ENDOCRINE SOCIETY
Hormone Science to Health

Endocrine Society response to public consultation on new CLP hazard class for endocrine disruptors

Re: Commission delegated Regulation, incl. Annexes, amending the CLP Regulation

The Endocrine Society appreciates the opportunity to comment on the proposal to amend the regulation on Classification, Labeling, and Packaging (CLP) for hazardous chemicals and mixtures. We enthusiastically support the new hazard classes for endocrine disruptors (EDs), and multiple categories for EDs based on the strength of available evidence. We offer several suggestions to clarify and improve the ability of the regulation to effectively identify hazardous EDs for restriction.

- **Sec. 3.11.1.1, point (a)** – We note a difference between the WHO definition of an endocrine disruptor: "alters the functioning of the endocrine system" and the definition in the proposal which refers to "one or more functions of the endocrine system." This is a critical distinction – a substance that alters thyroxine concentrations alters functioning and would confer adversity, but the definition as written implies that a specific function of the reduced thyroxine concentration such as a threshold of change would need to be identified. The proposal should be changed to align with the WHO definition so that it reads "'endocrine disruptor' means a substance or a mixture that alters the functioning of the endocrine system" and similarly throughout this section. The notion of alteration of the functioning of the endocrine system (i.e., biological or clinical consequences) is covered by the other part of the definition referring to adverse effects.

- **Sec. 3.11.1.1, point (f)** – The notion of biological plausibility is relative to a body of knowledge that can be both empirical and theoretical. When used as a criterion, the establishment of biological plausibility should be extremely permissive given that gaps in knowledge about the mechanisms of chemical interference with endocrine systems may persist as new mechanisms and sensitive endpoints are uncovered. This sentence should be revised to read as: "'biologically plausible link' means an empirically explicable or theoretically possible correlation between one or a series of..." Final text "where …. Existing knowledge" should be deleted.

- **Sec. 3.11.2.1, table 3.11.1, Category 1 –** The final sentence in the criteria for classification, beginning with 'However…' is vague and inconsistent with the intent of the statement in Sec. 3.11.1.2. We expect it serves a similar purpose as point (b) in the criteria for classification in category 2, but the ambiguity presents unnecessary confusion. We strongly recommend that this sentence be deleted.

- **Sec. 3.11.2.1, table 3.11.1, Category 1/2 –** For category 1 point (b) and category 2 point (a), a revision is needed: "an adverse effect in an intact organism or its offspring ~~and~~or future generations."

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- **Sec. 3.11.2.3.1.** – The case of bisphenols illustrates the issue of regrettable substitutions. While data from analogue substances is useful in identifying such substitutions, this point should be expanded by encouraging use of information from read-across and group-based approaches to identifying EDs. We caution that negative data from read-across or SAR should not exclude a substance from Category 1 where there is already evidence of endocrine disruption.

- **Sec. 3.11.3.1.1, table 3.11.2** – Because endocrine disruptors often have non-monotonic dose responses and effects at extremely low concentrations, there may be no safe threshold for use for single substances or mixtures. For category 1 substances we recommend that there be no generic concentration limit of an ED as a component of a mixture.

We commend the Commission's efforts to amend the CLP regulation to better protect human and environmental health from endocrine disruption and are encouraged that the European Union is recognized as the global leader in establishing such measures. These criteria will prove their worth if they are able to effectively identify EDs with appropriate levels of evidence so that action can be taken under REACH and other EU legislation to minimize exposure to these hazardous substances.