EUROPEAN
COMMISSION

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COMMISSION IMPLEMENTING DECISION

of XXX

on the identification of resorcinol as a substance of very high concern pursuant to Article 57, point (f), of Regulation (EC) No 1907/2006 of the European Parliament and of the Council

(Text with EEA relevance)

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on the identification of resorcinol as a substance of very high concern pursuant to Article 57, point (f), of Regulation (EC) No 1907/2006 of the European Parliament and of the Council

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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 Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC[1], and in particular Article 59(9) thereof,

Whereas:

(1) On 25 February 2020, France submitted to the European Chemicals Agency ('the Agency'), in accordance with Article 59(3) of Regulation (EC) No 1907/2006, a dossier prepared in accordance with Annex XV to that Regulation ('Annex XV dossier') for the identification of resorcinol (EC No 203-585-2, CAS No 108-46-3) as a substance of very high concern in accordance with Article 57, point (f), of that Regulation due to its endocrine disrupting properties, for which there is scientific evidence of probable serious effects to human health, which give rise to an equivalent level of concern to those of other substances listed in Article 57, points (a) to (e), of Regulation (EC) No 1907/2006.

(2) On 12 June 2020, the Member State Committee of the Agency (MSC) adopted its opinion[2] on the Annex XV dossier. While a majority of the MSC members considered that, because of its thyroid disrupting properties causing serious effects to human health, resorcinol should be identified as a substance of very high concern pursuant to Article 57, point (f), of Regulation (EC) No 1907/2006, the MSC did not reach unanimous agreement. Eight members abstained from the vote and three members were of the opinion that there is not sufficient scientific evidence of probable serious effects to human health which give rise to an equivalent level of concern to those of other substances listed in Article 57, points (a) to (e), of Regulation (EC) No 1907/2006. Furthermore, two members that abstained from the vote made statements expressing concerns that in some studies the administration of resorcinol did not lead to adverse effects and that the specific exposure conditions in the human case studies

[1] OJ L 396, 30.12.2006, p. 1.

[2] https://echa.europa.eu/documents/10162/23665416/svhc_msc_opinion_recorcinol_16293_en.pdf/5ff2f41c-409e-7ab8-636e-e74aa17c49f0

impeded a clear conclusion on whether resorcinol gives rise to an equivalent level of concern to those substances listed in Article 57, points (a) to (e).

(3) On 16 July 2020, pursuant to Article 59(9) of Regulation (EC) No 1907/2006, the Agency referred the MSC opinion to the Commission for a decision on the identification of resorcinol as a substance of very high concern on the basis of Article 57, point (f), of that Regulation.

(4) The Commission notes, in line with the majority of the MSC members, that medical case reports provide evidence that the application of ointments containing high concentrations of resorcinol to ulcerated or to undamaged skin over long periods led to hypothyroidism in patients, which was reversible upon cessation of exposure. Although most of these results were based on exposure via ulcerated skin, they are of high relevance for hazard identification in a regulatory context since they provide direct information that resorcinol results in serious adverse effects in humans.

(5) The Commission considers that inconsistent findings in a two-generation reproductive toxicity study as well as the lack of effects seen in reliable animal studies with dermal exposure or with resorcinol administered via gavage, as referred to in the minority opinion, do not invalidate the available evidence on serious effects from other studies. Reliable *in vivo* studies with animals exposed via drinking water resulted in histopathological changes in the thyroid gland and in changes of circulating levels of thyroid hormones and thus provide evidence that resorcinol affects the regulation of the thyroid function inducing hypothyroidism in humans. Results of those studies are consistent with thyroid disruption via the inhibition of thyroperoxidase (TPO), a key enzyme in the synthesis of thyroid hormones. Furthermore, a reliable study with animals exposed sub-cutaneously caused histopathological changes in the thyroid gland. While, as indicated in the minority opinion, the sub-cutaneous exposure route is considered a non-physiological route of exposure, the Commission notes that it is established under Regulation (EC) No 1272/2008 of the European Parliament and of the Council[3] for other toxicological endpoints that information received via a non-physiological route of exposure can be used as supportive evidence for the purpose of hazard identification. Moreover, skin absorption has also been demonstrated *in vitro*. Therefore, the findings provide supportive evidence on the serious adverse effects of resorcinol.

(6) The Commission notes that most MSC members explicitly agreed that data from *in vitro* tests show that resorcinol inhibits TPO. Histopathological changes in the thyroid gland and changes of circulating levels of thyroid hormones observed in humans and in animals support the conclusion that resorcinol acts via an endocrine mode of action affecting the thyroid hormone system by inhibiting TPO.

(7) The Commission concurs with the majority of the MSC members that the biological plausibility between the evidenced thyroid mode of action of resorcinol and the observed adverse effects is strong and that resorcinol fulfils the World Health Organisation/International Programme on Chemical Safety (WHO/IPCS)[4] definition of an endocrine disruptor.

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[3] Regulation (EC) No 1272/2008 of the European Parliament and of the 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).

[4] World Health Organisation/International Programme on Chemical Safety (WHO/IPCS), 2002. Global Assessment of the State-of-the-science of Endocrine Disruptors. WHO/PCS/EDC/02.2, publicly available at http://www.who.int/ipcs/publications/new_issues/endocrine_disruptors/en/

(8) In light of all the above information, the Commission concludes that there is scientific evidence of probable serious effects to human health for resorcinol.

(9) The Commission considers that the adverse effects are of a severity similar to those of other substances, which have been identified as substances of very high concern pursuant to Article 57, point (f), of Regulation (EC) No 1907/2006 due to their endocrine disrupting properties with probable serious effects to human health. Hypothyroidism has clinical implications related to nearly all major organs. Although generally considered reversible, hypothyroidism raises concerns due to the delay of the onset of symptoms and because it may result in severe forms that appear after long-term exposure and that may lead to reduced quality of life.

(10) It is scientifically accepted that TPO inhibition results in decreased thyroid hormone synthesis. That leads to a reduction in circulating concentrations of those hormones, which are essential for normal human brain development, both prenatally and postnatally. Thyroid hormones modulate the expression of genes that are critical for a normal neuroanatomical development, with subsequent effects on neurophysiological and neurological functions. Substances that interfere with the thyroid hormone synthesis have thus the potential to affect neural functions controlled by the hippocampus, which is involved in cognitive, emotional, and memory functions. The fact that resorcinol inhibits TPO raises therefore a serious concern, for potential neurodevelopmental alteration as regards the cognitive, emotional and memory function.

(11) Based on the above information, resorcinol should be identified pursuant to Article 57, point (f), of Regulation (EC) No 1907/2006 as a substance of very high concern due to its endocrine disrupting properties, for which there is scientific evidence of probable serious effects to human health which give rise to an equivalent level of concern to those of other substances listed in that Article, points (a) to (e).

(12) The measures provided for in this Decision are in accordance with the opinion of the Committee established pursuant to Article 133 of Regulation (EC) No 1907/2006,

HAS ADOPTED THIS DECISION:

Article 1

1. Resorcinol is identified as a substance of very high concern pursuant to Article 57, point (f), of Regulation (EC) No 1907/2006 due to its endocrine disrupting properties, with probable serious effects to human health which give rise to an equivalent level of concern to those of other substances listed in Article 57, points (a) to (e), of that Regulation.

2. The substance referred to in paragraph 1 shall be included in the candidate list referred to in Article 59(1) of Regulation (EC) No 1907/2006 with the following indication under ‘Reason for inclusion’: ‘Endocrine disrupting properties (Article 57, point (f) – human health)’.

Article 2

This Decision is addressed to the European Chemicals Agency.

Done at Brussels,

For the Commission
Thierry Breton
Member of the Commission