HEAL response to ANSES proposal to classify resorcinol (1,3-benzenediol) as an endocrine disruptor for human health

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General comments

The Health and Environment Alliance (HEAL) welcomes the opportunity to comment on France's proposal to classify resorcinol as having endocrine disrupting properties for human health (ED HH Cat. 1) and fully supports this initiative.

In June 2020, ECHAs Member States Committee did not reach a consensus on the proposal to identify resorcinol as a Substance of Very High Concern (SVHC) based on endocrine properties for human health (Article 57(f) REACH). Considering the available scientific evidence, HEAL voiced its concerns about this decision at the time [1] and considers it crucial to swiftly reach a favourable decision on the proposed harmonized ED HH Cat. 1 classification for this high-tonnage substance. While the Member States Committee already acknowledged in 2020 that the World Health Organization (WHO) definition of an endocrine disruptor can be met by resorcinol [2], we welcome the current classification initiative based on the updated Regulation (EC) No 1272/2008 (CLP Regulation).

Comments on the proposed classification

The CLH dossier is comprehensive, and the methodology used to report on the scientific evidence available on different classification criteria is very clear and transparent.

- **Endocrine activity**: We are in agreement with the proposal that strong evidence exists for thyroperoxidase (TPO) inhibition by resorcinol. Numerous *in vitro* studies support TPO inhibition in rat, porcine and human systems and subsequent mechanistic effects on thyroxine (T4) and thyroid-stimulating hormone (TSH) were demonstrated *in vivo* in rodents and humans.
- **Adverse effect in an intact organism or its offspring or future generations**: We agree that human case data can be considered as conclusive evidence of hypothyroidy, enlarged thyroid gland, myxoedema and hyperplasia in humans. Additionally, we regard the increased thyroid weight with hyperplasia in some rodent studies but not all, as strong supportive evidence of adverse thyroid-mediated effects. Observed T-sensitive but not diagnostic effects for developmental neurobehavioural changes in rodents (i.e. modified locomotor activity and indications for brain weight) further underline the clear adversity of the reported effects.

- **A biologically plausible link**: We endorse the conclusion on the presence of a biologically plausible link between the endocrine activity and the adverse effects of resorcinol, as both the endocrine activity and the effects were observed in human cases. Furthermore, the reported adverse effects are highly consistent with TPO inhibition (i.e. the reduction in T4, increase in TSH and enlarged thyroid gland), providing further support for the proposed classification. Finally, we agree with the proposal's assessment that due to the observation of adverse effects on the thyroid gland, no additional mechanistic information is required to meet the CLP criteria for endocrine disruption (see also Guidance on the Application of the CLP Criteria part 3, 2024). We see no reason for questioning the relevance of the described adverse effects to humans.

Based on the above, HEAL supports the proposed classification: ED HH 1; EUH380; May cause endocrine disruption in humans.

[1] See for example: https://www.env-health.org/heal-regrets-echa-member-states-committee-failure-to-recognise-endocrine-disrupting-resorcinol-as-a-substance-of-very-high-concern/

[2] https://echa.europa.eu/-/resorcinol-not-identified-as-a-substance-of-very-high-concern