

Committee for Risk Assessment
RAC

Annex 2

Response to comments document (RCOM)
to the Opinion proposing harmonised classification and
labelling at EU level of

**tetrasodium 4-amino-5-hydroxy-3,6-bis[[4-[[2-
(sulphonatooxy)ethyl]sulphonyl]phenyl]
azo]naphthalene-2,7-disulphonate; [1]**

**Reaction products of 4-amino-5-
hydroxynaphthalene-2,7-disulfonic acid, coupled
twice with diazotized 2-[(4-
aminophenyl)sulfonyl]ethyl hydrogen sulfate,
sodium salts; [2]**

**disodium 4-amino-5-hydroxy-3,6-bis{[4-
(vinylsulfonyl)phenyl]diazenyl}naphthalene-2,7-
disulfonate [3]**

EC Number: 241-164-5 [1], - [2], - [3]
CAS Number: 17095-24-8 [1], - [2], 100556-82-9 [3]

CLH-O-0000007139-70-01/F

Adopted
2 June 2022

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON TETRASODIUM 4-AMINO-5-HYDROXY-3,6-BIS[[4-[[2-(SULPHONATOXY)ETHYL]SULFONYL] PHENYL]AZO]NAPHTHALENE-2,7-DISULPHONATE; [1] REACTION PRODUCTS OF 4-AMINO-5-HYDROXYNAPHTHALENE-2,7-DISULFONIC ACID, COUPLED TWICE WITH DIAZOTIZED 2-[(4-AMINOPHENYL)SULFONYL]ETHYL HYDROGEN SULFATE, SODIUM SALTS; [2] DISODIUM 4-AMINO-5-HYDROXY-3,6-BIS{[4-(VINYSULFONYL) PHENYL]DIAZENYL}NAPHTHALENE-2,7-DISULFONATE [3]

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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**Substance name: tetrasodium 4-amino-5-hydroxy-3,6-bis[[4-[[2-(sulphonatooxy)ethyl]sulphonyl] phenyl]azo]naphthalene-2,7-disulphonate; [1] Reaction products of 4-amino-5-hydroxynaphthalene-2,7-disulfonic acid, coupled twice with diazotized 2-[(4-aminophenyl)sulfonyl]ethyl hydrogen sulfate, sodium salts; [2] disodium 4-amino-5-hydroxy-3,6-bis{[4-(vinylsulfonyl) phenyl]diazanyl}naphthalene-2,7-disulfonate [3]
**EC number: 241-164-5 [1] - [2] - [3]
CAS number: 17095-24-8 [1] - [2] 100556-82-9 [3]
Dossier submitter: Germany****

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
14.10.2021	Germany	Huntsman Textile Effects (Germany) GmbH	Company-Importer	1
Comment received				
The classification as proposed by ECHA is slightly different from the one we, as lead registrant, have filed in our dossier. However, we as lead registrant of substance 701-365-5 do support the harmonised classification as proposed.				
Dossier Submitter's Response				
The Dossier Submitter thanks for the comment and appreciates the support of the lead registrant of substance [2] (List no. 701-365-5) to classify the substance as proposed (Resp. Sens. 1A).				
RAC's response				
Noted. Thank you for commenting.				

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RESPIRATORY SENSITISATION

Date	Country	Organisation	Type of Organisation	Comment number
04.11.2021	France		MemberState	2
Comment received				
<p>Volatility is an essential parameter for a substance to reach respiratory tract and possibly induce respiratory sensitisation. However, there is no clear value of vapour pressure for these substances. There is no toxicokinetics data performed by inhalation route to estimate pulmonary absorption.</p> <p>The overall conclusion remains inconclusive for respiratory sensitisation based on in vivo and in vitro experimental studies. However, we agree that there is currently no validated methods for this endpoint. Thus, respiratory sensitisation property is mainly identified from human data. There are consistent results regarding induction of respiratory sensitisation in humans from different occupational studies and case reports, where there is general evidence that RB5 is the causative agent. On this basis, we agree that RB5 should be classified as Resp. Sens.1. Regarding subcategory, there is no clear threshold value for considering "high frequency" of occurrence in humans in CLP guidance. However, taken into account what is considered as high frequency for skin sensitisation, we agree with the proposal as category 1A.</p>				
Dossier Submitter's Response				
<p>The Dossier Submitter thanks the FR CA for the comment and for pointing out that there is a lack of clear values for the vapour pressures or toxicokinetic data via inhalation route on the substances addressed in the CLH proposal. The support of the proposal to classify the substances as Resp. Sens. category 1A is appreciated.</p>				
RAC's response				
<p>Noted. Thank you for commenting.</p> <p>The frequencies of occurrence of respiratory sensitisation were around 1.2-3.3 % among dye powder exposed workers (Docker et al. (1987), Park et al. (1991b), Nilsson et al. (1993)), thus considered as high. In addition, severity of the symptoms reported in the case studies is high taking into account the need for relocation of employees to other workplaces. In addition, the long-term study of Park et al. (2007) demonstrated that in cases with severe occupational asthma, even after long-time avoidance of the causative dyes, there is no recovery in lung function, i.e. effects are irreversible.</p>				

Date	Country	Organisation	Type of Organisation	Comment number
14.10.2021	Germany	Huntsman Textile Effects (Germany) GmbH	Company-Importer	3
Comment received				
<p>We have filed Resp. Sens. 1 rather than Resp. Sens. 1A as proposed in the CLH report. To both classifications H334 is allocated.</p> <p>The main difference is the threshold for classification of mixtures containing this substance. As the formulation containing it are at a level of > 1%, the impact is negligible</p>				

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Dossier Submitter's Response
Thank you very much for clarification. However, classification of the substances as Resp. Sens. 1 subcategory 1A might be relevant for other formulators, which have to verify the classification of their mixtures as respiratory sensitiser (component classified as Resp. Sens. 1, category 1A: GCL \geq 0.1 % for classification of the mixture; category 1/1B: GCL \geq 1.0 % for classification of the mixture).
RAC's response
Noted. Thank you for commenting. Taking into account high severity of symptoms reported in the case studies, GCL \geq 0.1 % for classification of the mixture corresponding to sub-category 1A of Resp. Sensitisation will be more appropriate for this hazard class.

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
04.11.2021	France		MemberState	4
Comment received				
Skin sensitisation: We agree with the proposal Skin Sens. 1 without subcategorization based on the positive LLNA and human data.				
Dossier Submitter's Response				
The Dossier Submitter thanks the FR CA for the comment. The support of the proposal to classify the substances as Skin Sens. 1 (without sub-categorisation) is appreciated.				
RAC's response				
Noted. Thank you for commenting.				

Date	Country	Organisation	Type of Organisation	Comment number
14.10.2021	Germany	Huntsman Textile Effects (Germany) GmbH	Company-Importer	5
Comment received				
Identical to what we have filed in the lead dossier				
Dossier Submitter's Response				
As written in the endpoint summary for sensitisation of the registration dossier, it is agreed between members of the Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers (ETAD) to classify the substance [2] (List no. 701-365-5) as respiratory sensitiser based on literature data on symptoms of respiratory sensitisation in workers after occupational exposure to reactive dyes. The test substance was not sensitising in a guinea pig sensitisation test by the inhalation route, submitted by the registrant (study listed in the CLH proposal). Furthermore, based on comment 1, the lead registrant supports classification of the substance as proposed in the CLH dossier, as Resp. Sens. category 1A.				
RAC's response				
Noted. Thank you for commenting.				