are being developed, but
5 have not yet been agreed by OECD. It should be noted that concluding that there is lack of or
6 reduced bioavailability has a high burden of evidence and needs to be supported by robust data
7 and expert evaluation.

8 Bioavailability of a substance or a substance in mixtures is normally assumed if there are *in*
9 *vitro* studies available which show the solubility of a substance or mixture in body fluids or
10 artificial simulated body fluids. Furthermore, conclusions on bioavailability of a substance or a
11 mixture may be based on considerations of the physical properties of a substance or derived
12 from Structural Activity Relationships (SAR). Note also that bioavailability is not limited to
13 solubility, local bioavailability and the uptake of (nano)particles also has to be taken into
14 account. Further, a substance or mixture can be transformed, e.g. by gastric fluid so that the
15 substance absorbed may differ from the substance delivered. In certain exceptional
16 circumstances it may be possible that a substance on its own or in a mixture can be considered
17 to be non-bioavailable, based on either appropriate *in vitro* data, e.g. from skin absorption
18 models, SAR considerations or consideration of the physical properties of the substance, if the
19 respective requirements described above have been taken into account in an adequate analysis.

20 **1.3.2.2. Environmental hazards**

21 The hazard classification for the aquatic environment is based on the three elements aquatic
22 toxicity, bioaccumulation and degradation. The measurement of toxicity to aquatic organisms
23 and its use within a hazard classification system introduces a number of compounding
24 problems. The substance is not dosed directly into the organism but rather into water in which
25 the organism lives. While this reflects more accurately the manner in which the organism will
26 receive the dose in the environment, it does not allow the direct control of the dose which is an
27 important part of much mammalian toxicity testing. The dose is limited by the bioavailability of
28 the substance, the maximum dose being determined by the level of water solubility.

29 It is usually assumed that toxic effects are only measured following exposure to the dissolved
30 fraction, i.e. organisms are exposed to substances dissolved in water. It is assumed that the
31 substances will either be absorbed by the organisms through passive diffusion or taken up
32 actively by a specific mechanism. Bioavailability may, therefore, vary between different
33 organisms. In the case of bioaccumulation, oral exposure could also be considered for
34 substances with high Log K_{ow} . Further guidance of the impact of bioavailability caused by the
35 size of the molecule and how this is considered for aquatic hazard classification can be found in
36 Annex [III](#) to this document.

37 In general, there are no specific environmental test methods developed to measure biological
38 availability of substances or mixtures. This aspect is built into the testing methodology for
39 toxicity and if adverse effects are identified the substance should be classified accordingly.
40 Substances which lack bioavailability would not be absorbed by the exposed organisms and
41 therefore due to lack of toxic effects these substances would not be classified, unless they are
42 known to degrade or transform to hazardous products. For example see the strategy for metals
43 classification in Annex [IV](#) to this document.

44 **1.4. USE OF SUBSTANCE CATEGORISATION (READ ACROSS AND** 45 **GROUPING) AND (Q)SARS FOR CLASSIFICATION AND LABELLING**

Article 5 (1) *Manufacturers, importers and downstream users of a substance shall identify the relevant available information for the purposes of determining whether the substance*

entails a physical, health or environmental hazard as set out in Annex I, and, in particular, the following:

[...]

(c) any other information generated in accordance with section 1 of Annex XI to Regulation (EC) No 1907/2006;

Article 6 (1) *Manufacturers, importers and downstream users of a mixture shall identify the relevant available information on the mixture itself or the substances contained in it for the purposes of determining whether the mixture entails a physical, health or environmental hazard as set out in Annex I, and, in particular, the following:*

[...]

(c) any other information generated in accordance with section 1 of Annex XI to Regulation (EC) No 1907/2006 for the mixture itself or the substances contained in it;

Article 9 (1) *Manufacturers, importers and downstream users of a substance or a mixture shall evaluate the information identified in accordance with Chapter 1 of this Title by applying to it the criteria for classification for each hazard class or differentiation in Parts 2 to 5 of Annex I, so as to ascertain the hazards associated with the substance or mixture*

Article 9 (3) *Where the criteria cannot be applied directly to available identified information, manufacturers, importers and downstream users shall carry out an evaluation by applying a weight of evidence determination using expert judgement in accordance with section 1.1.1 of Annex I to this Regulation, weighing all available information having a bearing on the determination of the hazards of the substance or the mixture, and in accordance with section 1.2 of Annex XI to Regulation (EC) No 1907/2006.*

Article 13 *If the evaluation undertaken pursuant to Article 9 and Article 12 shows that the hazards associated with the substance or mixture meet the criteria for classification in one or more hazard classes or differentiations in Parts 2 to 5 of Annex I, manufacturers, importers and downstream users shall classify the substance or mixture in relation to the relevant hazard class or classes or differentiations by assigning the following:*

(a) one or more hazard categories for each relevant hazard class or differentiation;

(b) subject to Article 21, one or more hazard statements corresponding to each hazard category assigned in accordance with (a).

1 Section 1 of Annex XI to REACH provides a list of data that can be used instead of testing when
2 standard data are missing. This Annex specifies the conditions under which results of (Q)SARs,
3 read across and grouping may be used in order to fulfil the information requirements under
4 REACH and refers to the adequacy of the information for the purpose of classification of
5 substances. It states e.g. that results of (Q)SARs may be used instead of testing when the
6 (Q)SAR models have been scientifically validated, 'the substance falls within the applicability
7 domain', the 'results are adequate for the purpose of classification and labelling' and 'adequate
8 and reliable documentation of the applied method is provided'. Results generated by read-
9 across and grouping may, according to the same principles, be used for classification and
10 labelling if they are 'adequate for classification and labelling', 'have adequate and reliable
11 coverage of the key parameters addressed in the corresponding test method', 'cover an
12 exposure duration comparable to or longer than the corresponding test method', and 'adequate
13 and reliable documentation of the applied method' is provided.

1 According to CLP Article 9(3), a weight of evidence determination using expert judgement has
2 to be applied where the criteria cannot be applied directly to the available data. This
3 determination is further described in CLP Annex I, 1.1.1.

4 It is important to note that most of the criteria for classification are directly related to specific
5 test methods. Thus, the adequacy of results of (Q)SARs, read across and grouping should be
6 evaluated against the criteria taking into account that normally the individual method attempts
7 to estimate the same hazard as the criterion. Nevertheless, when grouping, read-across and
8 (Q)SARs are being used alone or as a part of the basis for classification, it is normally necessary
9 to do so employing weight of evidence and expert judgement in order to be able to apply the
10 criteria to the information leading to a decision on the classification when the criteria are met
11 (article 13, CLP).

12 CLP Annex I, 1.1.1.3 refers to the consideration of any information that is relevant for the
13 determination of a hazard including the category approach. The latter encompasses grouping
14 and read-across to help in a weight of evidence determination which is needed when the
15 application of the criteria is not straightforward and cannot be applied directly to the available
16 information (article 9(1)(3), recital (33)).

Annex I: 1.1.1.3. *A weight of evidence determination means that all available information bearing on the determination of hazard is considered together, such as the results of suitable in vitro tests, relevant animal data, information from the application of the category approach (grouping, read across), (Q)SAR results, human experience such as occupational data and data from accident databases, epidemiological and clinical studies and well documented case reports and observations. The quality and consistency of the data shall be given appropriate weight. Information on substances or mixtures related to the substance or mixture being classified shall be considered as appropriate, as well as site of action and mechanism or mode of action study results. Both positive and negative results shall be assembled together in a single weight of evidence determination.*

17 IR/CSA, Chapter R.6 provides extensive advice on the use of (Q)SARs and grouping of
18 substances including guidance on read across, for developing the data set for hazard evaluation.
19 Guidance on the use of (Q)SAR and grouping for specific hazard classes is given in IR/CSA,
20 Chapter R.7.

21 In general, read across, grouping and use of (Q)SARs as the sole information elements to
22 obtain data on basic physical-chemical properties is not recommended, since reliable data
23 should normally be available or is easily obtainable through testing. However, there may
24 occasionally be practical problems with testing of substances for physical-chemical properties,
25 especially for UVCBs where the properties may be dependent on the variable composition.
26 Therefore, the appropriateness of using read across, categorisation and (Q)SARs for physical-
27 chemical assessment should be considered on a case by case basis. This should also be the case
28 when such data are considered for the evaluation of health and environmental hazards in order
29 to apply the criteria for classification.

30 Given the availability of extensive guidance only a brief overview of each approach is presented
31 below. For classification of mixtures see Section [1.6](#) of this document.

32 **1.4.1. (Q)SAR**

33 Structure Activity Relationships and Quantitative Structure Activity Relationships, collectively
34 referred to as (Q)SARs, are defined in IR/CSA, Chapter R.6.1.1 as theoretical models that can
35 be used to predict in a qualitative or quantitative manner the physico-chemical, biological (e.g.
36 toxicological) or environmental fate properties of compounds from knowledge of their chemical
37 structure.

1 It should be noted that the use of (Q)SAR results requires the user to be sufficiently skilled to
2 understand the applicability of the selected (Q)SAR and to interpret the results in terms of
3 reliability and adequacy for the purpose of classification and labelling.

4 Extensive guidance on the use of (Q)SAR for hazard identification is given in IR/CSA, Chapter
5 R.6.1. Guidance on the use of (Q)SARs for classification and labelling is also given in IR/CSA,
6 Chapter R.6.1.4.2. This guidance is directly applicable to CLP. It should be noted that the
7 (Q)SAR approach is not directly applicable to inorganic substances.

8 **1.4.2. Grouping**

9 Guidance on grouping of substances for the purpose of hazard evaluation is given in IR/CSA,
10 Chapter R.6.2. Annex XI to REACH opens the possibility of evaluating substances not on a one-
11 by-one basis, but by grouping substances in categories. A substance category is a group of
12 substances whose physico-chemical, human health, environmental and/or environmental fate
13 properties are expected to be similar or to follow a regular pattern as a result of structural
14 similarity.

15 The use of grouping for hazard evaluation in the grouping approach means that not every
16 substance needs to be tested for every hazard. Read across by interpolation can be used to fill
17 data gaps, as well as trend analysis and (Q)SAR, and in addition the overall data for that
18 category must prove adequate to support the hazard assessment.

19 In some cases it is necessary to create sub-groups within a category of substances, e.g. when
20 there is a consistent trend within a group with regard to the potency of an effect which may
21 justify different classifications or setting of SCLs (see also IR/CSA, R.6.2.1.2).

22 **1.4.3. Read across**

23 Read across is the use of hazard specific information for one substance ('source') to predict the
24 same hazard for another substance ('target'), which is considered to have similar physico-
25 chemical, human health, environmental fate and/or (eco)toxicological properties. This can be
26 based on structural similarity with a parent substance or its transformation products, and their
27 bioavailability, bioaccessibility, or known physico-chemical properties such as water solubility.
28 For certain substances without test data, the formation of common significant metabolites or
29 information on metabolites of tested substances or information from precursors, may be
30 valuable information (IR/CSA, Chapter R.6.2.5.2 and OECD 2004). For any hazard, read across
31 may be performed in a qualitative or quantitative manner. Extensive guidance on the use of
32 read across is given in IR/CSA, Chapter R.6.2.2.1.

33 Specific guidance for certain types of substances such as reaction products and multi-
34 constituent substances, complex substances, isomers, metals and metal compounds and other
35 inorganic compounds is given in IR/CSA, Chapter R.6.2.5.

36 **1.5. SPECIFIC CONCENTRATION LIMITS AND M-FACTORS**

37 **1.5.1. Specific concentration limits**

Article 10(1) *Specific concentration limits and generic concentration limits are limits assigned to a substance indicating a threshold at or above which the presence of that substance 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.*

Specific concentration limits shall be set by the manufacturer, importer or downstream user where adequate and reliable scientific information shows that the hazard of a substance is evident when the substance is present at a level below the concentrations set for any hazard

class in Part 2 of Annex I or below the generic concentration limits set for any hazard class in Parts 3, 4 and 5 of Annex I.

In exceptional circumstances specific concentration limits may be set by the manufacturer, importer or downstream user where he has adequate, reliable and conclusive scientific information that a hazard of a substance classified as hazardous is not evident at a level above the concentrations set for the relevant hazard class in Part 2 of Annex I or above the generic concentration limits set for the relevant hazard class in Parts 3, 4 and 5 of that Annex.

Article 10(3) *Notwithstanding paragraph 1, specific concentration limits shall not be set for harmonised hazard classes or differentiations for substances included in Part 3 of Annex VI.*

The specific concentration limit (SCL) concept allows a fine tuning of the contribution of certain hazardous substances to the classification of mixtures based on the potency of the substances, as well as a classification of other substances containing these substances as impurities, additives or individual constituents. The SCL concept is generally only applicable to health hazards. For physical hazards, classification must normally be established on the basis of test data for the respective mixture, where applicable.

The procedure of derivation of SCLs is different for every health hazard class and therefore guidance on how to set SCLs is provided in the respective chapters of the different health hazard classes. A general overview on the applicability of SCLs and guidance availability for setting SCLs for health hazards is illustrated by [Table 1.5.1–a](#) below.

SCLs should take precedence over the generic concentration limits (GCLs) given in the relevant health hazard sections of Annex I to CLP. In case specific concentration limits have been set in Annex VI to CLP, these must be applied. Moreover, manufacturers, importers or downstream users may not set their own SCLs for hazards subject to harmonised classifications in Annex VI to CLP.

However, if not included in Annex VI, SCLs should be set by a manufacturer, importer or downstream user in accordance with CLP and be available in the C&L Inventory. SCLs should be communicated via the SDS.

Table 1.5.1–a Possibilities for setting SCL for health hazards addressed in relevant sections of the guidance

Hazard class	Category	Lower SCL than GCL	Higher SCLs than GCL (in exceptional circumstances)	Guidance
Acute toxicity	all	not applicable	not applicable	not necessary
Skin corrosion/irritation	all	yes	yes	available in Section 3.2
Serious damage/eye irritation	eye	yes	yes	available in Section 3.3
Respiratory sensitisation	all	yes*	yes*	see Section 3.4 *currently not available;
Skin sensitisation	all	yes	yes*	available in Section 3.4 *currently not available

Hazard class	Category	Lower SCL than GCL	Higher SCLs than GCL (in exceptional circumstances)	Guidance
Germ mutagenicity cell	all	yes*	yes*	see Section 3.5 *currently not available
Carcinogenicity	all	yes	yes	available in Section 3.6
Reproductive toxicity	all	yes	yes	available in Section 3.7 and in Annex IV
STOT-SE	1	yes	no	available in Section 3.8
	2	no	no	see Section 3.8
	3	yes	yes	available in Section 3.8
STOT-RE	1	yes	no	available in Section 3.9
	2	no	no	see Section 3.9
Aspiration hazard	1	not appropriate	not appropriate	not necessary

1 **1.5.2. Multiplying factors (M-factors)**

Article 10(2) *M-factors for substances classified as hazardous for the aquatic environment, acute category 1 or chronic category 1, shall be established by manufacturers, importers and downstream users.*

2

Article 10(4) *Notwithstanding paragraph 2, M-factors shall not be set for harmonised hazard classes or differentiations for substances included in Part 3 of Annex VI for which an M-factor is given in that Part.*

However, where an M-factor is not given in Part 3 of Annex VI for substances classified as hazardous to the aquatic environment, acute category 1 or chronic category 1, an M-factor based on available data for the substance shall be set by the manufacturer, importer or downstream user. When a mixture including the substance is classified by the manufacturer, importer or downstream user using the summation method, this M-factor shall be used.

3 For the hazard class 'Hazardous to the Aquatic Environment', SCLs are not applicable. Instead
4 the M-factors concept is used.

5 The M-factors are used in the application of the summation method for classification of mixtures
6 containing substances that are classified as very toxic. The concept of M-factors has been
7 established to give an increased weight to very toxic substances when classifying mixtures. M-
8 factors are only applicable to the concentration of a substance classified as hazardous to the
9 aquatic environment (categories Acute 1 and Chronic 1) and are used to derive by the
10 summation method the classification of a mixture in which the substance is present. They are,
11 however, substance-specific and it is important that they are being established already when
12 classifying substances.

13 For further guidance on how to establish the M-factor see Section 4.1.3.3.3 of this document.

1 M-factors should have been established in accordance with Article 10 of CLP and be available in
2 the C&L Inventory.

3 For the harmonised classifications in Annex VI to CLP, M-factors must be set by the
4 manufacturer, importer or downstream user in case there is no M-factor provided, in accordance
5 with CLP Article 10(4).

6 **1.5.3. Harmonised ATE values**

7 From 2016 harmonised ATE values may be included in annex VI of CLP. These values has to be
8 used, just as any other harmonised item.

9 **1.6. MIXTURES**

10 **1.6.1. How to classify a mixture**

11 The classification of mixtures under CLP is for the same hazards as for substances. As a general
12 rule and as is the case with substances, available relevant data on the mixture as a whole
13 should primarily be used to determine classification where applicable, also considering the
14 validity and suitability of the used test method, with regard to testing mixtures in general and
15 the specific mixture of concern. Not all the test methods relevant for substances may be
16 suitable for (all) mixtures and for this reason care has to be taken. Note that for skin
17 sensitisation, care has to be taken so that the doses used do not render the results unreliable. If
18 this cannot be done, further approaches to mixture classification may be applied. For mixtures
19 containing CMR or rapidly biodegradable or bioaccumulative ingredient substances, classification
20 should according to Article 6 (3) and (4) always be based on the ingredient substances for these
21 particular hazard classes. However, if data on a mixture show CMR properties even in absence
22 of data on possible CMR ingredients, the mixture has to be classified appropriately following
23 Article 6(3).

24 It is important to choose the most appropriate method to determine the classification for a
25 mixture for each hazard class, differentiation or category. The method will depend on whether
26 the mixture is being assessed for physical, health or environmental hazards and on the type and
27 quality of information that is available (see also Section [1.2.3](#) of this document on form or
28 physical state).

29 It is important to get a clear picture on which substances and mixtures are contained in a
30 mixture. Basic information on substances would include the substance identity, its classification
31 and any assigned SCLs or M-factors, and concentration in the mixture and, where relevant,
32 details of any impurities and additives including their identity, classification and concentration.
33 Where an ingredient in a mixture is itself a mixture, it is necessary to get information on the
34 ingredient substances of that mixture together with their concentrations, classifications and any
35 applied SCLs or M-factors.

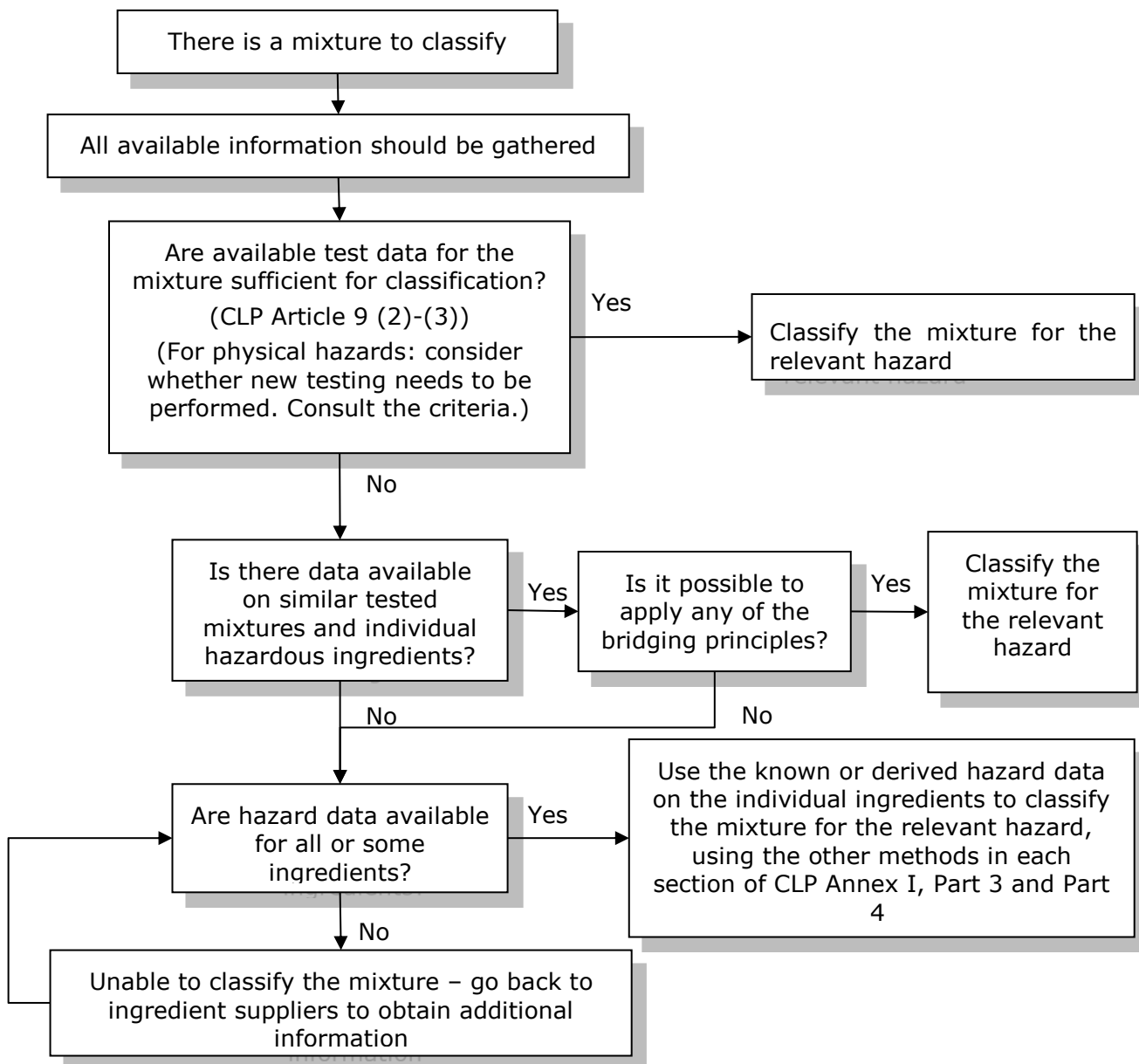
36 Useful sources for such information are the SDS from the supplier of the substance or the
37 mixture, and the C&L Inventory provided by ECHA, which also includes the harmonised
38 classifications of substances listed in Annex VI to CLP. Also data from registration dossiers are a
39 valuable source of information.

40 It should be noted that an SDS should also be provided in some cases when the mixture does
41 not meet the criteria for classification but certain specific criteria are met (see Article 31(3) of
42 REACH).

43 Further dialogue with the supplier may be necessary to obtain additional information. For
44 example on compositional information for the mixture supplied.

45 The classification of mixtures follows the sequence displayed in [Figure 1.6.1–a](#), for each hazard
46 class independently (except for CMR, biodegradable or bioaccumulative ingredient substances):

1 **Figure 1.6.1—a How to classify a mixture**



2

⚠ Note: The principles for using expert judgement and weight of evidence determination (CLP Article 9 (3) and (4)) and Annex I, section 1.1.1.) should be taken into account.

3 **1.6.2. Classification for physical hazards**

4 The majority of the physical hazards of mixtures should be determined through testing based on
 5 the methods or standards referred to in CLP Annex I, Part 2. In few cases, the classification of
 6 mixtures can also be derived through a calculation, if sufficient appropriate data are available
 7 (see CLP Annex I 2.2.4.1 and ISO 10156 for flammable gases, CLP Annex I 2.4.4 and ISO
 8 10156 for oxidizing gases and CLP Annex I, 2.6.4.2 and 2.6.4.3 for flammable liquids).

9 Test methods for physical hazards are referred to in each physical hazard class chapter of CLP.
 10 Most of these test methods can be found in the UN Manual of Tests and Criteria, see the website
 11 http://www.unece.org/trans/danger/publi/manual/manual_e.html. A few of these test methods

1 are contained in standards which are also referred to in CLP (see particularly flammable gases,
2 oxidizing gases and flammable liquids). When test result, based on other methods or standards
3 (which are not referred to in CLP) are available, then these data may still be used, provided
4 they are adequate for the purpose of hazard determination. Expert judgement is necessary to
5 conclude whether there is sufficient documentation to assess the suitability of the test used, and
6 whether the test was carried out using an acceptable level of quality assurance and thus on the
7 adequacy of such data for the purposes of classification according to CLP.

8 Please note that in practice the physical hazards of a substance or mixture may differ from
9 those shown by tests, e.g. in case of certain ammonium-nitrate-based compounds (explosive /
10 oxidising properties) and certain halogenated hydrocarbons (flammable properties). Such
11 experience must be taken into account for the purpose of classification (CLP Article 12(a)).

12 The information available or generated must be checked to determine if it is directly comparable
13 to the respective hazard criteria and if it is, then it can be used to derive the classification
14 immediately. Where the criteria cannot be directly applied to the available data, expert
15 judgement should be used for the evaluation of the available information in a weight of
16 evidence determination (CLP Article 9(3) and CLP Annex I, 1.1.1.).

17 **1.6.3. Health and environmental hazards**

18 For the purpose of classification for health or environmental hazards, check whether or not for
19 each hazard there is information:

- 20 • on the mixture itself;
- 21 • on similar tested mixtures and ingredient substances; or
- 22 • on the classification of ingredient substances and their concentrations in the mixture.

23 As pointed out in the introduction to this chapter, the supplier should be contacted if it is
24 considered that the information on the substances or mixtures supplied is not sufficient for
25 classification purposes.

26 The information available on the hazard under consideration, will determine if the mixture
27 should be classified using the approaches below in the following sequence (CLP Article 9):

- 28 a. Classification derived using data on the mixture itself (see Section [1.6.3.1](#) of this
29 document), by applying the substance criteria of Annex I to CLP;
- 30 b. Classification based on the application of bridging principles (see Section [1.6.3.2](#) of this
31 document), which make use of test data on similar tested mixtures and ingredient
32 substances; and
- 33 c. Classification based on calculation or on concentration thresholds, including SCLs and M-
34 factors.

35 **1.6.3.1. Classification derived using data on the mixture itself**

36 Classification derived using data on the mixture itself, by applying the substance criteria of
37 Annex I to CLP, is applicable for all hazards, except: CMR hazards (see CLP Article 6(3)),
38 bioaccumulation and biodegradation properties within the evaluation of the 'hazardous to the
39 aquatic environment' hazard class referred to in sections 4.1.2.8 and 4.1.2.9 of Annex I to CLP
40 (see CLP Article 6(4)).

Article 6 (3) For the evaluation of mixtures pursuant to Chapter 2 of this Title in relation to the 'germ cell mutagenicity', 'carcinogenicity' and 'reproductive toxicity' hazard classes referred to in sections 3.5.3.1, 3.6.3.1 and 3.7.3.1 of Annex I, the manufacturer, importer or

downstream user shall only use the relevant available information referred to in paragraph 1 for the substances in the mixture.

Further, in cases where the available test data on the mixture itself demonstrate germ cell mutagenic, carcinogenic or toxic to reproduction effects which have not been identified from the information on the individual substances, those data shall also be taken into account.

Article 6(4) *For the evaluation of mixtures pursuant to Chapter 2 of this Title in relation to the 'biodegradation and bioaccumulation' properties within the 'hazardous to the aquatic environment' hazard class referred to in sections 4.1.2.8 and 4.1.2.9 of Annex I, the manufacturer, importer or downstream user shall only use the relevant available information referred to in paragraph 1 for the substances in the mixture.*

1 Where the criteria cannot be directly applied to the available data, expert judgement should be
2 used for the evaluation of the available information in a weight of evidence determination (CLP
3 Article 9(3) and CLP Annex I, 1.1.1). Note that the test method used must be suitable for the
4 mixture tested.

5 **1.6.3.2. Bridging principles**

6 In the case of a classification for health or environmental hazards, relevant information on the
7 mixture itself may not always be available. However, where there are sufficient data on similar
8 tested mixtures and individual hazardous ingredient substances, CLP allows bridging principles
9 to be used to classify the mixture (CLP Annex I, 1.1.3). To apply these bridging principles
10 certain conditions should be considered for their application. The conditions are summarised
11 below.

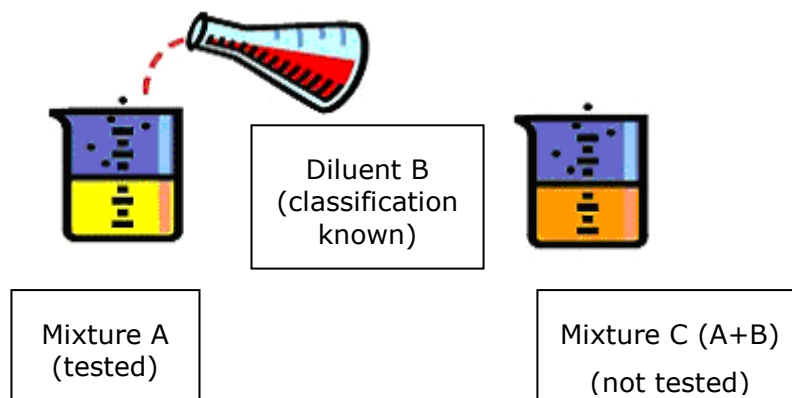
12 It is necessary to consult Annex I of CLP, Part 3 for health hazards and Part 4 for environmental
13 hazards, before undertaking any of these assessments.

14 In case it is not possible to classify the mixture by applying bridging principles and a weight of
15 evidence determination using expert judgement by applying the criteria in Annex I to test
16 results of a mixture, then the mixture should be classified using the other methods described in
17 CLP Annex I, Parts 3 and 4.

18 **1.6.3.2.1. Dilution**

19 Where the tested mixture is diluted with a substance (diluent) that has an equivalent or lower
20 hazard category than the least hazardous original ingredient substance, then it can be assumed
21 that the respective hazard of the new mixture is equivalent to that of the original tested
22 mixture. The application of dilution for determining the classification of a mixture is illustrated
23 by [Figure 1.6.3—a](#).

1 **Figure 1.6.3—a Application of the bridging principle: dilution for determining the acute**
2 **toxicity classification of a mixture**



3
4

5 Example: Mixture A, which has been classified as acute toxic category 2 based on test data, is
6 subsequently diluted with diluent B to form mixture C. If diluent B has an equivalent or lower
7 acute toxicity classification than the least acutely toxic ingredient in mixture A and is not
8 expected to affect the hazard classification of other ingredients, then mixture C may be also
9 classified as acutely toxic category 2. However, this approach may over-classify mixture C, thus
10 the supplier may choose to apply the additivity formula described in CLP Annex I, 3.1.3.6 (see
11 Section [1.6.3.3.1](#) of this document).

12 Note that also the diluent of the tested mixture is considered a relevant ingredient.

13 Consider using this particular bridging principle also when, for example,

- 14 • diluting an irritant mixture with water,
- 15 • diluting an irritant mixture with a non-classified ingredient, or
- 16 • diluting a corrosive mixture with a non-classified or irritant ingredient.

17 In case a mixture is diluted with another mixture, see Section 1.6.4.1 of this document.

18 Within the 'hazardous to the aquatic environment' hazard class, if a mixture is formed by
19 diluting another classified mixture or substance with water or other totally non-toxic material,
20 the toxicity of the mixture can also be calculated from the original mixture or substance (see
21 section 4.1.3.4.3 of Annex I to CLP and mixture example C in Section 4.1.4.7 of this document).

22 **1.6.3.2.2. Batching**

23 Where a batch of a mixture is produced under a controlled process, then it can be assumed that
24 the hazards of each new batch are equivalent to those of previous batches. This method must
25 not be used where there is reason to believe that the composition may vary significantly,
26 affecting the hazard classification.

27 **1.6.3.2.3. Concentration of highly hazardous mixtures**

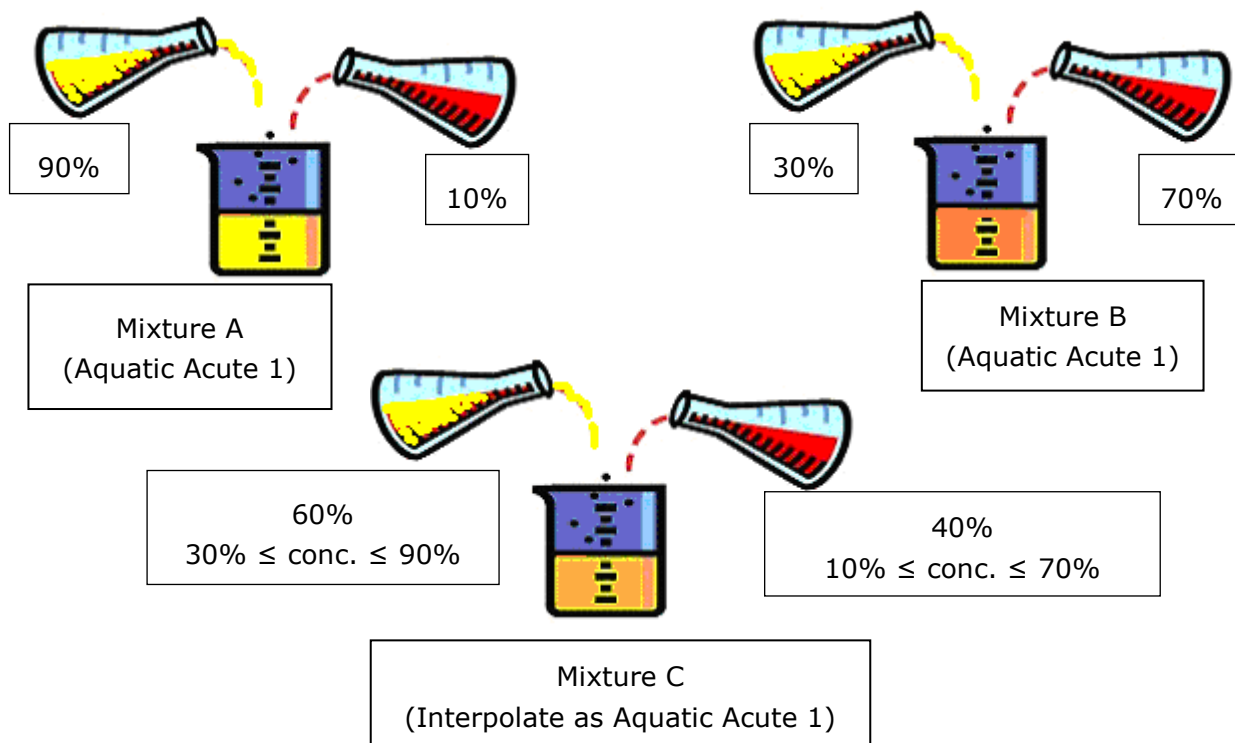
28 Where a tested mixture is already classified in the highest hazard category or sub-category, an
29 untested mixture which contains a higher concentration of those ingredient substances that are
30 in that category or sub-category should also be classified in the highest hazard category or sub-
31 category (CLP Annex I, 1.1.3.3).

32 **1.6.3.2.4. Interpolation within one toxicity category**

33 Assume there are three mixtures (A, B and C) which contain identical hazardous components. If
34 mixtures A and B have been tested and are in the same hazard category, and mixture C is not

1 tested and has concentrations of those hazardous components intermediate to the
2 concentrations in mixtures A and B, then mixture C is assumed to be in the same hazard
3 category as A and B. The application of interpolation for determining the classification of a
4 mixture is illustrated by [Figure 1.6.3—b](#) (CLP Annex I, 1.1.3.4).

5 **Figure 1.6.3—b Application of the bridging principle: interpolation for determining the**
6 **aquatic acute hazard classification of a mixture**

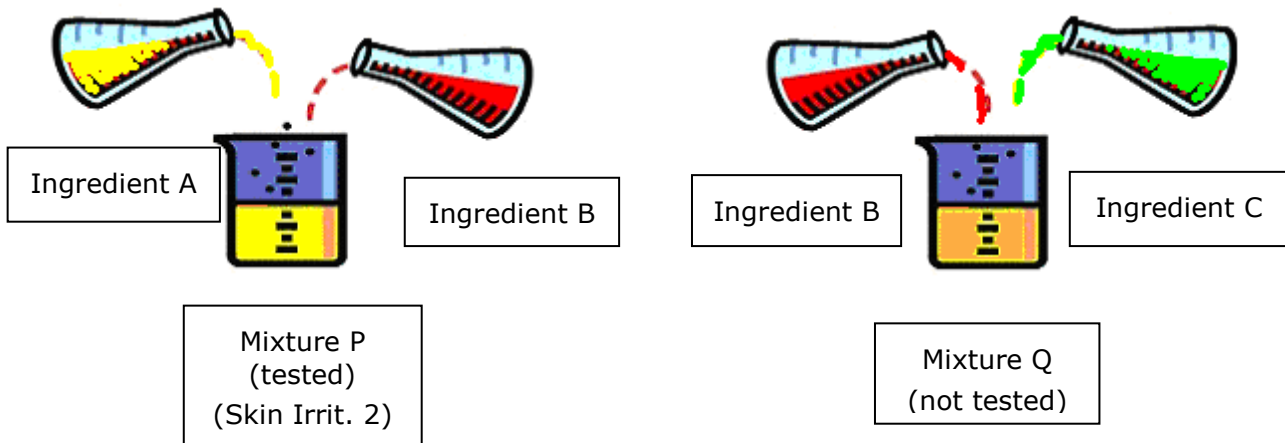


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8 **1.6.3.2.5. Substantially similar mixtures**

9 Two mixtures contain an identical ingredient at the same concentration. Each of the two
10 mixtures contains an additional ingredient which is not identical with each other; however they
11 are present in equivalent concentrations and the hazard category of these two ingredients is the
12 same and neither of them is expected to affect the hazard classification of the other ingredient.
13 If one of the mixtures is classified based on test data it may be assumed that the hazard
14 category of the other mixture is the same. The application of substantially similar mixtures for
15 determining the classification of a mixture is illustrated by [Figure 1.6.3—c](#) (CLP Annex I,
16 1.1.3.5).

1 **Figure 1.6.3—c Application of the bridging principle: substantially similar mixtures for**
2 **determining the skin irritation classification of a mixture**



3
4 Example: If the Ingredient C has the same hazard category and the same potency as Ingredient
5 A, then Mixture Q can be classified as Skin Irrit. 2 like Mixture P. Potency may be expressed by,
6 for example, differences in the specific concentration limits of Ingredients A and C. This method
7 should not be applied where the irritancy of Ingredient C differs from that of Ingredient A.

8 **1.6.3.2.6. Review of classification where the composition of a mixture has changed**

Article 15(2) *Where the manufacturer, importer or downstream user introduces a change to a mixture that has been classified as hazardous, that manufacturer, importer or downstream user shall carry out a new evaluation in accordance with this Chapter where the change is either of the following:*

(a) a change in the composition of the initial concentration of one or more of the hazardous constituents in concentrations at or above the limits in Table 1.2 of Part 1 of Annex I;

(b) [...]

9

Annex I: 1.1.3.6 *Review of classification where the composition of a mixture has changed*
The following variations in initial concentration are defined for the application of Article 15(2)(a):

Table 1.2

Bridging Principle for changes in the composition of a mixture

<i>Initial concentration range of the constituent</i>	<i>Permitted variation in initial concentration of the constituent</i>
$\leq 2,5 \%$	$\pm 30 \%$
$2,5 < C \leq 10 \%$	$\pm 20 \%$
$10 < C \leq 25 \%$	$\pm 10 \%$
$25 < C \leq 100 \%$	$\pm 5 \%$

! **NOTE:** *The guidance below explaining Table 1.2 in the green box relates to a change in the composition of mixtures already classified as hazardous. A change in the composition of*

*non-hazardous mixtures may result in concentration thresholds being reached and a need to classify the changed mixture as hazardous. Where the manufacturer, importer or downstream user introduces a change to a mixture **not** classified for a specific hazard, that manufacturer, importer or downstream user must therefore always carry out a new evaluation for that hazard in accordance with Chapter 2 of Title II to CLP (see Article 15(1) of CLP).*

1 When a manufacturer, importer or downstream user introduces a change in the composition of
2 the initial concentration of one or more of the hazardous constituents of a mixture classified as
3 hazardous, that manufacturer, importer or downstream user must carry out a new evaluation, if
4 the change in concentrations is at or above the limits in Table 1.2 of Part 1 of Annex I to CLP.

5 However, where the variations of the initial concentrations of the constituents lie within the
6 permitted variation, manufacturer, importer or downstream user does not need to carry out a
7 new evaluation and may use the current classification of the mixture.

8 The following example is to illustrate what is meant by the permitted variations in Table 1.2.

9 Example: Mixture A is classified as hazardous based on the initial concentration of two
10 hazardous constituents, substance A and substance B. The initial concentrations in the mixture
11 of substance A and substance B are 2 % and 12 %, respectively. The permitted variation
12 according to table 1.2 is for substance A ± 30 % of the initial concentration and for substance B
13 ± 10 % of the initial concentration. This means that the concentration in the mixture may for
14 substance A vary between 1.4 % and 2.6 % and for substance B between 10.8 % and 13.2 %,
15 without having to carry out a new evaluation in accordance with Chapter 2 of Title II to CLP:

16 Substance A: $2 \times \pm 0.3 = \pm 0.6 \rightarrow 1.4 - 2.6$

17 Substance B: $12 \times \pm 0.1 = \pm 1.2 \rightarrow 10.8 - 13.2$

18 **1.6.3.2.7. Aerosols (some health hazards only)**

19 A mixture in aerosol form is considered to have the same classification as the non-aerosolised
20 form of a mixture, provided that the propellant used does not affect these hazards upon
21 spraying and data demonstrating that the aerosolised form is not more hazardous than the non-
22 aerosolised form is available (see CLP Annex I, 1.1.3.7.).

23 **1.6.3.3. Classification based on calculation or concentration thresholds**

24 In most cases, test data on the mixture itself will not be available for a mixture, therefore
25 bridging principles and weight of evidence determination using expert judgement for all of the
26 necessary health and environmental hazard assessments may not be applied. In these cases,
27 classification must be based on calculation or on concentration thresholds referring to the
28 classified substances present in the mixture.

29 In the case where one or more mixtures are added to another mixture, the same requirement
30 applies: it is necessary to know all ingredient substances, their hazard classifications and their
31 concentrations to be able to derive a correct hazard classification of the final mixture. For
32 further details see Section [1.6.4](#) of this document.

33 **1.6.3.3.1. Classification based on calculation**

34 More detailed guidance on the selection of the most appropriate method is provided in the
35 specific section for each hazard class.

36 An example is the hazard class acute toxicity where a calculation formula is used which is based
37 on acute toxicity estimates and concentrations, and a modified formula for determining the
38 classification of a mixture containing substances of unknown acute toxicity.

Annex I: 3.1.3.6.1.

[...]

The ATE of the mixture is determined by calculation from the ATE values for all relevant ingredients according to the following formula for Oral, Dermal or Inhalation Toxicity:

$$\frac{100}{ATE_{\text{mix}}} = \sum_n \frac{C_i}{ATE_i}$$

where:

C_i = concentration of ingredient i (% w/w or % v/v)

i = the individual ingredient from 1 to n

n = the number of ingredients

ATE_i = Acute Toxicity Estimate of ingredient i .

1

Annex I: 3.1.3.6.2.3. If the total concentration of the ingredient(s) with unknown acute toxicity is ≤ 10 % then the formula presented in section 3.1.3.6.1 shall be used. If the total concentration of the ingredient(s) with unknown toxicity is > 10 %, the formula presented in section 3.1.3.6.1 shall be corrected to adjust for the total percentage of the unknown ingredient(s) as follows:

$$\frac{100 - (\sum C_{\text{unknown}} \text{ if } > 10\%)}{ATE_{\text{mix}}} = \sum_n \frac{C_i}{ATE_i}$$

- 2 For more information on the CLP calculation formulae for this hazard, please see Section 3.1.3.3.3
3 of this document.
4 Another example is provided by hazard class 'hazardous to the aquatic environment', namely the
5 additivity formula:

Annex I: 4.1.3.5.2. Mixtures can be made of a combination of both components that are classified (as Acute Category 1 and/or Chronic Category 1, 2, 3 or 4) and others for which adequate toxicity test data are available. When adequate toxicity data are available for more than one component in the mixture, the combined toxicity of those components is calculated using the following additivity formulas(a) and (b), depending on the nature of the toxicity data:

(a) Based on acute aquatic toxicity:

$$\frac{\sum C_i}{L(E)C_{50m}} = \sum_{\eta} \frac{C_i}{L(E)C_{50i}}$$

where:

C_i = concentration of component i (weight percentage)

$L(E)C_{50i}$ = (mg/l) LC_{50} or EC_{50} for component i

η = number of components

$L(E)C_{50m}$ = $L(E)C_{50}$ of the part of the mixture with test data

The calculated toxicity may be used to assign that portion of the mixture a short-term (acute) hazard category which is then subsequently used in applying the summation method;

(b) Based on chronic aquatic toxicity:

$$\frac{\sum C_i + \sum C_j}{Eq\ NOEC_m} = \sum_n \frac{C_i}{NOEC_i} + \sum_n \frac{C_j}{0,1 \times NOEC_j}$$

Where:

C_i = concentration of component i (weight percentage) covering the rapidly degradable components

C_j = concentration of component i (weight percentage) covering the non-rapidly degradable components


$NOEC_i$ = NOEC (or other recognised measures for chronic toxicity) for component i covering the rapidly degradable components, in mg/l;

$NOEC_j$ = NOEC (or other recognised measures for chronic toxicity) for component i covering the non-rapidly degradable components, in mg/l;

n = number of components, and i and j are running from 1 to n ;

$EqNOEC_m$ = Equivalent NOEC of the part of the mixture with test data;

[...]

 NOTE: The full use of this approach requires access to the whole aquatic toxicity data set and the necessary knowledge to select the best and most appropriate data. CLP has limited the use of the additivity formulae to those circumstances where the substance hazard category is not known, although the acute and/or chronic toxicity data are available. With the aquatic toxicity data at hand the ingredient substance classification and M-factor(s) could easily be gained by a direct comparison with the substance criteria, which then could be fed straight into the summation method. It will therefore usually not be necessary to use the additivity formulae.

1 For more information on the CLP calculation formulae for this hazard please see Section 4.1.4.3
2 of this document.

3 **1.6.3.3.2. Classification based on concentration thresholds**

4 Generic concentration thresholds

5 For most hazard classes or differentiations, classification based on concentration thresholds may
6 be applicable. CLP distinguishes between two different kinds of generic concentration
7 thresholds:

- 8 • **Generic cut-off values:** these values are the minimum concentrations for a substance to
9 be taken into account for classification purposes. These substances are also referred to
10 as relevant ingredients in some hazard classes (see Sections [3.1](#), [3.2](#) and [3.3](#)). When a
11 classified substance is present in a concentration above the generic cut-off value it
12 contributes to the mixture classification even if it does not trigger classification of the
13 mixture directly. The generic cut-off values are defined for some hazard classes and
14 categories only and are listed in Table 1.1 of Annex I to CLP;
- 15 • **Generic concentration limits (GCL):** these values are the minimum concentrations for a
16 substance which trigger the classification of a mixture if exceeded by the individual
17 concentration or the sum of concentrations of relevant substances (where the individual
18 substance concentrations can be 'added' to each other in a straight forward way); they
19 are set out in parts 2-5 of Annex I for those hazard classes where they apply.

20 Generic concentration thresholds are generic for a hazard class, differentiation or category. The
21 difference between a generic cut-off value and a generic concentration limit is demonstrated
22 through the example of the skin irritation hazard: while Table 1.1 of Annex I to CLP defines the
23 generic cut-off value to be 1 % for a skin irritant substance which is present in a mixture, Table
24 3.2.3 of Annex I to CLP shows that a GCL of the skin irritant substance above or equal to the
25 concentration limit of 10% triggers classification of the mixture for skin irritation. However, at \geq
26 1 % and below 10 %, the substance may still contribute to the classification of the mixture as

1 skin irritant. This because the concentration would be taken into account if other skin
2 corrosive/irritant substances are present in the mixture below the relevant generic
3 concentration limits. If additivity applies, classification as provided by the summation in CLP
4 Annex I, Table 3.2.3 may be applicable, i.e.:

5 $(10 \times \text{Skin Corrosive Categories 1A, 1B, 1C}) + \text{Skin Irritant Category 2}$ should be $\geq 10 \%$

6 Specific concentration thresholds

7 In contrast to generic thresholds, 'Specific Concentration Limits' (SCLs) and/or specific cut-off
8 values may be established for individual substances:

- 9 1. SCLs are described in section 1.5.1 of this document and where they have been
10 established they are included in Tables 3.1 and 3.2 of Annex VI to CLP and/or in the C&L
11 Inventory (CLP Article 42). For 'hazardous to the aquatic environment' the Multiplying
12 factors (M-factors) concept⁴³ is used instead of SCLs, see section 1.5.2 of this guidance.
13 SCLs and M-factors included in Tables 3.1 must be used where applicable and, for
14 classifications not included in Annex VI, SCLs and M-factors notified to the C&L Inventory
15 can be considered and used where applicable.
- 16 2. Cut-off values that may be different from the generic values and that are to be used in
17 specific cases are given in 1.1.2.2.2(a) and (b) of Annex I to CLP. For example
18 concerning aquatic hazard, for a substance with an established M-factor, the cut-off
19 value is always the generic cut-off value divided by the M-factor; hence, $(0.1/M) \%$ (see
20 1.1.2.2.2(b) and 4.1.3.1 of Annex I to CLP).

21 22 **1.6.3.3.3. Additivity Vs. non additivity of hazards**

23 For some hazard classes additivity concepts are normally not applicable. In these cases, the
24 general approach is that if a substance or mixture contains two substances each present at a
25 concentration below the GCL defined for that hazard class or differentiation, even if the sum of
26 the substances' concentrations is above this limit, the mixture will not be classified, as far as no
27 lower SCL has been set.

28 Additivity is normally not applied for the following hazard classes:

- 29 a. skin and respiratory sensitisation;
- 30 b. germ cell mutagenicity;
- 31 c. carcinogenicity;
- 32 d. reproductive toxicity;
- 33 e. specific target organ toxicity, single and repeated exposure, categories 1 and 2;
- 34 f. skin corrosion/irritation in certain cases (see CLP Annex I, 3.2.3.3.4); and
- 35 g. serious eye damage/eye irritation in certain cases (see CLP Annex I, 3.3.3.3.4).

36 However, in certain cases for these hazard classes additivity may be scientifically justified.
37 Expert judgement is needed.

38 If the mode of action (MoA) of two substances is the same, additivity can reasonably be
39 assumed. Examples of cases where additivity applies is reprotoxicity of anticoagulant

⁴³ M-factors are used to derive, by means of the summation method, the classification of a mixture in which the substance is present for which the M-factor has been established. For further guidance on how to establish and use M-factors see sections 4.1.3.3.2 and 4.1.4.5, respectively.

1 rodenticides (a group of substances affecting the same enzyme in the same way), reprotoxicity
2 of substances releasing boron ions, skin sensitisation by nickel substances and carcinogenicity
3 and mutagenicity of formaldehyde releasers. For the latter group of substances there are
4 notes⁴⁴ in Annex VI stating that the levels of releasable formaldehyde from different
5 components of a mixture must be added. This applies regardless whether the substances have a
6 harmonised classification or not, whether the purpose of the substance is to act as a
7 formaldehyde releaser or not and it includes formaldehyde itself.

8 When the MoA is different, there may be some cases where it is deemed appropriate to assume
9 additive or synergistic effects. In other cases, there may be no cause for additivity.

10 For STOT SE-RE 1 and 2 additivity may be assumed for substances with the same target organ,
11 especially if the MoAs are similar. Again, in other cases there may be no reason to assume
12 additivity.

13 Additivity is used for the following hazard classes or differentiations:

- 14 a. Acute toxicity (according to specific formula);
- 15 b. skin corrosion/irritation (besides the cases mentioned in CLP Annex I, 3.2.3.3.4);
- 16 c. serious eye damage/eye irritation (besides the cases mentioned in CLP Annex I,
17 3.3.3.3.4);
- 18 d. specific target organ toxicity, single exposure Category 3 (respiratory tract irritation);
- 19 h. specific target organ toxicity, single exposure Category 3 (narcotic effects);
- 20 e. aspiration hazard (plus consideration of viscosity of the final mixture) and
- 21 f. short-term (acute) and long-term (chronic) aquatic toxicity.

22 In these cases, as well as in the specific cases described above when additivity may be
23 scientifically justified, if the sum of the concentrations of one or several substances classified for
24 the same hazard class/category in the mixture equals or exceeds the GCL set out for this hazard
25 class/category, the mixture must be classified for that hazard. For substances that have an SCL
26 or M-factor(s), these should be taken into account when applying the summation methods. The
27 method described in section 3.2.3.2.3.2 can be used when one or more substances in a mixture
28 have SCLs.

29
30 If the sum of $(\text{ConcA} / \text{cIA}) + (\text{ConcB} / \text{cIB}) + \dots + (\text{ConcZ} / \text{cIZ})$ is ≥ 1 then the mixture needs
31 to be classified for the hazard class in question.

32 Where ConcA = the concentration of substance A in the mixture;

33 cIA = the concentration limit (either specific or generic) for substance A;

34 ConcB = the concentration of substance B in the mixture;

35 cIB = the concentration limit (either specific or generic) for substance B; etc.

36 An example is provided for the hazard class serious eye damage /eye irritation: in case there
37 are only substances classified as eye irritation Category 2 present in a mixture, then their sum
38 must be equal to or exceed the generic concentration limit of 10 % in order for the mixture to

⁴⁴ The 10th ATP added the following notes in Annex I to CLP:

"Note 8: The classification as a carcinogen need not apply if it can be shown that the maximum theoretical concentration of releasable formaldehyde, irrespective of the source, in the mixture as placed on the market is less than 0,1%."

"Note 9: The classification as a mutagen need not apply if it can be shown that the maximum theoretical concentration of releasable formaldehyde, irrespective of the source, in the mixture as placed on the market is less than 1%."

1 be classified in Category 2 as well. Note that only relevant substances (i.e. for eye irritants,
2 above the generic cut-off value of 1%) should be summed up and contribute to mixture
3 classification. Further guidance on the application of SCLs when using the summation method to
4 derive conclusions on skin corrosion / irritation or serious eye damage/eye irritation hazards can
5 be found in Sections [3.2](#) and [3.3](#) of this document.

6 **1.6.4. Classification of mixtures in mixtures**

7 For physical hazards, an adequate hazard classification is generally derived by testing. To
8 determine the classification of a mixture for health or environmental hazards using the
9 additivity or summation methods, information on all the component substances, including their
10 individual hazard classification and concentration, is generally required. In the case where one
11 or more mixtures are added to another mixture, the same requirement applies: it is generally
12 necessary to know all component substances, their hazard classifications and their
13 concentrations to be able to derive a correct hazard classification of the final mixture. It is
14 generally not possible to derive the correct hazard classification for the final mixture by using
15 only the hazard classification(s) of the mixtures that were combined to make it. For example, a
16 mixture containing 1% of a Carc. Cat. 1B substance would be classified as Carc. Cat. 1B. Taking
17 1% of this mixture into another mixture would lead to a concentration of the ingredient causing
18 the carcinogenic classification of 0.01%, i.e. below the GCL. The same situation may occur also
19 for substances classified due to an impurity.

20 However, there is one exception. If the acute toxicity estimate (ATE) of a mixture is known
21 (either actual or derived), this value can be used to derive a correct classification for acute
22 toxicity if this mixture is added to another mixture.

23 Thus, it is very important that suppliers of mixtures communicate the necessary information
24 listed above on component substances (including their individual hazard classification and
25 concentration) down the supply chain, normally in the SDS, to enable a correct classification to
26 be established by downstream users formulating new mixtures from their products. However,
27 the information provided in the SDS may not be sufficient, for example where only a
28 concentration range is quoted for a particular substance or where the mixture contains other
29 substances classified as hazardous but which are present below the concentration which triggers
30 the obligation to indicate the substance in the SDS. Thus further dialogue with the supplier of
31 the mixture may be necessary to obtain additional information on the constituent substances to
32 ensure correct classification and labelling of the new mixture.

33 In situations, where tested mixtures are added to other tested or untested mixtures, an
34 adequate hazard classification can only be derived by taking account of the test data as well as
35 the knowledge on all ingredient substances, their hazard classifications, and their
36 concentrations in these mixtures. Such an approach is a case-by-case analysis and requires
37 expert judgement.

38 **1.6.4.1. Example: Classification of Mixture A**

39 Note that the example only addresses health hazards. For compositional details see [Table](#)
40 [1.6.4–a](#) and [Table 1.6.4–b](#) below.

41 Mixture A is a water solution containing a surfactant, a thickening agent dye and a fragrance
42 mixture. Classification of components and composition of the fragrance mixture are known.

43 No test data are available on Mixture A and it is not possible to apply bridging principles due to
44 lack of data on similar tested mixtures. Therefore it is necessary to identify the ingredients in
45 Mixture A (including their % w/w and classification).

46 Mixture A does not contain any ingredients classified as a respiratory sensitiser, CMR, STOT or
47 aspiration hazard. Therefore it is possible to conclude that Mixture A will not be classified as
48 hazardous for these particular hazard classes.

1 Acute toxicity

2 As indicated in CLP Annex I, point 3.1.3.3(b), there are two options to calculate the acute
3 toxicity of Mixture A: (i) treat the 'fragrance mixture' as an ingredient when calculating the ATE
4 for Mixture A, or (ii) break the 'fragrance mixture' down into its component ingredients and only
5 take over the relevant ingredients (CLP Annex I, 3.1.3.3(a) and 3.1.3.6.1) into the calculation
6 for the ATE of Mixture A.

7 Following option (i) it is first necessary to calculate ATE_{mix} of the 'fragrance mixture' (see [Table](#)
8 [1.6.4–b](#)) taking into account 'FM component 1' and 'FM component 2' (other components can
9 be excluded as their LD₅₀ values are > 2000 mg/kg):

$$\frac{100}{ATE_{mix}} = \sum_n \frac{C_i}{ATE_i} \rightarrow$$

$$ATE_{mix} = \frac{100}{\sum_n \frac{C_i}{ATE_i}} \rightarrow$$

$$ATE_{mix} = \frac{100}{\frac{35.2}{1230} + \frac{17.0}{500}} = 1597 \text{ mg/kg}$$

10

11 The ATE_{mix} for the 'fragrance mixture' can then be included in the calculation of the ATE_{mix} for
12 Mixture A:

$$ATE_{mix} = \frac{100}{\frac{8.0}{1800} + \frac{5.0}{1597}} = 13300 \text{ mg/kg}$$

13

14 Following option (ii) it is only necessary to include 'FM component 1' from the 'fragrance
15 mixture' (present in Mixture A at 1.76 %), as 'FM component 2' is present in a concentration <
16 1%). Calculation of the ATE_{mix} for Mixture A according to option (ii):

$$ATE_{mix} = \frac{100}{\frac{8.0}{1800} + \frac{1.76}{1230}} = 17200 \text{ mg/kg}$$

17

18 Both options indicate that the calculated ATE_{mix} of Mixture A is > 2000 mg/kg thus mixture A is
19 not classified as hazardous for acute toxicity by the oral route.



NOTE: If an acute oral toxicity test (i.e. an actual LD₅₀ value) was available for the fragrance mixture, then this should be used in the calculation for the ATE of Mixture A.

20 Skin corrosion/irritation

21 Work out the actual levels of the 'fragrance mixture' ingredients in Mixture A and carry out the
22 summation method (CLP Annex I, Table 3.2.3) using the relevant ingredients.

23 Mixture A does not contain any ingredient classified as Skin Corr. 1A, B or C. Therefore Mixture
24 A is not classified as Skin Corr. 1A, B or C.

1 The 'fragrance mixture' contains ingredients classified as Skin Irrit. 2, but these are all present
2 in Mixture A at concentrations < 1 % and can be disregarded (generic cut-off values to be taken
3 into account, CLP Annex I, Table 1.1). Mixture A does also contain 8 % of the 'anionic
4 surfactant' classified as Skin Irrit. 2, but as the concentration of the 'anionic surfactant' < 10 %
5 (GCL, CLP Annex I, Table 3.2.3), Mixture A is not classified as Skin Irrit. 2.

6 Serious eye damage/eye irritation

7 Work out the actual levels of the 'fragrance mixture' ingredients in Mixture A and carry out the
8 summation method (CLP Annex I, Table 3.3.3) using the relevant ingredients:

9 Mixture A contains 8 % of an ingredient classified as Eye Dam. 1, thus Mixture A must also be
10 classified as Eye Dam. 1 (i.e. the relevant ingredient is present in a concentration above the
11 GCL of 3 %). The 'fragrance mixture' also contains an ingredient classified as Eye Dam. 1, but
12 this is present in Mixture A at a concentration < 1 % and can be disregarded.

13 Skin sensitisation

14 The 'fragrance mixture' contains four ingredients classified as skin sensitisers (cat 1) but their
15 actual levels in Mixture A are below the GCL of 1 % thus Mixture A is not classified as a skin
16 sensitiser. However, the four skin sensitiser ingredients are present above 0.1 %, thus
17 additional labelling information EUH208 (CLP Annex II, 2.8) would be required on the label for
18 Mixture A.

19 In summary, mixture A is classified as Eye Dam.1 and additional labelling information is needed
20 on the label. EUH208 – 'Contains (name of sensitising substance). May produce an allergic
21 reaction'.

22 **Table 1.6.4–a Ingredients in Mixture A**

Ingredient	% w/w	Oral LD ₅₀ (rat)	Classification
Anionic surfactant	8.00	1800 mg/kg	Acute Tox. 4 (oral) Eye Dam. 1 Skin Irrit. 2
Thickening agent	0.80	> 5000 mg/kg	Not classified
Dye	0.05	> 5000 mg/kg	Not classified
Fragrance mixture (see list of ingredients below)	5.00	not tested	Acute Tox. 4 (inhalation, oral) Skin Sens. 1 Eye Dam. 1 Skin Irrit. 2 Aquatic Chronic 2
Water	86.15		Not classified
Total:	100.00		

23 **Table 1.6.4–b Ingredient 'Fragrance mixture'**

Ingredient	% w/w	% in Mixture A	Oral LD ₅₀ (rat)	Classification
FM component 1	35.20	1.76	1230 mg/kg	Acute Tox. 4 (inhalation, oral)

Ingredient	% w/w	% in Mixture A	Oral LD ₅₀ (rat)	Classification
FM component 2	17.00	0.85	not available (use cATpE 500)	Acute Tox. 4 (oral) Skin Sens. 1
FM component 3	16.00	0.8	3600 mg/kg	Skin Sens. 1 Skin Irrit. 2
FM component 4	13.40	0.67	3100 mg/kg	Skin Sens. 1
FM component 5	7.00	0.35	> 2000 mg/kg	Eye Dam. 1 Aquatic Chronic 2
FM component 6	6.00	0.3	4400 mg/kg	Flam. Liq. 3 Skin Sens. 1 Skin Irrit. 2 Aquatic Chronic 1
FM component 7	2.80	0.14	> 5000 mg/kg	Not classified
FM component 8	2.60	0.13	> 5000 mg/kg	Aquatic Chronic 1
Total:	100.00	5.00		

1

2 **1.6.4.2. Example: Classification of Mixture B**

3 Note that the example only addresses health hazards.

4 Mixture B is a powder form detergent containing a base powder, oxygen bleach, silicates,
5 carbonate and inorganic processing aid. The compositional details are provided in [Table 1.6.4–c](#)
6 and [Table 1.6.4–d](#) below.

7 No test data are available on Mixture B and it is not possible to apply bridging principles due to
8 lack of data on similar tested mixtures. Therefore it is necessary to identify the ingredients in
9 Mixture B (including their % w/w and classification).

10 Mixture B does not contain any ingredients classified as a skin sensitiser, CMR or aspiration
11 hazard. Therefore it is possible to conclude that Mixture A will not be classified as hazardous for
12 these particular hazard classes.

13 Acute toxicity

14 As indicated in CLP Annex I, 3.1.3.3(b), there are two options to calculate acute toxicity of
15 Mixture B: (i) treat the 'base powder' as an ingredient when calculating the ATE for Mixture B,
16 or (ii) break the 'base powder' down into its component ingredients and only take over the
17 relevant ingredients (CLP Annex I, 3.1.3.3(a) and 3.1.3.6.1) into the calculation for the ATE of
18 Mixture B.

19 Following option (i) it is first necessary to calculate the ATE_{mix} of the 'base powder' taking into
20 account the non-ionic surfactant (other components can be excluded as LD₅₀ values are > 2000
21 mg/kg):

$$\frac{100}{ATE_{mix}} = \sum_n \frac{C_i}{ATE_i} \rightarrow$$

$$ATE_{mix} = \frac{100}{\sum_n \frac{C_i}{ATE_i}} \rightarrow$$

$$ATE_{mix} = \frac{100}{\left(\frac{18.0}{500}\right)} = 2778\text{mg/kg}$$

1
2

3 The ATE_{mix} for the 'base powder' can then be used for the calculation of the ATE_{mix} for Mixture B:

$$ATE_{mix} = \frac{100}{\frac{20.0}{2778} + \frac{18.0}{770} + \frac{8.0}{1800}} = 2860\text{mg/kg}$$


4
5

6 Following option (ii) it is only necessary to include the non-ionic surfactant from the 'base
7 powder' (present in Mixture B at 3.6%). Other ingredients in the 'base powder' can be excluded
8 as $LD_{50} > 2000$ mg/kg for all of them. The calculation of the ATE_{mix} for Mixture B applying option
9 (ii):

$$ATE_{mix} = \frac{100}{\frac{3.6}{500} + \frac{18.0}{770} + \frac{8.0}{1800}} = 2860\text{mg/kg}$$

10
11

12 Both options indicate that the calculated ATE_{mix} of Mixture B is > 2000 mg/kg. Therefore Mixture
13 B is not classified as hazardous for acute toxicity by the oral route.

 NOTE: If an acute oral toxicity test (i.e. an actual LD_{50} value) was available for the 'base powder' then this should be used in the calculation for the ATE of Mixture B.

14 Skin corrosion/irritation

15 Work out the actual levels of the 'base powder' ingredients in Mixture B and carry out the
16 summation method (CLP Annex I, Table 3.2.3) using the relevant ingredients:

17 Mixture B does not contain any ingredients classified as Skin Corr. 1A, B or C thus Mixture B is
18 not classified as Skin Corr. 1A, B or C.

19 Mixture B does however contain 23 % ingredients classified as Skin Irrit. 2 (11% silicates, 8%
20 anionic surfactant and 4% anionic surfactant from the 'base powder'), as the content of
21 classified ingredients are $> 10\%$ also Mixture B is classified as Skin Irrit. 2.

1 Serious eye damage/eye irritation

2 Work out the actual levels of the 'base powder' ingredients in Mixture B and carry out the
3 summation method (CLP Annex I, Table 3.3.3) using the relevant ingredients:

4 Mixture B contains 40.6 % ingredients classified as Eye Dam.1 (18% oxygen bleach, 11%
5 silicates, 8 % anionic surfactant and 3.6 % non-ionic surfactant), thus Mixture B is also
6 classified as Eye Dam.1.

7 Respiratory sensitisation

8 Mixture B contains 0.7% of the ingredient 'enzymes' classified for respiratory sensitisation
9 category 1. However this is below the concentration triggering classification (CLP Annex I, Table
10 3.4.5) thus Mixture B is not classified as a respiratory sensitiser. However ingredient 'enzymes'
11 trigger additional labelling information EUH208 (CLP Annex II, 2.8).

12 STOT

13 Mixture B does not contain any ingredients classified as STOT RE or STOT SE 1 or 2, but it
14 contains 11% of an ingredient classified as STOT SE 3 (respiratory tract irritation). The generic
15 concentration limit is 20 % for extrapolating the classification as STOT SE 3 from an ingredient
16 to the mixture (CLP Annex I, 3.8.3.4.5.), thus Mixture B does not trigger classification as STOT
17 SE 3 (respiratory tract irritation).

18 In summary, mixture B is classified as Skin Irrit. 2, Eye Dam. 1 and additional labelling
19 information is needed on the label. EUH208 – 'Contains (name of sensitising substance). May
20 produce an allergic reaction'.

21 **Table 1.6.4—c Ingredients in Mixture B**

Ingredient	% w/w	Oral LD ₅₀ (rat)	Classification
Base powder (see list of ingredients below)	20.00	not tested	Eye Dam.1 Skin Irrit. 2
Oxygen bleach	18.00	770 mg/kg	Ox. Sol. 1 Acute Tox. 4 (oral) Eye Dam. 1
Silicates	11.00	3400 mg/kg	Eye Dam. 1 Skin Irrit. 2 STOT SE 3 (respiratory tract irritation)
Carbonate	7.00	4090 mg/kg	Eye Irrit. 2
Inorganic processing aid	11.30	> 5000 mg/kg	Not classified
Builder	16.00	> 5000 mg/kg	Not classified
Anionic surfactant	8.00	1800 mg/kg	Acute Tox. 4 (oral) Eye Dam. 1 Skin Irrit. 2
Bleach activator	5.00	> 5000 mg/kg	Not classified
Enzymes	0.70	> 2000 mg/kg	Resp. Sens. 1

Ingredient	% w/w	Oral LD ₅₀ (rat)	Classification
Polycarboxylate	3.00	> 5000 mg/kg	Not classified
Total:	100.00		


1 **Table 1.6.4—d Ingredients 'base powder'**

Ingredient	% w/w	% in Mixture B	Oral LD ₅₀ (rat)	Classification
Non-ionic surfactant	18.00	3.6	500 mg/kg	Acute Tox. 4 (oral) Eye Dam. 1 Aquatic Acute 1
Anionic surfactant	20.00	4.0	> 2000 mg/kg	Skin Irrit. 2 Eye Irrit. 2
Builder	50.00	10.0	> 5000 mg/kg	Not classified
Carbonate	8.00	1.6	4090 mg/kg	Eye Irrit. 2
Inorganic processing aid	4.00	0.8	> 5000 mg/kg	Not classified
Total:	100.00	20.00		

2

3 **1.7. ANNEX VII TO CLP**

Article 61(5) *Where a substance or mixture has been classified in accordance with Directive 67/548/EEC or 1999/45/EC before 1 December 2010 or 1 June 2015 respectively, manufacturers, importers and downstream users may amend the classification of the substance or mixture using the conversion table in Annex VII to this Regulation.*

 NOTE: Article 61 uses the term 'conversion table' and Annex VII uses the term 'translation table'. These terms have the same meaning i.e. the tables in Annex VII that relate classifications according to DSD or DPD to a classification according to CLP.

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5 The tables contained in Annex VII to CLP show how classifications in accordance with the DSD
6 were converted into the corresponding classification under CLP and included in Table 3.1 of
7 Annex VI to CLP⁴⁵. The tables also aimed to support translation of existing self-classifications in
8 accordance with DSD into classifications in accordance with CLP.

9 Although conceptually similar, the coverage of CLP and the DSD or DPD is different. In some
10 cases, the relationship between the category of danger and corresponding R-phrases and the
11 hazard categories and corresponding hazard statements is clear, but in other cases, it is less

⁴⁵ Note that the 8th ATP has corrected the Annex VII to CLP. The current Annex VII suggests R34 = Skin Corr. 1 whereas the original translation was to Skin Corr. 1B.

1 well defined. Additionally, CLP introduced new hazard classes reflecting hazards that were not
2 covered or were only partly covered by DSD and DPD.

3 While the tables explicitly point out where no translation was possible or where minimum
4 classification would be applied, they do not identify situations where CLP hazard classes or
5 categories, not covered by the DSD and DPD, are required under CLP. In the particular case of
6 'no classification' under the DPD, the table would not provide any indication for a reasonable
7 translation to a CLP classification.

8 As mentioned, the Annex VII translation tables did not always give a direct translation. For
9 certain hazard classes, including acute toxicity and STOT repeated exposure, a translation from
10 DSD to CLP according to Annex VII, resulted in a recommended minimum classification. This
11 minimum classification is also indicated as such in Table 3.1 in Annex VI, and should only be
12 used if no additional hazard information is available (see also CLP Annex VI, 1.2.1).

13 It should be noted that whenever data for a substance or mixture is available for a hazard class,
14 the substance or mixture must be classified in accordance with the CLP criteria and the Annex
15 VII tables must no longer be used.

16 [Table 1.7-a below](#) identifies where no direct translation was possible according to the Annex VII
17 translation tables for substances and mixtures requiring classification under DSD or DPD.

18 In addition to the differences indicated in Table 1.7-a, it should be noted that for some hazards,
19 the generic concentration limits to be applied for mixtures, were lowered under CLP as
20 compared to DPD. Lower generic concentration limits were set for skin corrosion (R34 and R35),
21 severe eye damage and eye irritation (R41 and R36), skin irritancy (R38) and reproductive
22 toxicity (R60, R61, R62 and R63).

23

24 **Table 1.7-a Hazard classes where the translation tables in Annex VII to CLP indicate that**
25 **no direct translation was possible from DSD to CLP**

Classifications under DSD or DPD	Potential translation outcomes	Comments
E, R2 E, R3	1) Explosive. 2) Organic peroxide 3) Flammable solid 4) Oxidising solid 5) Self-reactive 6) No classification	Change of classification criteria and method; case-by-case considerations See Annex VII for additional information on transport classifications
O, R8 (liquid)	Oxidising liquid	All liquid substances or mixtures classified O,R8 are classified as oxidising liquids under CLP. See Annex VII for additional information on transport classifications
O, R8 (solid)	Oxidising solid	The test methods for oxidising solids in 67/548/EEC and CLP were different. Most solids classified O, R8 are also classified as oxidising solids under CLP. See Annex VII for additional information on transport classifications
F, R11 (solid)	1) Flammable solid	Solid substances or mixtures classified F, R11 may be classified as flammable solids or self reactives

Classifications under DSD or DPD	Potential translation outcomes	Comments
	1a) Possibly self-heating in addition 2) Self-reactive	under CLP. If classified as flammable solids, they may additionally be classified as self-heating. See Annex VII for additional information on transport classifications
F, R15	Substance or mixture which, in contact with water, emit(s) flammable gas(es)	See Annex VII for additional information on transport classifications

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1 **2. PART 2: PHYSICAL HAZARDS**

2 *[See separate document for the specific sections of Part 2 under consultation]*

3 **2.0. INTRODUCTION**

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5 **2.1. EXPLOSIVES**

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1 **2.2. FLAMMABLE GASES (INCLUDING CHEMICALLY UNSTABLE GASES)**

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1 2.3. AEROSOLS

1 **2.4. OXIDISING GASES**

2 **2.5. GASES UNDER PRESSURE**

3 **2.6. FLAMMABLE LIQUIDS**

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1 **2.7. FLAMMABLE SOLIDS**

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1 **2.8. SELF-REACTIVE SUBSTANCES AND MIXTURES**

2 **2.9. PYROPHORIC LIQUIDS**

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1 **2.10. PYROPHORIC SOLIDS**

2

1 **2.11. SELF-HEATING SUBSTANCES AND MIXTURES**

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1 **2.12. SUBSTANCES AND MIXTURES WHICH, IN CONTACT WITH WATER,**
2 **EMIT FLAMMABLE GASES**
3

1 **2.13. OXIDISING LIQUIDS**

2

1 **2.14. OXIDISING SOLIDS**

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3 **2.15. ORGANIC PEROXIDES**

4

1 **2.16. CORROSIVE TO METALS**

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1 **3. PART 3: HEALTH HAZARDS**

2 *[See separate document for the specific sections of Part 3 under consultation]*

3 **3.1. ACUTE TOXICITY**

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1 **3.2. SKIN CORROSION/IRRITATION**

2 **3.3. SERIOUS EYE DAMAGE/EYE IRRITATION**

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1 **3.4. RESPIRATORY OR SKIN SENSITISATION**

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3 **3.5. GERM CELL MUTAGENICITY**

4 **3.6. CARCINOGENICITY**

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7 **3.7. REPRODUCTIVE TOXICITY**

8 **3.8. SPECIFIC TARGET ORGAN TOXICITY – SINGLE EXPOSURE (STOT-**
9 **SE)**

10 **3.9. SPECIFIC TARGET ORGAN TOXICITY – REPEATED EXPOSURE**
11 **(STOT-RE)**

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1 **4. PART 4: ENVIRONMENTAL HAZARDS**

2 *[Please note, Part 4 is **not** under consultation]*

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4 **4.1. HAZARDOUS TO THE AQUATIC ENVIRONMENT**

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2 **5. ADDITIONAL HAZARDS**

3 *[Please note, Part 5 is **not** under consultation]*

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5 **5.1. HAZARDOUS TO THE HOZONE LAYER**

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11 **ANNEXES**

12 *[Please note, Annexes are **not** under consultation]*

13

14 **I ANNEX I: AQUATIC TOXICITY**

1 **II ANNEX II: RAPID DEGRADATION**
2

1 **III ANNEX III: BIOACCUMULATION**

2

1 **IV ANNEX IV: METALS AND INORGANIC METAL COMPOUNDS**

2 **V ANNEX V: COLLECTION OF INTERNET LINKS FOR THE**
3 **USERS OF THE GUIDANCE**

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**VI ANNEX VI: BACKGROUND DOCUMENT TO THE GUIDANCE
FOR SETTING SPECIFIC CONCENTRATION LIMITS FOR
SUBSTANCES CLASSIFIED FOR REPRODUCTIVE TOXICITY
ACCORDING TO REGULATION (EC) NO 1272/2008**

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