Industry Position on Endocrine Disruptors

Industry favours a single category 'scheme' (confirmed endocrine disruptor of regulatory concern). The identification of substances having endocrine disrupting properties must separate substances of high regulatory concern from those that present little/no concern. Substances should only be considered as endocrine disruptors when they produce clear adverse effects in vivo (pathology or functional impairment) unambiguously caused by an endocrine mode of action. We consider a **one category (confirmed endocrine disruptor of regulatory concern)** 'scheme' the most appropriate.

Please note that for the purpose of the Cosmetics regulation only those substances that are relevant for Human Health and deemed confirmed endocrine disrupters are relevant – substances which are endocrines in the environment and/or wildlife are regulated via REACH

Also we could compromise with two sets of criteria – one set to define the confirmed endocrine disrupters (with the possibility to distinguish between high and low potency) and another set of criteria to 'flag' substances for further evaluation but without any regulatory consequences

What needs to be avoided is we end up with 2 categories that are treated in the Cosmetics regulation as CMR (this is what some MS have indicated) because if that would be the case we will lose both categories 1 & 2 substances (at least ingredients that are applied in cosmetics only re. full ban in place 2013).

DG Environment Proposal to identify Endocrine Disruptors

Currently, DG Environment proposes a two categories scheme:
- Category 1 – Proven EDs;
- Category 2 – Suspected EDs;

The proposed categorisation scheme appears to be similar to the CMR classification system, although there are fundamental differences. CMR's are classified on the basis of defined toxicological endpoints, whereas endocrine disruption addresses a mode of action that may or may not produce an adverse effect depending on the dose, potency and part of the endocrine system affected.
In general we recommend that for a substance to be allocated in **category 1**, it should present clear and unequivocal evidence, from epidemiological studies or in wildlife,

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of endocrine-mediated adverse effects or when there is clear evidence of endocrine -mediated effects from high tier whole animal studies.
Furthermore, we recommend that this category should be divided in two subcategories according to the potency of each chemical. Substances that present clear evidence of endocrine disruption and have high potency (present high concern) should be allocated to category 1A. For the purpose of the Cosmetics Regulation this category should follow similar regulatory consequences as CMR's category 1.
On the contrary, if the substance is a confirmed endocrine disruptor but has low potency (poses little or no concern) it should be allocated to category 1B. For the purpose of the Cosmetics Regulation this category should follow similar regulatory consequences as CMR's category 2.

When there is e.g. mechanistic information that raises doubt about the relevance of the effect for humans (e.g. effects on rat thyroid hormones) or animal species living in the environment, the substance should not be allocated to any category.

For **category 2**, and since these are chemicals where the existing data shows insufficient evidence and/or doubtful relevance for humans or environment requiring further testing, they should be called substances under evaluation. Using Endocrine Disruptor in the title might raise unjustified awareness as the chemical poses no clear concern to the public.
We recommend that substances should be placed in **category 2** (Substances under evaluation) when there is some evidence for adverse effects in humans, or wildlife or from in vivo studies, but where the evidence of ED-mediated effects is not sufficiently convincing to place the substance in category 1. If, for example, limitations in the study (or studies) make the quality of evidence less convincing, category 2 may be more appropriate. Such effects should be observed in the absence of other toxic effects, or if occurring together with other toxic effects, the ED-mediated effect should be considered not to be a secondary non-specific consequence of other toxic effects.
Evidence from in vivo studies not specifically indicating ED-mediated adverse effects as well as in vitro/in silico data indicating a potential for endocrine disruption-mediated effects should not be sufficient to place the substance in category 2.

Criteria

It is critical that the criteria of adversity (using an agreed definition), relevance to humans/non target populations, potency, irreversibility and specificity (lead toxicity) will form the basis of any regulatory decision in relation to endocrine disruption. Only careful assessment of the combination of these factors in a weight of evidence approach will lead regulators to scientifically robust decisions.
To increase consumer safety we have to separate substances of high regulatory concern from those that present little/no concern. The potency of a substance is a factor of both the dose level at which adverse effects are caused and the duration required to cause the adverse effects. High regulatory concern is only warranted if the endocrine-mediated adverse effects have been observed at exposure levels of relevance to potential human contact with the endocrine substance. Potency along with other criteria such as severity and irreversibility provide key information that will prioritise substances for further action according to the relevant framework. As a frame of orientation, naturally occurring substances to which a substantial proportion of humans is exposed via food could be used to derive a potency cut-off.
The consequence of classification of weakly potent substances without differentiation according to potency forces replacement by other substances which may not be safer for the consumer for other reasons. Lack of potency criteria may also lead to overregulation, thus diluting the objective of the classification.

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