Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

lithium sodium 3-amino-10-{4-(10-amino-6,13-dichloro-4,11-disulfonatobenzo[5,6][1,4]oxazino[2,3-b]phenoxazine-3-ylamino)-6-[methyl(2-sulfonato-ethyl)amino]-1,3,5-triazin-2-ylamino}-6,13-dichlorobenzo[5,6][1,4]oxazino[2,3-b]phenoxazine-4,11-disulfonate; (Direct Blue FC 57087)

EC number: 418-870-9
CAS number: 154212-58-5

CLH-O-0000003528-69-03/F

Adopted

14 March 2014

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ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DIRECT BLUE FC 57087

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in this table as submitted by the webform. Please note that some attachments received may have been copied in the table below. The attachments received have been provided in full to the dossier submitter and RAC.

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Substance name: lithium sodium 3-amino-10-{4-(10-amino-6,13-dichloro-4,11-disulfonatobenzo[5,6][1,4]oxazino[2,3-b]phenoxazine-3-ylamino)-6-[methyl(2-sulfonato-ethyl)amino]-1,3,5-triazin-2-ylamino}-6,13-dichlorobenzo[5,6][1,4]oxazino[2,3-b]phenoxazine-4,11-disulfonate;
Direct Blue FC 57087
EC number: 418-870-9
CAS number: 154212-58-5
Dossier submitter: Germany

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
30.04.2013	France		MemberState	1
Comment received				
We agree with the classification proposal.				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Thank you for your opinion				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
07.05.2013	Belgium		MemberState	2
Comment received				
The Dossier Submitter proposed removal of the current CLH classification for acute toxicity (Acute Tox. 4: H332, H312 and H302) basing on the analytically measured much lower concentration of methanol in the substance (typical concentration of 0.5% w/w) than it was initially used for the classification purposes. This proposal was done when the criteria for classification were based on the directives on dangerous substances and dangerous preparations. At that time, a concentration of 3% in methanol triggered the classification of Direct Blue FC 57087 as harmful Xn; R20/21/22 for acute toxicity. According to the new criteria of the CLP regulation (Article 11), 'Where a substance contains another substance, itself classified as hazardous, whether in the form of an identified impurity, additive or individual constituent, this shall be taken into account for the purposes of classification, if the concentration of the identified impurity, additive or individual constituent is equal to, or greater than, the applicable cut-off value '. The relevant cut-off value for methanol, classified in Acute Tox.3 is 0.1% (see Table 1.1. of CLP Annex I). The conclusion can be drawn that no classification for Acute Tox. 4 is further required basing on the typical methanol concentration of 0.5% w/w. However, we would like to point out that the upper limit of methanol concentration range mentioned in the Dossier (< 1.5% w/w) is still above the generic cut-off value from table 1.1., which would in some cases imply possibility for classification basing on the methanol toxicity. In the view of that we would like to kindly ask the Dossier Submitter for addressing our concern.				

Additionally, results presented by the Dossier Submitter for acute toxicity testing indicate that the Direct Blue FC 57087 has no toxic character according to the CLP criteria (LD50 > 2000 mg/kg bw) what confirms the conclusion of no classification. However, it has to be noted that rat is an insensitive species towards the methanol toxicity due to different effect/mode of action than in humans (LD50 > 5000 mg/kg bw), hence no effects from methanol toxicity at the dose ranges applied in the presented studies are expected. This implies that data provided by the Dossier submitter can be questioned. In order to verify the reliability of it, we would like to ask whether some additional information on other species could be provided by the Dossier Submitter?
Dossier Submitter's Response
During the original substance synthesis process, the first step of the synthesis was done in a methanol/water mixture. In the new synthesis process, the first step is done in water only, therefore the end product does not contain methanol. According to our analytical result of a typical substance batch, the concentration of methanol is < 10 mg/kg. Therefore the new specification of the test substance regarding methanol is upper limit < 0.1%; typical concentration < 0.01%. Concerning the suggestion to provide test result in other species, there are only the skin and eye irritation studies in rabbit available, where neither systemic nor local toxicity was observed. According to the IUCLID 4 file for methanol available in ESIS, the oral LD_{50} values for all tested species (rat, mouse, rabbit, dog) were above 5000 mg/kg. Therefore, no other test result in the oral toxicity testing would be expected using a different species from rats.
RAC's response
Thank you for your comment. Since in the new technical specification of the Direct Blue FC 57087 the upper limit for methanol as an impurity is < 0.1%, Direct Blue FC 57087 should not be classified for acute toxicity by any route on the basis of the presence of methanol as impurity. The oral and dermal LD_{50} in rats for Direct Blue FC 57087 itself are above CLP and DSD classification criteria therefore they do not warrant classification for acute toxicity.

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
07.05.2013	Belgium		Member State	3
Comment received				
The Dossier Submitter proposed removal of the current CLH classification for STOT SE (STOT SE 2: H371). This was supported by findings of Bomhard (1994a,b) in single exposure acute toxicity studies (oral and dermal) on rats, where no target organ toxicity was observed. Similarly to acute toxicity studies, no effects from methanol toxicity on rat are expected at the dose ranges applied in the presented studies due to its insensitivity towards methanol, therefore the reliability of information provided can be questioned. In order to verify that, studies on other species could be presented by the Dossier Submitter.				
Dossier Submitter's Response				
see comment 2				
RAC's response				
Thank you for the comment. Since in the new technical specification of the Direct Blue FC 57087 the upper limit for methanol as impurity is < 0.1%, Direct Blue FC 57087 should not be classified for Specific Target Organ Toxicity- Single Exposure by any route on the basis of the presence of methanol as impurity. No new studies of acute toxicity of Direct Blue are justified.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
07.05.2013	Belgium		Member State	4
Comment received				
No classification as STOT RE is proposed by the Dossier Submitter, as no target organ toxicity was observed in the repeated dose toxicity rat study of Jekat and Sander (1995). Similarly to our remarks in other sections, we would like to underline that at the tested concentration levels no effects related to methanol toxicity in rats are expected, due to well-known species insensitivity. Hence, in order to verify the reliability of provided data, results from studies on other species could be presented.				
Dossier Submitter's Response				
In the new synthesis process, the first step is done in water only, therefore the end product does not contain methanol. According to our analytical result of a typical substance batch, the concentration of methanol is < 10 mg/kg. Therefore the new specification of the test substance regarding methanol is upper limit < 0.1%; typical concentration < 0.01%. Therefore, the content of 1.2% methanol in the original test substance has no relevance for the newly produced batches.				
RAC's response				
The classification into class of STOT RE was not proposed by the Dossier Submitter therefore RAC does not provide comments on this issue.				