**Committee for Risk Assessment**

**RAC**

Annex 2

**Response to comments document (RCOM)**

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

# dichlofluanid (ISO); N-[(Dichlorofluoromethyl)thio]-N',N'-dimethyl-N-phenylsulfamide

**EC Number: 214-118-7**
**CAS Number: 1085-98-9**

**Adopted**
**3 June 2015**

CLH-O-0000001412-86-57/F

**ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON DICHLOFLUANID (ISO); N-[(DICHLOROFLUOROMETHYL)THIO]-N',N'-DIMETHYL-N-PHENYLSULFAMIDE**

**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: dichlofluanid (ISO); N-[(Dichlorofluoromethyl)thio]-N',N'-dimethyl-N-phenylsulfamide**
**CAS number: 1085-98-9**
**EC number: 214-118-7**
**Dossier submitter: United Kingdom**

**GENERAL COMMENTS**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 11.12.2014 | France | | MemberState | 1 |
| Comment received | | | | |
| MS-FR agrees with the classification proposed for Human Health Hazard.<br>Environmental hazards are not reported in this CLH report. However environmental data are available in the biocide Competent Authority Report (March 2007). According to these data, MS-FR agrees that dichlofluanid can be considered as rapidly degradable (DT50 for hydrolysis below 2 days, and the degradation product does not fulfill the criteria for classification as hazardous to the aquatic environment). However, in the biocide dossier, chronic data lead to a classification Aquatic chronic 1 (M-factor = 1) with a NOEC = 2.65 µg/L for daphnia. Therefore, the classification for the environment should be revised.<br><br>*ECHA comment: See ECHA comment in box #2.* | | | | |
| Dossier Submitter's Response | | | | |
| Thank you, we have noted your comments and will consider this further. However, the current CLH report does not contain a proposal for environmental classification and can not be addressed in the context of this current proposal. | | | | |
| RAC's response | | | | |
| RAC shares the view of ECHA - see ECHA comment under Comment no 2. | | | | |

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 12.12.2014 | Germany | | MemberState | 2 |
| Comment received | | | | |
| The German CA recommends a modifiction of the classification of Diclofluanide as compared to the CLH dossier by the UK CA.<br>The following aspects were observed:<br><br>- The substance may require additional classification for STOT RE. A discussion of the repeated dose toxicity studies should therefore be added.<br><br>- The current CLH dossier does not address the environmental hazard classification of dichlofluanid and no change of the current Annex VI entry of "Aquatic Acute 1, H400" with an M-factor of 10 is proposed. | | | | |

However, available acute data suggest the need to update the acute M-factor from 10 to 100. Additionally, available chronic data suggest the addition of classification as Aquatic chronic 1 (H410) with the chronic M-factor of 1.

*ECHA comment: Neither STOT RE nor environmental hazard classification were considered in the CLH report and hence those hazard classes were not opened for comments during public consultation and cannot be changed in the context of this CLH proposal. In order to address the classification of dichlofluanid for those hazard classes, a new CLH proposal including relevant information would need to be submitted.*

Dossier Submitter's Response

Thank you for your comments, we will consider these further. However, the current CLH report does not contain a proposal for STOT-RE or environmental classification and can not be updated at this stage. It should also be noted that classification for repeat dose effects has been considered by the EU experts previously and no new data are available.

RAC's response

RAC shares the view of ECHA.

**OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 12.12.2014 | Germany | | MemberState | 3 |

Comment received

Classification in Category 1 should be retained rather than sub-classification in Category 1B.

Justification: As noted by the dossier submitter classification in Category 1A could not be excluded as doses below 1% were not tested in the GPMT. In addition, the Human Information as presented in chapter 4.6.1.2 of the CLH report did not include the case report by Hansson C &, Wallengren (1995) Allergic contact dermatitis from dichlofluanid. Contact Dermatitis 32(2): 116-117. In contrast to the study described in the CLH report, Hansson & Wallengreen reported a strong reaction (+++) to 0.1%, a moderate reaction (++) to 0.01% and no reaction (-) to 0.01 % dichlofluanid in patch testing of a patient. In addition, Björkner et al. reported on 13 patients that became sensitised by dichlofluanid (Biörkner B, Bruze M and Gruvberger B (1990) Sensitization to dichlofluanide. Contact Dermatitis 23(4): 246). This study was apparently also not cited in the CLH report. Hence, there is evidence for sensitisation in human, while the information provided in the reports is not sufficient for subcategorisation.
According to Section 3.4.2.2.1.2. of the Guidance on the Application of the CLP criteria (version 4.0): "Classification into sub-categories is only allowed if data are sufficient. Therefore care should be taken when classifying substances into category 1B when category 1A cannot be excluded. In such cases classification into category 1 should be considered. This is particularly important if only data are available from certain tests showing a high response after exposure to a high concentration but where lower concentrations which could show the presence of such effects at lower doses are … When considering human evidence, it is necessary to take into account the size of the population exposed and the extent of exposure and frequency, and thus the consideration is on a case by case basis..."

Dossier Submitter's Response

Thank you for your comments and additional information. As stated in the report, it could be that classification in Category 1A cannot be excluded and a simple argument for retaining Category 1 could also be made. Full rationale are provided in the CLH report.

| RAC's response |
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| RAC is of the view that the data provided in the CLH report is insufficient for subcategorisation and that the current classification (Skin Sens. 1) should be retained.<br><br>The case reports published in the open literature are considered in the RAC Opinion. RAC agrees with the CA that the information provided in these reports is not sufficient for subcategorisation. |

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 12.12.2014 | Finland | | MemberState | 4 |
| Comment received | | | | |
| The Finnish CA does not agree with the proposed classification of Dichlofluanid as Skin Sens. 1B; H317 according to Regulation (EC) No 1272/2008 (CLP).<br><br>In the guinea pig study, which was considered comparable to OECD TG 406, 87 % of animals gave positive response when tested with 10 % induction dose. Although the result meets the criteria for sub-category 1B, it remains unknown whether lower concentration of the substance would give positive result which would meet the criteria for sub-category 1A. We also noticed that the description, purity and stability of the test substance and the use of Freund´s complete adjuvant were not documented at all and positive control was not included in the study. In addition, according to OECD TG 406 the induction dose should be the highest causing mild-to-moderate skin irritation. However, no skin irritation reactions observed during the induction phase were documented. It´s also stated in the report that the 25 % concentration was determined to be the maximum non-irritant concentration. Thus it´s unclear whether the 10 % induction dose caused even mild skin irritation.<br><br>In conclusion, the Finnish CA does not agree with the proposed classification in sub-category 1B because the sub-category 1A cannot be excluded. Therefore retaining classification Skin Sens. 1; H317 is proposed. | | | | |
| Dossier Submitter's Response | | | | |
| Thank you for your comments. The GPMT was conducted prior to guideline but the method is considered to be comparable to the OECD 406. However, it is the case that information on purity was not available and positive controls were not included. As stated in the CLH report, it could be that classification in Category 1A cannot be excluded and a simple argument for retaining Category 1 could also be made. Full information is provided in the CLH report. | | | | |
| RAC's response | | | | |
| RAC is of the view that the data provided in the CLH report is insufficient for subcategorisation and that the current classification as Skin Sens. 1 should be retained. | | | | |

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 21.11.2014 | Sweden | | MemberState | 5 |
| Comment received | | | | |
| In the Guinea Pig study by Bomhard et al. (1980) 87% of the animals were sensitized at an i.d. test concentration of 10%. From this result it is not possible to conclude on a 1A or 1B classification as the degree of sensitization at lower i.d. concentrations is unknown. In such cases Cat. 1 should be the default classification (see Guidance on the application of the CLP criteria, as pointed out in the proposal). Therefore, the classification in Skin Sens Cat. 1 should be retained. | | | | |

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| It could be noted that the non-guideline test by Bomhard and Loeser (1980a) gives an indication that dichlofluanide could be a Cat. 1A sensitizer as i.d. injections of 0.1% sensitized 100% of the animals. |
| Dossier Submitter's Response |
| Thank you for your comments. As stated in the report, it could be that classification in Category 1A cannot be excluded and a simple argument for retaining Category 1 could also be made. Full rationale are provided in the CLH report. |
| RAC's response |
| RAC is of the view that the data provided in the CLH report is insufficient for subcategorisation and that the current classification as Skin Sens. 1 should be retained. |

**OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 12.12.2014 | Germany | | MemberState | 6 |
| Comment received | | | | |
| According to the submitted data package, namely DocIIA Chapter 3.5, classification for STOT RE2 may be required.<br><br>Justification: In the oral 90day study in dogs, increased BUN (m+f), ALT (f), creatinine (f); focal periportal vacuolization, necrosis, pigmentation and inflammation was reported at 34 mg/kg bw/d.<br>Findings in dogs are confirmed by a 1 year study with the following effects: At 12.5 mg/kg and above: changes in body weight gain, food consumption, clinical chemistry parameters (liver enzymes, cholesterol, urea nitrogen and creatinine increased) occurred.<br>Histopathological changes at 12.5 mg/kg and above: chronic nephropathy and thyroid follicular cell degeneration. At 37 mg/kg decreased T3, T4 levels. In males at 37.5 mg/kg: decreased thyroid and testicular weights and anaemia. Histopathological changes at 37.5 mg/kg, liver changes, hyperplasia of the pituitary gland's basophils, testicular degeneration and thymic atrophy.<br>An oral 90 day study in rats was not reported in DocIIA Chapter 3.5, but the following relevant effects were reported in the 2-yr studies:<br>At 9.4 mg/kg bw/d and above: changes characteristic of fluorosis (i.e., whitish and hardened cranium, increase of osteosclerosis, increase of fluoride in teeth and bones).<br><br>*ECHA comment: See ECHA comment in box #2.* | | | | |
| Dossier Submitter's Response | | | | |
| Thank you for your comments. However, as noted above, classification for STOT-RE is not considered in this report and therefore cannot be addressed in the context of this proposal. Further, classification for repeat dose effects has previously been considered within the EU. | | | | |
| RAC's response | | | | |
| RAC shares the view of ECHA - see ECHA comment under Comment no 2. | | | | |

**OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| 12.12.2014 | Germany | | MemberState | 7 |
| Comment received | | | | |
| For dichlofluanid the need to reassess the actuality of the environmental hazard classification is triggered by the introduction of new criteria for the long-term aquatic hazard classification with the 2nd ATP in 2011.<br>In view of product authorisations (e.g. mutual recognition of biocidal products containing dichlofluanid within European member states) it is important to have a harmonised Annex VI entry (inclusive appropriate M-factors) which should reflect the latest scientific results. Therefore we strongly recommend to amend the environmental classification and labelling in the dossier.<br>In the CLH report, p.24 chapter 5.6 a conclusion on classification and labeling for environmental hazards is provided:<br>The current Annex VI entry for classification of dichlofluanid for environmental hazards is "Aquatic Acute 1; H400" with an M-factor of 10.<br>There is no change of this classification proposed by the dossier submitter.<br>However, the lowest acute effect value for fish (Oncorhynchus mykiss) is LC50 (4 days) of 0.01 mg/L (nominal).<br>Therefore an acute M-factor of 100 should be applied.<br>In addition, also the available long-term effect values for aquatic organisms should be considered for a revised classification.<br>The lowest available long-term effect value is the NOEC (21 days) of 0.0064 mg/L (nominal) obtained for fish (Oncorhynchus mykiss) and NOEC of 0.00265 mg/L (nominal) obtained for invertebrates (Daphnia magna).<br>As these values are between the trigger value of 0.01 mg/L and 0.001 mg/L for rapidly degradable substances, classification as "Aquatic Chronic 1; H410" with the chronic M-factor of 1 is necessary.<br><br>*ECHA comment: See ECHA comment in box #2.* | | | | |
| Dossier Submitter's Response | | | | |
| Thank you for your comments, we will consider these further. However, the current CLH report does not contain a classification for the environment and cannot be addressed in the context of this proposal. | | | | |
| RAC's response | | | | |
| RAC shares the view of ECHA - see ECHA comment under Comment no 2. | | | | |