Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

1-amino-4-hydroxy-2-phenoxyanthraquinone

EC Number: 241-442-6
CAS Number: 17418-58-5

CLH-O-0000007415-74-01/F

Adopted

14 March 2024

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

14 March 2024

CLH-O-0000007415-74-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted on **14 March 20214** by **consensus** an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **1-amino-4-hydroxy-2-phenoxyanthraquinone**

EC Number: **241-442-6**

CAS Number: **17418-58-5**

Rapporteur, appointed by RAC: **Anna Biró**

Administrative information

Sweden has submitted on **26 April 2023** a CLH dossier containing a proposal together with the justification and background information documented in a CLH report.

The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **22 May 2023**.

Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **21 July 2023**.

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The following table provides a summary of the Current Annex VI entry, Dossier submitter proposal, RAC opinion and potential Annex VI entry if agreed by the Commission.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	1-amino-4-hydroxy-2-phenoxyanthraquinone	241-442-6	17418-58-5	Skin Sens. 1A	H317	GHS07 Wng	H317			
RAC opinion	TBD	1-amino-4-hydroxy-2-phenoxyanthraquinone	241-442-6	17418-58-5	Skin Sens. 1A	H317	GHS07 Wng	H317			
Resulting Annex VI entry if agreed by COM	TBD	1-amino-4-hydroxy-2-phenoxyanthraquinone	241-442-6	17418-58-5	Skin Sens. 1A	H317	GHS07 Wng	H317			

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

1-amino-4-hydroxy-2-phenoxyanthraquinone, also known as Disperse Red 60, has no current Annex VI entry. The only endpoint discussed in the CLH dossier is skin sensitisation. The substance is used as a dye: the main uses are for dyeing textiles (especially to dye/print polyester), leather and paper.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of skin sensitisation

Summary of the Dossier Submitter's proposal

The DS proposed to classify 1-amino-4-hydroxy-2-phenoxyanthraquinone (Disperse Red 60) as Skin Sens. 1A; H317 on the basis of a Guinea Pig Maximisation Test performed according to OECD TG 406 (Study report, 2000). The DS did not propose to set an SCL, as a conclusion on extreme potency could not be made from the study available.

Comments received during consultation

Two MSCAs commented, both in support of the proposed classification.

There were 6 comments from Industry, all supporting/not questioning the proposed classification, but pointing out that Disperse Red 60 has been on the market for at least 60 years and despite its broad and long-term use, there is no epidemiological evidence of allergic reactions from exposure to dyed textiles. Industry submitted a Final Report on the Project titled *"Prospective investigation on frequency and spectrum of contact allergy to textile dyes"*. They report a two-year monitoring of cases of allergic contact dermatitis reported to 15 dermatological centres, all members of the German Information Network of Departments of Dermatology. The aim of the study was to ascertain the relevance of dyes used in textiles as cause of allergic contact dermatitis and, if necessary, to clarify the precise identity of any suspected dye. In the course of the 2-year study (2009-2011), there were no reported cases ascribable to the presence of dyes.

Assessment and comparison with the classification criteria

Animal data

There is one Guinea Pig Maximisation Test described in the CLH dossier, performed according to OECD TG 406 (Study report, 2000) with 15 (10 test and 5 negative control) male albino guinea pigs. The test was preceded by a range-finding test using 3 animals to determine the appropriate concentrations for induction and challenge. Intradermal induction in the test group was performed with a 1 % dilution of 1-amino-4-hydroxy-2-phenoxyanthraquinone in PEG 400 and 1 % in an emulsion of Freund's Complete Adjuvant (FCA)/physiological saline. Epidermal induction was conducted at 50 % in PEG 400 for 48 hours under occlusion with following pre-treatment of the test areas with 10 % Sodium-Lauryl-Sulfate (SLS). The animals in the negative control group were intradermally induced with PEG 400 and FCA/physiological saline and epidermally induced with PEG 400 under occlusion following pre-treatment with 10 % SLS. Challenge was performed by epidermal application of the substance at 25 % in PEG 400 and PEG

400 alone under occlusive dressing on the other flank of the animals. Cutaneous reactions were recorded at 24 and 48 hours after removal of the dressing.

In the test group, 10/10 animals showed a positive reaction 24 h and 48 h after treatment with 1-amino-4-hydroxy-2-phenoxyanthraquinone, and 0/10 animals showed a positive reaction at 24 h and 48 h with vehicle treatment. All test animals showed moderate/confluent to intense erythema and swelling after challenge treatment. In the negative control group, 0/5 animals showed a positive reaction 24 h and 48 h after treatment with 1-amino-4-hydroxy-2-phenoxyanthraquinone on the left flank, and 0/5 animals showed a positive reaction 24 h and 48 h after vehicle treatment.

No mortality occurred, and no toxic symptoms were evident in the guinea pigs of the control or test group.

Positive controls were treated with the known sensitizer 2-mercaptobenzothiazole following the same protocol as described above, using 15 animals (10 test and 5 negative control). The study used 5 % 2-mercaptobenzothiazole in mineral oil as well as FCA/physiological saline as intradermal induction dose. The epidermal induction dose was 50 %, and the challenge dose was 10 %, both in mineral oil. All test animals had positive reactions to 2-mercaptobenzothiazole (9/10 animals and 10/10 animals showed a positive reaction at 24 h and 48 h respectively), thereby confirming the validity of the test protocol.

Human data

Only one case study was found reporting a dye factory worker allergic to Disperse Red 60. The case is mentioned in Feinman and Doyle (2008)[1].

Conclusion

In a Guinea Pig Maximisation Test done according to OECD TG 406, Disperse Red 60 at an intradermal induction concentration of 1.0 % (w/v) induced positive skin reaction in 100 % of the animals 24 and 48 hours after challenge.

According to the CLP criteria[2], 1-amino-4-hydroxy-2-phenoxyanthraquinone fulfils the criteria for sub-categorisation into Skin Sens category 1A (≥ 60 % responding at > 0.1 % to ≤ 1 % intradermal induction dose in a GPMT).

Therefore, RAC concludes that **classification as Skin Sens. 1A; H317 (may cause allergic skin reactions)** is warranted (in agreement with the DS proposal).

Further, RAC agrees with the DS that an SCL cannot be set for 1-amino-4-hydroxy-2-phenoxyanthraquinone. In a GPMT the criterion for extreme potency is fulfilled when ≥ 60 % of the animals are sensitised at a ≤ 0.1 % intradermal induction dose. Since the intradermal induction dose used in the GPMT assessed is 1 %, a conclusion on extreme potency cannot be made.

---

1 *E. Feinman Susan and A. Doyle Elizabeth (1988) Sensitization to dyes in textiles and other consumer products, Journal of Toxicology: Cutaneous and Ocular Toxicology, 7:3, 195-222, DOI: 10.3109/15569528809052329*

2 *Regulation EC (No) 1272/2008, Annex I, table 3.4.3*

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).