CLP revision: ED criteria

CASG-ED

Which revisions of CLP are we looking at?

New Hazard classes

- New hazard class for ED for human health and one for the environment with a categorisation system for both;
- New hazard class for PBT and one for vPvB on the basis of REACH Annex XIII criteria and potentially a categorisation system;
- New hazard class for PMT and one for vPvM and potentially a categorisation system.

Chemicals Strategy for Sustainability Towards a Toxic-free Environment

- The Commission will make a “proposal to amend the CLP Regulation to introduce new hazard classes on endocrine disruptors, PBTs/vPvBs and persistent and mobile substances, and apply them across all legislation”, with a targeted date fixed in 2021.

Harmonised Classification

- Inclusion of a mandate for COM to request ECHA to initiate, develop and submit a proposal for CLH dossiers.
- Harmonisation of human health and environment based safety values (e.g., PNEC, DNEL)

Which supporting actions or studies are we planning?

Supporting study/actions for Impact Assessment

- An IA will be carried out to identify and assess which effects the various options are expected to have (protection of HH/Env, economic costs, internal market and other social impacts);
- Stakeholder consultations: existing relevant fora (Caracal, and its subgroup on EDs, FORUM, Helpnet, ECHA PBT expert group)
- Supporting study.

Indicative timing

Indicative timing of actions

- Inception Impact Assessment (roadmap) for 4 weeks stakeholder consultation – April 2021
- Public stakeholder consultation for 12 weeks is planned in all EU languages – Q1 2021 to Q2
- Supporting actions – Q1 2021 to Q2
- Impact Assessment – June 2021
- Drafting proposal for revision of CLP – September 2021
- Commission adoption of proposal – end 2021

First Draft Proposal of criteria

General considerations

- Initial draft proposal that will evolve in the future
- Separate hazard classes for endocrine disruptors (human health/environment)
- Introduction of categories
  - Category 1: Known or presumed endocrine disruptors (ED HH 1 and ED ENV 1)
  - Category 2: Suspected endocrine disruptors (ED HH 2 and ED ENV 2)

Further considerations

- Case of double classification
- Further changes needed in CLP (for example update of category codes)
- Need to develop a guidance after the adoption, taken into account the guidance developed under PPP/BPR

Draft criteria for Human Health

Colour explanation:

- YYY: Wording taken from CLP Regulation
- YYY: Wording taken from PPP Criteria (Regulation (EC) 1107/2009, Annex II, 3.6.5)
- YYY: Adaption of wording to ED

Text proposal	Comments
3.11 Endocrine disrupting property for human health	To follow CLP naming, it should be the name of the hazard (and not the substance) as for example “carcinogenicity”
3.11.1 Definitions and general considerations	Wording from Repro. 3.7.1
3.11.1.1 Endocrine disruptor means a substance or a mixture of substances that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.	Definition from WHO/PCS/EDC/02.2: https://www.who.int/ipcs/publications/en/ch1.pdf?ua=1

3.11.1.2 A substance is considered to be an endocrine disruptor if it meets all of the following criteria : (1) it shows an adverse effect in an intact organism or its progeny; (2) it shows endocrine activity; (3) the substance has an endocrine disrupting mode of action, i.e. there is a biologically plausible link between the endocrine activity and the adverse effect".	

3.11.1.3 An adverse effect is defined in this context as a change in morphology, physiology, growth, development, reproduction or lifespan of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences.	Definition from WHO/IPCS Environmental Health Criteria 240, Principles and Methods for the Risk Assessment of Chemicals in Food. Environmental Health Criteria 240: https://apps.who.int/iris/bitstream/handle/10665/44065/WHO_EHC_240_13_eng_Annex1.pdf?sequence=13 (Glossary)
3.11.1.4 An endocrine activity is defined as an interaction with the endocrine system that can potentially result in a response of the endocrine system, target organs and tissues. A substance that has an endocrine activity has the potential to alter the function(s) of the endocrine system.	Definition from the ECHA/EFSA guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009 .

3.11.2 Classification criteria for substances	
3.11.2.1 Hazard categories For the purpose of classification for endocrine disrupting properties for human health, substances are allocated to one of two categories based on strength of evidence and additional considerations in a weight of evidence approach.	

Table 3.11.1 Hazard categories for endocrine disruptors for human health	Wording adapted from Repro. 3.7.2.1.1 (Table 3.7.1(a))
Categories	Criteria
CATEGORY 1	Known or presumed endocrine disruptors for human health A substance is classified in Category 1 for endocrine disrupting properties for human health if it is known or presumed to meet the criteria defined in 3.11.1.2. The classification in Category 1 is based on evidence from human and/or on data from animal studies. Such data shall provide clear evidence of an adverse effect, endocrine activity and that the adverse effect is a consequence of the endocrine activity. However, when there is information that raises doubt about the relevance of the endocrine disrupting mode of action for humans, classification in Category 2 may be more appropriate.

CATEGORY 2	Suspected endocrine disruptors for human health A substance is classified in Category 2 for endocrine disrupting properties for human health when there is some evidence of an adverse effect, which is a consequence of the endocrine activity, and where the evidence is not sufficiently convincing to place the substance in Category 1.

Categories	Criteria
CATEGORY 1	Known or presumed endocrine disruptors for human health A substance is classified in Category 1 for endocrine disrupting properties for human health if it is known or presumed to meet the criteria defined in 3.11.1.2. The classification in Category 1 is based on evidence from human and/or on data from animal studies. Such data shall provide clear evidence of an adverse effect, endocrine activity and that the adverse effect is a consequence of the endocrine activity. However, when there is information that raises doubt about the relevance of the endocrine disrupting mode of action for humans, classification in Category 2 may be more appropriate.
CATEGORY 2	Suspected endocrine disruptors for human health A substance is classified in Category 2 for endocrine disrupting properties for human health when there is some evidence of an adverse effect, which is a consequence of the endocrine activity, and where the evidence is not sufficiently convincing to place the substance in Category 1.

Where there is evidence demonstrating that the adverse effects identified are not relevant to humans, the substance should not be considered an endocrine disruptor for human health.	

3.11.2.2 Basis of classification	
Classification is made on the basis of the appropriate criteria, outlined above, and an assessment of the total weight of evidence (see 1.1.1). Classification as an endocrine disruptor for human health is intended to be used for substances which have an intrinsic, specific property to produce an endocrine-related adverse effect. Endocrine-related adverse effects shall have been observed in the absence of other toxic effects, or if occurring together with other toxic effects the endocrine-related adverse effect is considered not to be solely secondary non-specific consequence of the other toxic effects.	Wording adapted from Repro 3.7.2.2.1

3.11.2.3 Weight of evidence	
Classification as an endocrine disruptor for human health is made on the basis of an assessment of the total weight of evidence, see section 1.1.1. This means that all available relevant scientific data (in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro, or, if applicable, in silico studies and data from analogous substances using structure-activity relationship (SAR), informing about endocrine modes of action) are considered together, including peer-reviewed published studies and additional acceptable data.	Wording adapted from Repro 3.7.2.3.1 For further information, please refer to ECHA/EFSA guidance on in silico prediction methods and read-across approaches and categories (page 52-53) “peer-reviewed …” from Carc. 3.6.2.2.1

In applying the weight of evidence determination, the assessment of the scientific evidence shall, in particular, consider all of the following factors: (a) both positive and negative results; (b) the relevance of the study designs, for the assessment of adverse effects and of the endocrine mode of action; (c) the quality and consistency of the data, considering the pattern and coherence of the results within and between studies of a similar design and across different species; (d) the route of exposure, toxicokinetic and metabolism studies; (e) the concept of the limit dose, and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity;	

Using a weight of evidence approach, the link between the adverse effect(s) and the endocrine activity shall be established based on biological plausibility, which shall be determined in the light of current scientific knowledge.	
Evidence used for the classification of a substance as an endocrine disruptor for the environment in section 4.2 should be considered to assess the classification of the substance as endocrine disruptor for human health in the current section 3.11.	

3.11.2.4 [List of evidences that can be used for classification]	This is a placeholder for a future list of evidence that can be used in the weight of evidence to assess the classification. This list will be developed in a second step on the basis of the discussion on the hazard categories.

3.11.2.5 Evidence considered not to support classification for endocrine disruption It is recognised that evidence may be seen in humans, animals and/or in vitro that do not justify classification. Such effects include, but are not limited to: (a) evidence on adversity, endocrine activity or biological plausibility such as i. the available information is sufficient to postulate a non -endocrine MoA where an endocrine MoA can conclusively be excluded; ii. the structural or functional relationship between the KEs is not understood and considered unplausible. (b) substance-induced species-specific mechanisms of toxicity, i.e. demonstrated with reasonable certainty to be not relevant for human health, shall not justify classification.	

3.11.3 Classification criteria for mixtures	Wording from Repro
3.11.3.1 Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture	Wording from Repro
3.11.3.1.1 The mixture shall be classified as an endocrine disruptor for human health when at least one ingredient has been classified as a Category 1 or Category 2 endocrine disruptor for human health and is present at or above the appropriate generic concentration limit as shown in Table 3.11.2 for Category 1 and Category 2, respectively.	Wording adapted from Repro

Table 3.11.2 Generic concentration limits of ingredients of a mixture classified as endocrine disruptor for human health that trigger classification of the mixture			Wording adapted from Repro
Ingredient classified as:	Generic concentration limits triggering classification of a mixture as:		Wording adapted from Carc. This table defines the GCL (Generic Concentration Limit). However SCL (Specific Concentration Limit) could be set on a case-by-case basis.
	Category 1 endocrine disruptor for human health	Category 2 endocrine disruptor for human health	
Category 1 endocrine disruptor for human health	≥ 0.1 %		
Category 2 endocrine disruptor for human health		≥ 1 %	

Note: The concentration limits in Table 3.11.2 apply to solids and liquids (w/w units) as well as gases (v/v units).

3.11.3.2 Classification of mixtures when data are available for the complete mixture	Wording from Repro
3.11.3.2.1 Classification of mixtures will be based on the available test data for the individual ingredients of the mixture using concentration limits for the ingredients classified as endocrine disruptor for human health. On a case-by-case basis, test data on mixtures may be used for classification when demonstrating effects that have not been established from the evaluation based on the individual ingredients. In such cases, the test results for the mixture as a whole must be shown to be conclusive taking into account dose and other factors such as duration, observations, sensitivity and statistical analysis of endocrine disrupting test systems. Adequate documentation supporting the classification shall be retained and made available for review upon request.	Wording adapted from Repro

3.11.3.3 Classification of mixtures when data are not available for the complete mixture: bridging principles	Wording from Repro
3.11.3.3.1 Where the mixture itself has not been tested to determine its endocrine disrupting properties for human health, but there are sufficient data on the individual ingredients and similar tested mixtures (subject to paragraph 3.11.3.2.1) to adequately characterise the hazards of the mixture, these data shall be used in accordance with the applicable bridging rules set out in section 1.1.3.	Wording adapted from Repro

3.11.4 Hazard Communication	Wording from Repro
3.11.4.1 Label elements shall be used in accordance with Table 3.11.3, for substances or mixtures meeting the criteria for classification in this hazard class.	Wording from Repro

Table 3.11.3 Label elements of endocrine disrupting properties for human health	Wording adapted from Repro	
Classification	Category 1	Category 2
Symbol/pictogram		
Signal Word	Danger	Warning
Hazard Statement	EUHXXX: May cause endocrine-related adverse effects on human health	EUHXXX: Suspected of causing endocrine-related adverse effects on human health
Precautionary Statement Prevention	P201 P202 P260 P263 P264 P270 P280	P201 P202 P260 P263 P264 P270 P280
Precautionary Statement Response	P308 + P313	P308 + P313
Precautionary Statement Storage	P405	P405
Precautionary Statement Disposal	P501	P501

Draft criteria for the Environment

Colour explanation:

- YYY: Difference from hazard class for human health

4.2 Endocrine disrupting property for the environment
4.2.1 Definitions and general considerations
4.2.1.1 Endocrine disruptor means a substance or a mixture of substances that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.
4.2.1.2 A substance is considered to be an endocrine disruptor if it meets all of the following criteria : (1) it shows an adverse effect in an intact organism or its progeny; (2) it shows endocrine activity; (3) the substance has an endocrine disrupting mode of action, i.e. there is a biologically plausible link between the endocrine activity and the adverse effect".

4.2.1.3 An adverse effect is defined in this context as a change in morphology, physiology, growth, development, reproduction or lifespan of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences.
3.11.1.4 An endocrine activity is defined as an interaction with the endocrine system that can potentially result in a response of the endocrine system, target organs and tissues. A substance that has an endocrine activity has the potential to alter the function(s) of the endocrine system.
4.2.2 Classification criteria for substances
4.2.2.1 Hazard categories For the purpose of classification for endocrine disrupting properties for the environment, substances are allocated to one of two categories based on strength of evidence and additional considerations in a weight of evidence approach.

Table 4.2.1 Hazard categories for endocrine disruptors for the environment	
Categories	Criteria
CATEGORY 1	Known or presumed endocrine disruptors for the environment A substance is classified in Category 1 for endocrine disrupting properties for the environment if it is known or presumed to meet the criteria defined in 4.2.1.2. The classification in Category 1 is based on evidence from human and/or on data from animal studies. Such data shall provide clear evidence of an adverse effect that is relevant for the (sub-)population level and which is a consequence of the endocrine activity. However, when there is information that raises doubt about the relevance of the effect for the (sub-)population level, classification in Category 2 may be more appropriate.
CATEGORY 2	Suspected endocrine disruptors for the environment A substance is classified in Category 2 for endocrine disrupting properties for the environment when there is some evidence of an adverse effect that is relevant for the (sub-)population level and which is a consequence of the endocrine activity, and where the evidence is not sufficiently convincing to place the substance in Category 1.

~~Where there is evidence demonstrating that the adverse effects identified are not relevant at the (sub)population level for non-target organisms, the substance should not be considered an endocrine disruptor for the environment.~~	This paragraph coming from PPP criteria is not relevant for a horizontal system in CLP.

4.2.2.2 Basis of classification
Classification is made on the basis of the appropriate criteria, outlined above, and an assessment of the total weight of evidence (see 1.1.1). Classification as an endocrine disruptor for the environment is intended to be used for substances which have an intrinsic, specific property to produce an endocrine-related adverse effect. Endocrine-related adverse effects shall have been observed in the absence of other toxic effects, or if occurring together with other toxic effects the endocrine-related adverse effect is considered not to be solely secondary non-specific consequence of the other toxic effects.

4.2.2.3 Weight of evidence
Classification as an endocrine disruptor for the environment is made on the basis of an assessment of the total weight of evidence, see section 1.1.1. This means that all available relevant scientific data (in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro, or, if applicable, in silico studies and data from analogous substances using structure-activity relationship (SAR), informing about endocrine modes of action) is considered together, including peer-reviewed published studies and additional acceptable data.

In applying the weight of evidence determination, the assessment of the scientific evidence shall, in particular, consider all of the following factors:

(a) both positive and negative results;

(b) the relevance of the study design for the assessment of adverse effects and its relevance at the (sub-)population level, and for the assessment of the endocrine mode of action;

(c) the adverse effects on reproduction, growth/development, and other relevant adverse effects which are likely to impact on (sub-)populations. Adequate, reliable and representative field or monitoring data and/or results from population models shall as well be considered where available;

(d) the quality and consistency of the data, considering the pattern and coherence of the results within and between studies of a similar design and across different taxonomic groups;

(e) the route of exposure, toxicokinetic and metabolism studies;

(f) the concept of the limit dose, and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity;

Using a weight of evidence approach, the link between the adverse effect(s) and the endocrine activity shall be established based on biological plausibility, which shall be determined in the light of current scientific knowledge.
Evidence used for the classification of a substance as an endocrine disruptor for human health in section 3.11 should be considered to assess the classification of the substance as endocrine disruptor for the environment in the current section 4.2.

4.2.2.4 [List of evidences that can be used for classification]
4.2.2.5 Evidence considered not to support classification for endocrine disruption It is recognised that evidence may be seen in humans, animals and/or in vitro that do not justify classification. Such effects include, but are not limited to: (a) evidence on adversity, endocrine activity or biological plausibility such as i. the available information is sufficient to postulate a non -endocrine MoA where an endocrine MoA can conclusively be excluded; ii. the structural or functional relationship between the KEs is not understood and considered unplausible. (b) substance-induced species-specific mechanisms of toxicity, i.e. demonstrated with reasonable certainty to be not relevant for human health, shall not justify classification.

4.2.3 Classification criteria for mixtures
4.2.3.1 Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture
4.2.3.1.1 The mixture shall be classified as an endocrine disruptor for the environment when at least one ingredient has been classified as a Category 1 or Category 2 endocrine disruptor for the environment and is present at or above the appropriate generic concentration limit as shown in Table 4.2.2 for Category 1 and Category 2, respectively.

Table 4.2.2 Generic concentration limits of ingredients of a mixture classified as endocrine disruptor for the environment that trigger classification of the mixture		
Ingredient classified as:	Generic concentration limits triggering classification of a mixture as:	
	Category 1 endocrine disruptor for the environment	Category 2 endocrine disruptor for the environment
Category 1 endocrine disruptor for the environment	≥ 0.1 %	
Category 2 endocrine disruptor for the environment		≥ 1 %

Note: The concentration limits in Table 4.2.2 apply to solids and liquids (w/w units) as well as gases (v/v units).

4.2.3.2 Classification of mixtures when data are available for the complete mixture
4.2.3.2.1 Classification of mixtures will be based on the available test data for the individual ingredients of the mixture using concentration limits for the ingredients classified as endocrine disruptor for the environment. On a case-by-case basis, test data on mixtures may be used for classification when demonstrating effects that have not been established from the evaluation based on the individual ingredients. In such cases, the test results for the mixture as a whole must be shown to be conclusive taking into account dose and other factors such as duration, observations, sensitivity and statistical analysis of endocrine disrupting test systems. Adequate documentation supporting the classification shall be retained and made available for review upon request.

4.2.3.3 Classification of mixtures when data are not available for the complete mixture: bridging principles
4.2.3.3.1 Where the mixture itself has not been tested to determine its endocrine disrupting properties for the environment, but there are sufficient data on the individual ingredients and similar tested mixtures (subject to paragraph 4.2.3.2.1) to adequately characterise the hazards of the mixture, these data shall be used in accordance with the applicable bridging rules set out in section 1.1.3.

4.2.4 Hazard Communication		
4.2.4.1 Label elements shall be used in accordance with Table 4.2.3, for substances or mixtures meeting the criteria for classification in this hazard class.		
Table 4.2.3 Label elements of endocrine disrupting properties for the environment		
Classification	Category 1	Category 2
Symbol/pictogram		
Signal Word	Danger	Warning
Hazard Statement	EUHXXX: May cause endocrine-related adverse effects on the environment	EUHXXX: Suspected of causing endocrine-related adverse effects on the environment
Precautionary Statement Prevention	P273	P273
Precautionary Statement Response	P391	P391
Precautionary Statement Storage		
Precautionary Statement Disposal	P501	P501

Thank you

Deadline for comments: 26/04/2021

Slide xx: element concerned, source: e.g. Fotolia.com; Slide xx: element concerned, source: e.g. iStock.com

European Commission