Committee for Risk Assessment

RAC

Annex 1
Background document
to the 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

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It is based on the official CLH report submitted to consultation and additional information (if applicable).

Adopted

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CLH report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

Chemical name:

1-amino-4-hydroxy-2-phenoxyanthraquinone

EC Number: 241-442-6

CAS Number: 17418-58-5

Index Number: -

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ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON 1-AMINO-4-HYDROXY-2-PHENOXYANTHRAQUINONE

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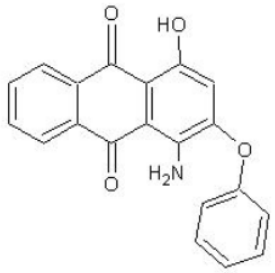
ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON 1-AMINO-4-HYDROXY-2-PHENOXYANTHRAQUINONE

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	1-amino-4-hydroxy-2-phenoxyanthraquinone
Other names (usual name, trade name, abbreviation)	Disperse Red 60 Keyplast Red FB Solvent Red 146
ISO common name (if available and appropriate)	-
EC number (if available and appropriate)	241-442-6
EC name (if available and appropriate)	1-amino-4-hydroxy-2-phenoxyanthraquinone
CAS number (if available)	17418-58-5
Other identity code (if available)	-
Molecular formula	C20H13NO4
Structural formula	
SMILES notation (if available)	NC1=C(OC2=CC=CC=C2)C=C(O)C2=C1C(=O)C1=CC=CC=C1C2=O
Molecular weight or molecular weight range	Ca. 331.3
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	-
Description of the manufacturing process and identity of the source (for UVCB substances only)	-
Degree of purity (%) (if relevant for the entry in Annex VI)	-

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3 (CLP)	Current self-classification and labelling (CLP)
1-amino-4-hydroxy-2-phenoxyanthraquinone	>=80.0 - <100.0 % (w/w)	-	Skin Irrit. 2, H315 Skin Sens. 1, H317 Skin Sens. 1A, H317 Eye Dam. 1, H318 Eye Irrit. 2, H319 Aquatic Chronic 3, H412 Aquatic Chronic 4, H413

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
-	-	-	-	-

Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
-	-	-	-	-	-

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 5:

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATEs	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 submitter's proposal	TBD	1-amino-4-hydroxy-2-phenoxyanthraquinone	241-442-6	17418-58-5	Skin Sens. 1A	H317	GHS07 Wng	H317	-	-	-

Table 6: Reason for not proposing harmonised classification and status under consultation

Hazard class	Reason for no classification	Within the scope of consultation
Explosives	hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)	hazard class not assessed in this dossier	No
Oxidising gases	hazard class not assessed in this dossier	No
Gases under pressure	hazard class not assessed in this dossier	No
Flammable liquids	hazard class not assessed in this dossier	No
Flammable solids	hazard class not assessed in this dossier	No
Self-reactive substances	hazard class not assessed in this dossier	No
Pyrophoric liquids	hazard class not assessed in this dossier	No
Pyrophoric solids	hazard class not assessed in this dossier	No
Self-heating substances	hazard class not assessed in this dossier	No
Substances which in contact with water emit flammable gases	hazard class not assessed in this dossier	No
Oxidising liquids	hazard class not assessed in this dossier	No
Oxidising solids	hazard class not assessed in this dossier	No
Organic peroxides	hazard class not assessed in this dossier	No
Corrosive to metals	hazard class not assessed in this dossier	No
Acute toxicity via oral route	hazard class not assessed in this dossier	No
Acute toxicity via dermal route	hazard class not assessed in this dossier	No
Acute toxicity via inhalation route	hazard class not assessed in this dossier	No
Skin corrosion/irritation	hazard class not assessed in this dossier	No
Serious eye damage/eye irritation	hazard class not assessed in this dossier	No
Respiratory sensitisation	hazard class not assessed in this dossier	No
Skin sensitisation	**harmonised classification proposed;**	**Yes**
Germ cell mutagenicity	hazard class not assessed in this dossier	No
Carcinogenicity	hazard class not assessed in this dossier	No
Reproductive toxicity	hazard class not assessed in this dossier	No
Specific target organ toxicity-single exposure	hazard class not assessed in this dossier	No
Specific target organ toxicity-repeated exposure	hazard class not assessed in this dossier	No
Aspiration hazard	hazard class not assessed in this dossier	No
Hazardous to the aquatic environment	hazard class not assessed in this dossier	No
Hazardous to the ozone layer	hazard class not assessed in this dossier	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

1-amino-4-hydroxy-2-phenoxyanthraquinone has no previous harmonised classification and labelling.

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Justification that action is needed at Community level is required.

Reason for a need for action at Community level:

Differences in self-classification
Requirement for harmonised classification by other legislation or process.

Further detail on need of action at Community level
Only 38% (148/398) of the notifiers in the C&L Inventory have self-classified 1-amino-4-hydroxy-2-phenoxyanthraquinone as a skin sensitiser. 97% (144/148) of these have sub-categorised the substance in category 1A.

1-amino-4-hydroxy-2-phenoxyanthraquinone has professional and consumer uses, including home dyeing. Article service life is also reported, for example for textiles and leather.

In 2021, the Swedish Chemicals Agency published a report on harmful substances in textiles[1]. The aim of the report was to detect and quantify harmful substances in samples of textile available for purchase in Sweden. The amount of substance in textile was used as starting point for risk assessment. 1-amino-4-hydroxy-2-phenoxyanthraquinone was found in 20% of the textile samples of cotton, polyester, and elastane. The risk assessment revealed an increased risk (RCR = 3100) for skin sensitisation from the contact of the textile with skin. Harmonised classification was proposed as a first step to reduce the risk.

Harmonisation of the classification for skin sensitisation will enable 1-amino-4-hydroxy-2-phenoxyanthraquinone to be covered by the proposed scope of the restriction of skin sensitising substances in textile leather, fur and hide[2]. It should be noted that the restriction has not yet been adopted by the European Commission.

5 IDENTIFIED USES

1-amino-4-hydroxy-2-phenoxyanthraquinone is used as a dye. The main uses are for dyeing textiles, leather, and paper. Uses in plastics and rubber are also reported. Article service life is relevant for these uses and for textile and leather dyeing professional and/or consumer uses are also reported.

Further uses are in polymers and ink and toners. Regarding the use in polymers, article service life is registered. Moreover, both professional and consumer uses are reported.

Professional and/or consumer uses are also reported for other areas including coatings and photochemicals.

6 DATA SOURCES

Data for 1-amino-4-hydroxy-2-phenoxyanthraquinone are primarily taken from the publicly disseminated REACH Registration Dossier[3]. In addition, the scientific literature and websites were searched for additional studies addressing skin sensitisation. The searches included literature databases such as Google Scholar and PubMed. For identification of information from grey literature, the OpenGrey database was checked. General searches via Google have also been carried out.

[1] Rapport 4/21: Kartläggning av farliga kemiska ämnen i textil - Kemikalieinspektionen
[2] Registry of restriction intentions until outcome - ECHA (europa.eu)
[3] Registration Dossier - ECHA (europa.eu)

7 PHYSICOCHEMICAL PROPERTIES

Table 7: Summary of physicochemical properties

Property	Value	Reference*	Comment (e.g., measured or estimated)
Physical state at 20°C and 101.3 kPa	Solid	Study report, 2014	Observed
Melting/freezing point	181.9 °C	Study report, 2014	Measured
Boiling point	Study waived	-	-
Relative density	Not possible to define	-	-
Vapour pressure	9.53 × 10^-10, at 25 °C	Study report, 2015	Estimated
Surface tension	Study waived	-	-
Water solubility	<< 0.02 g/l at 20 °C	Study report, 2015	Measured
Partition coefficient n-octanol/water	1.7660 at 20 °C	Study report, 2015	Measured
Flash point	Study waived	-	-
Flammability	Non flammable	Study report, 1999	Measured
Explosive properties	Study waived	-	-
Self-ignition temperature	No information	-	-
Oxidising properties	Study waived	-	-
Granulometry	Mean mass diameter is 21.214 µm.	Study report, 2014	Measured
Stability in organic solvents and identity of relevant degradation products	No information	-	-
Dissociation constant	No information	-	-
Viscosity	No information	-	-

* All references are from the publicly disseminated REACH Registration Dossier

8 EVALUATION OF PHYSICAL HAZARDS

Not evaluated in this CLH proposal.

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

No toxicokinetic studies are available.

10 EVALUATION OF HEALTH HAZARDS

Acute toxicity

10.1 Acute toxicity - oral route

Not evaluated in this CLH proposal.

10.2 Acute toxicity - dermal route

Not evaluated in this CLH proposal.

10.3 Acute toxicity - inhalation route

Not evaluated in this CLH proposal.

10.4 Skin corrosion/irritation

Not evaluated in this CLH proposal.

10.5 Serious eye damage/eye irritation

Not evaluated in this CLH proposal.

10.6 Respiratory sensitisation

Not evaluated in this CLH proposal.

10.7 Skin sensitisation

Table 8: Summary table of animal studies on skin sensitisation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Results	Reference
Guinea Pig Maximization Test According to OECD TG 406 No GLP	Guinea Pig, GOHI, male, 10(test) + 5(negative control)	Disperse Red 60 Positive controls were treated with 2-mercaptobenzothiazole	Test group: Intradermal induction dose: 1% in PEG 400 and FCA/physiological saline Epidermal induction dose: 50% in PEG 400 Topical challenge dose: 25% in PEG 400 Negative control: Intradermal induction: PEG 400 Epidermal induction dose: PEG 400 Topical challenge dose: 25% test substance in PEG	Negative control group: 0/5 animals with positive reactions at 24 h and 48 h after challenge with Disperse Red 60. Test group: 10/10 animals with positive reactions at 24 h and 48 h after treatment with Disperse Red 60. Positive control: 9/10 and 10/10 animals with positive reactions at 24h and 48h after treatment with 2-mercaptobenzothiazole.	Study report, 2000

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Results	Reference
			400 Positive control: Intradermal induction dose: 5% in mineral oil and FCA/physiological saline Epidermal induction dose: 50% in mineral oil Topical challenge dose: 10 % in mineral oil		

Table 9: Summary table of human data on skin sensitisation

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
Report	Disperse Red 60	Not available	Contact allergy to Disperse Red 60 was described in a dye factory worker.	Feinman and Doyle. 2008 Original reference: Cywie et al. Les eczemas allergiques professionels dans l'industrie textile, Rapport No. 244lRI Inst. Nat. Recherche et Securite, France, 1977.

10.7.1 Short summary and overall relevance of the provided information on skin sensitisation

A Guinea Pig Maximisation Test was performed with Disperse Red 60 (1-amino-4-hydroxy-2-phenoxyanthraquinone), according to the OECD Guideline 406 (Study report, 2000). The study was performed with 15 (10 test and 5 negative control) male albino guinea pigs.

The intradermal induction of sensitization in the test group was performed in the nuchal region with a 1 % dilution of 1-amino-4-hydroxy-2-phenoxyanthraquinone in PEG 400 and in an emulsion of Freund's Complete Adjuvant (FCA)/physiological saline. The epidermal induction of sensitization was conducted for 48 hours under occlusion with 1-amino-4-hydroxy-2-phenoxyanthraquinone at 50 % in PEG 400 one week after the intradermal induction and following pre-treatment of the test areas with 10 % Sodium-Lauryl-Sulfate (SLS) approximately 23 hours prior to application of 1-amino-4-hydroxy-2-phenoxyanthraquinone.

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.

Two weeks after epidermal induction the negative control and test animals were challenged by epidermal application of 1-amino-4-hydroxy-2-phenoxyanthraquinone at 25 % in PEG 400 and PEG 400 alone under occlusive dressing. Cutaneous reactions were recorded at 24 and 48 hours after removal of the dressing.

After the challenge, the following reactions were observed:
In the negative control group, 0 out of 5 animals showed a positive reaction 24 h and 48 h after treatment with 1-amino-4-hydroxy-2-phenoxyanthraquinone on the left flank, after 24 h and 48 h. In the same group, 0 out of 5 animals showed a positive reaction 24 h and 48 h after vehicle treatment on the right flank.

In the test group, 10 out of 10 animals showed a positive reaction 24 h and 48 h after treatment with 1-amino-4-hydroxy-2-phenoxyanthraquinone on the left flank, after 24 h and 48 h. In the same group, 0 out of 10 animals showed a positive reaction 24 h and 48 h after vehicle treatment on the right flank.

No mortality occurred. No toxic symptoms were evident in the guinea pigs of the control or negative test group. All test animals showed moderate/confluent to intense erythema and swelling after challenge treatment with 1-amino-4-hydroxy-2-phenoxyanthraquinone.

Positive controls were treated with the known sensitizer 2-mercaptobenzothiazole following the same protocol as described above. 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, thereby confirming the validity of the test protocol.

The GPMT was preceded by a dose range finding test with 3 guinea pigs.

The DS has found one case study of a dye factory worker allergic to Disperse Red 60. The case is mentioned in Feinman and Doyle (2008)[4]. The DS has not been able to get hold of the original report.

10.7.2 Comparison with the CLP criteria

The CLP Regulation allows classification of skin sensitizers in one hazard category, Category 1, which comprises two sub-categories, 1A and 1B. For Category 1, when an adjuvant guinea pig test method is used, a response in at least 30% of the animals is considered positive. This criterion is fulfilled for 1-amino-4-hydroxy-2-phenoxyanthraquinone which has a positive response in 100% of the animals following the use of a 1% intradermal induction dose of 1-amino-4-hydroxy-2-phenoxyanthraquinone (Study report, 2000).

Classification into sub-categories should be performed if data is sufficient (CLP Annex I 3.4.2.2.1.1). Criteria for sub-categorisation into 1A and 1B includes data with the below indicated values (Table 9), according to the CLP Regulation (Table 3.4.3 and 3.4.4).

Table 9. Criteria for sub-category classification of skin sensitizers.

Sub-category	Assay	Response
1A	Buehler assay	≥ 15 % responding at ≤ 0.2 % topical induction dose or ≥ 60 % responding at > 0.2 % to ≤ 20 % topical induction dose
	Guinea Pig Maximization Test	≥ 30 % responding at ≤ 0.1 % intradermal induction dose or ≥ 60 % responding at > 0.1 % to ≤ 1 % intradermal induction dose
1B	Buehler assay	≥ 15 % to < 60 % responding at > 0,2 % to ≤ 20 % topical induction dose or ≥ 15 % responding at > 20 % topical induction dose
	Guinea Pig	≥ 30 % to < 60% responding at > 0.1 % to ≤ 1% intradermal induction dose or

[4] 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

	Maximization Test	≥ 30 % responding at > 1 % intradermal induction dose

According to Table 9, 1-amino-4-hydroxy-2-phenoxyanthraquinone fulfils the criteria for sub-categorisation into 1A (≥ 60 % responding at > 0.1% to ≤ 1% intradermal induction dose in a GPMT).

Specific concentration limits (SCLs) are generally applied for the most potent skin sensitisers classified in 1A ("extreme potency"). In a GPMT the criterion for extreme potency is when ≥ 60 % of the animals responds at a ≤ 0.1% intradermal induction dose (Table 3.7 of the Guidance on the application of the CLP criteria). Since the intradermal induction dose in the study presented herein (1%) is at the higher end of the range for category 1A, with a high number of animals responding positively (100%), a conclusion on extreme potency cannot be made. Hence, a specific concentration limit is not proposed.

10.7.3 Conclusion on classification and labelling for skin sensitisation

Classification of 1-amino-4-hydroxy-2-phenoxyanthraquinone as **Skin Sens. 1A, (H317)** is proposed.

10.8 Germ cell mutagenicity

Not evaluated in this CLH proposal.

10.9 Carcinogenicity

Not evaluated in this CLH proposal.

10.10 Reproductive toxicity

Not evaluated in this CLH proposal.

10.11 Specific target organ toxicity-single exposure

Not evaluated in this CLH proposal.

10.12 Specific target organ toxicity-repeated exposure

Not evaluated in this CLH proposal.

10.13 Aspiration hazard

Not evaluated in this CLH proposal.

11 EVALUATION OF ENVIRONMENTAL HAZARDS

Not evaluated in this CLH proposal.

12 EVALUATION OF ADDITIONAL HAZARDS

Not evaluated in this CLH proposal.

13 ADDITIONAL LABELLING

14 REFERENCES

All references in the CLH-proposal are given as footnotes.

15 ANNEXES

No annexes.