# Committee for Risk Assessment

# RAC

Annex 2

## Response to comments document (RCOM)

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

# Indoxacarb and Indoxacarb (enantiomeric reaction mass S:R 75:25)

ECHA/RAC/CLH-O-0000001735-72-01/A2

**Adopted**

**1 June 2011**

**COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION**

***[ECHA has compiled the comments received via internet that refer to several hazard classes and entered them under each of the relevant categories/headings as comprehensive as possible. Please note that some of the comments might occur under several headings when splitting the given information is not reasonable.]***

**Substance name: Indoxacarb and Indoxacarb (enantiomeric reaction mass S:R 75:25)**
**CAS number: 173584-44-6**
**EC number: -**

**General comments**

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
|---|---|---|---|---|
| 05/10/2010 | Denmark / DuPont Danmark ApS / Company-Manufacturer | Background and proposal.<br>page 5, 3rd. paragraph, lines 8-9, kindly replace<br>"may be used for product formulations in the future" with "is now used for product formulations"<br>Justification: A pesticide formulation based on the single enantiomer technical is now approved in Italy and Hungary. Applications have been made in several other EU Member States. | Thank you for the information. We have made the proposed replacement. | Noted. |
| 08/10/2010 | Germany / Member State | All references that are cited in section 5 Human health hazard assessment are not further mentioned in the literature list of the report. | As is stated in the introduction of section 5, all references to individual studies should be seen as references to the CAR and DAR and its addenda. | Noted. |
| 08/10/2010 | Spain / Member State | In general terms, Spain supports the UK proposal | Thank you for the support | Noted |
| 08/10/2010 | Sweden / Member State | SE supports classification of Indoxacarb (Cas No 173584-44-6) and Indoxacarb (enantiomeric reaction mass S:R 75:25) as specified in the proposal. SE agrees with the rationale for classification into the proposed hazard classes and differentiations. | Thank you for the support | Noted |
| 11/10/2010 | Norway / Climate and Pollution Agency / National Authority | Indoxcarb (enantiomeric reaction mass S:R 75:25) has recently been evaluated by the Norwegian Scientific Committee on Food Safety and approved as plant protection product by the Norwegian Food Safety | Thank you for the support | Noted |

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| | | Authority with the following classification according to directive 67/548/EC:<br>Xn; Harmful<br>N; Dangerous for the environment<br>R20/22 Harmful by inhalation and if swallowed.<br>R43 May cause sensitization by skin contact.<br>R48 Harmful: danger of serious damage to health by prolonged exposure if swallowed.<br>R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.<br><br>This classification is in accordance with the proposal for harmonised classification and labelling of indoxacarb (enantiomeric reaction mass S:R 75:25) and is based on the assessment of the same studies evaluated by the EU rapporteur member states (UK/NL). | | |
| 11/10/2010 | Portugal / Portuguese Environment Agency / National Authority | Considering the present proposal, we agree to establish a harmonised classification & labelling for Indoxacarb and Indoxacarb (enantiomeric reaction mass S:R 75:25).<br>The proposed environmental classification fulfills the criteria established both in CLP Regulation and Directive 67/548/EEC. However the proposed environment labeling doesn't include the N symbol, according to Directive 67/548/EEC. We therefore propose to update it accordingly. | Thank you, this appears to have been an error and we will update the dossier as suggested. | noted |

**Carcinogenicity**

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
|---|---|---|---|---|
| 05/10/2010 | Denmark / DuPont Danmark ApS / Company-Manufacturer | None | - | - |
| 08/10/2010 | Germany / Member | Page 44-45: Proposal for non-classification of Indoxacarb (DPX- | Thank you for the support | noted |

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| | State | MP062; enantiomeric reaction mass S:R 75:25) and Indoxacarb (DPX-KN 128; S-enantiomer) is supported. | | |

**Mutagenicity**

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
|---|---|---|---|---|
| 05/10/2010 | Denmark / DuPont Danmark ApS / Company-Manufacturer | None | - | - |
| 08/10/2010 | Germany / Member State | Page 43: Proposal for non-classification of Indoxacarb (DPX-MP062; enantiomeric reaction mass S:R 75:25) and Indoxacarb (DPX-KN 128; S-enantiomer) is supported. | Thank you for the support | noted |

**Toxicity to reproduction**

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
|---|---|---|---|---|
| 05/10/2010 | Denmark / DuPont Danmark ApS / Company-Manufacturer | None | - | - |
| 08/10/2010 | Germany / Member State | Page 47-48: Proposal for non-classification of Indoxacarb (DPX-MP062; enantiomeric reaction mass S:R 75:25) and Indoxacarb (DPX-KN 128; S-enantiomer) is supported. | Thank you for the support | noted |

**Respiratory sensitisation**

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
|---|---|---|---|---|
| 05/10/2010 | Denmark / DuPont Danmark ApS / | None | - | - |

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| | Company-Manufacturer | | | |

**Other hazards and endpoints**

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| 05/10/2010 | France / Elodie Pasquier / Member State | Physical hazards<br><br>FR agrees with UK/NL on the absence of classification for physical hazards of Indoxacarb according to the Dir. 67/548/CEE and the CLP criteria.<br><br>It is however noted that the IUPAC names noted in section 1.1 are not correct. To our information, the following names apply:<br>- Indoxacarb (S enantiomer ): methyl (S)-7-chloro-2,3,4a,5-tetrahydro-2-[methoxycarbonyl(4-trifluoromethoxyphenyl)carbamoyl]indeno[1,2-e][1,3,4]oxadiazine-4a-carboxylate<br>- Enantiomeric reaction mass S:R 75 :25 : methyl (S,R)-7-chloro-2,3,4a,5-tetrahydro-2-[methoxycarbonyl(4-trifluoromethoxyphenyl)carbamoyl]indeno[1,2-e][1,3,4]oxadiazine-4a-carboxylate<br><br>Health hazards<br><br>FR agrees with UK/NL on the Indoxacarb classification for health hazards according to the Dir. 67/548/CEE and the CLP criteria.<br><br>Environmental hazards<br><br>FR agrees with UK/NL on the Indoxacarb classification for environmental hazards according to the Dir. 67/548/CEE and the CLP criteria. | <br><br>Thank you for the support<br><br><br><br>Thank you for your comments. However, the IUPAC name included in the report was agreed with the ECHA substance identification team prior to submission of the dossier.<br><br><br><br><br><br>Thank you for the support<br><br><br><br>The test referred to was conducted according to OECD 219 (spiked water). | <br><br><br><br><br><br><br><br><br><br><br><br>Noted<br><br><br><br>Noted |

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| | | In section 7.1.1.4, of the CLH report it is however noted that the study on Chironomus riparius (midge larvae) conducted with Indoxacarb (enantiomeric reaction mass 75:25 S:R) was considered not valid in the proposal for harmonised classification. It is written that the study was not supported by analytical measurements to demonstrate the maintenance of the test concentrations of Indoxacarb (enantiomeric reaction mass 75:25 S:R).<br>However in the summary of the study reported in the DAR addendum_3_vol_3_B8_B9 (Janvier 2005) prepared by the Netherlands, analytic concentrations were provided that show the maintenance of the test concentrations of Indoxacarb: Analysis of the dose solutions in the aqueous phase showed that the applied doses were 99-109% of nominal. Therefore the results were considered valid and based on the nominal applied doses.<br><br>Reference of the study:<br>(Radford, K. (2001), DPX-MP062 : To Assess The Toxicity To The Sediment Dwelling Phase of the Midge Chironomus Riparius, Huntingdon Life Sciences Ltd, Woolley Road, Alconbury. Huntingdon, Cambridgeshire, UK, Report No. DuPont-4055, 05 December 2000) | For the biocides CAR, the CA did not use the result as concentrations in the sediment were not sufficiently characterised.<br><br>The measured water values noted by the French CA in the DAR refer to analysis made at the start of the test. The point being that 99-109% refers to the range of initial measured concentrations in comparison to the nominal values. The nature of the 219 test means that it was conducted under static conditions. During the study, measured water concentrations declined significantly. Specifically the concentration of indoxacarb in the overlying water decreased from 26-48% on day 0 to 13-23% on day 28. Results of all chemical analyses were based on total radioactivity measurements expressed as concentrations of the active ingredient.<br><br>The CLP dossier was | |

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| | | | originally based on the CAR. We will amend the dossier to include more details of the first sediment test.<br><br>The decline in water concentration, and possible partitioning to sediment, mean that it is difficult to be confident about the substance exposure the organisms received during the test. For this reason while the study provides useful supporting information, we do not think it should be used for classification. | |
| 05/10/2010 | Denmark / DuPont Danmark ApS / Company-Manufacturer | None | - | - |
| 08/10/2010 | Germany / Member State | Proposed labelling (according to Directive 67/548/EEC):<br>Concerning the S-phrases the German CA likes to comment as follows:<br>Indoxacarb (pure S enantiomer) is a toxic substance so we think that S45 is obligatory and should replace S46. In the same context S1/2 is more appropriate (obligatory) than S2 alone. Furthermore we recommend S36/37 instead of S24 and S37 because of R48/22.<br><br>Skin Sensitisation:<br>The German CA agrees with the proposed classification Xi; R43 and Skin Sens 1 – H317 for both Indoxacarb (pure S enantiomer) and Indoxacarb (enantiomeric reaction mass 75:25 S:R). Read-across to | We agree that for the S enantiomer, S1/2 instead of S2 and S45 instead of S46 is more appropriate. The replacements will be made in the CLH dossier. We do not agree with the replacement of S24 and S37 with S36/37. First of all, S24 and S37 are obligatory for substances to which R43 has been ascribed, while R36 is only obligatory | Noted |

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| | | Indoxacarb (pure S enantiomer) from the study with Indoxacarb (enantiomeric reaction mass 75:25 S:R) is accepted. | for very toxic substances or substances to which R21 or R24 has been ascribed, which is not the case.<br><br>Thank you for the support for the classification for skin sensitisation | |
| | | However, we question whether the alert "formaldehyde donor" from SAR analyses with DEREK is relevant as possible explanation for the skin sensitisation potential of Indoxacarb (enantiomeric reaction mass 75:25 S:R). Firstly, there is no evidence from toxicokinetic studies that formaldehyde is formed during metabolism (see chapter 5.1). Secondly, there is no evidence from in vitro genotoxicity studies that Indoxacarb (pure S enantiomer or enantiomeric reaction mass 75:25 S:R) or its metabolites are genotoxic (see chapter 5.7.1). In the presence of formaldehyde, however, this would be expected. | We agree that the alert "formaldehyde donor" from SAR analyses with DEREK is probably not relevant, since there is no evidence that formaldehyde is indeed formed. We will add this to the CLH dossier | Noted |
| | | Although it is currently not required within the scope of the classification of sensitisers, we propose to mention that the classification into potency categories according to the Guidance on the Application of the CLP-criteria has also been considered. | Test animals were induced with intradermal injections of 5% Indoxacarb, resulting in 35% of the guinea pigs sensitized. Thus, indoxacarb is a moderate skin sensitiser. This will be added to the CLH dossier. | Agreed |
| | | Acute Toxicity:<br>The German CA agrees with the proposed classification for Indoxacarb (pure S enantiomer) that is<br>T;R25 / Xn; R20 and Acute Tox 3 - H301 / Acute Tox 4 – H332, respectively.<br>We also agree with the proposed classification for Indoxacarb (enantiomeric reaction mass 75:25 S:R) that is Xn;R20/22 and Acute Tox 3 - H301 / Acute Tox 4 – H332 respectively.<br>The data are consistent with the toxicokinetics of the test substances. | Acute toxicity:<br>Thank you for the support<br><br>In the Sarver (1996b) study, | Noted |

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| | | Occasional read-across approach for classifying both substances is accepted.<br><br>Which species was used in the acute toxicity study with IN-JT333 by SARVER (1996b)?<br><br>Specific target organ toxicity – Single exposure:<br>The German CA agrees with the proposed non-classification.<br>However, it should be taken into consideration that the rat might not be the most sensitive mammalian species for studying neurotoxic effects induced by Indoxacarb (pure S enantiomer or enantiomeric reaction mass 75:25 S:R).<br>Considering the subchronic and chronic toxicity studies presented in the CLH-report (see chapter 5.6.1 table 5.6), it seems likely that mice express signs of neurotoxicity while rats already suffer death at comparable concentrations. Therefore this might indicate that mice are more appropriate for neurotoxicity studies than rats due to their lower sensitivity towards mortality.<br><br>Repeated dose toxicity:<br>The German CA agrees with the proposed classification Xn; R48/22 and STOT RE 1 – H372 for both Indoxacarb (pure S enantiomer) and Indoxacarb (enantiomeric reaction mass 75:25 S:R).<br><br>Classification is justified by substance-related deaths whereas reduced body weight (gain), altered haematologic parameters or microscopic findings (e.g. haemosiderosis, hyperplasia of spleen/bone marrow) are not considered severe enough for classification. In this context, we would appreciate a short notice that the relevant guidance has been taken into account (e.g. Guidance on the Application of Regulation (EC) 1272/2008 chapter 3.9.2.5.2 Hematotoxicity; Muller et al. (2006): Hazard classification of chemicals inducing haemolytic anaemia: An EU regulatory perspective, Regul Toxicol Pharmacol 45 | CD (SD)BR rats were used. We have added this to the CLH report.<br><br>STOT-SE: In repeated dose studies with Indoxacarb, neurotoxicity was observed in mice only at high doses which are not relevant for classification. Acute studies with mice (which are not available) would therefore probably not alter the classification for STOT-SE.<br><br>Repeated dose toxicity:<br>Thank you for the support<br><br>We have used the proposed reference by Muller et al., which is already mentioned in 5.6.5 (Summary & Discussion).<br><br>Additional data on temporal | Issue was addressed in summary and discussion on STOT-SE (BD).<br><br>Noted |

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| | | (2006) 229–241).<br><br>It might be useful for an unequivocal classification within the scope of R48/STOT RE, respectively, to give specific details about the temporal occurrence of mortality in the course of each (sub)chronic toxicity study. Taking into account gender specific properties (female individuals are prone to retain more metabolites in tissues than male individuals and they produce more of the metabolite IN-JT333 compared to males), it might be conceivable that already after few dose repetitions with the parent substance a lethal concentration of the highly acute toxic metabolite IN-JT333 is established in the organism and thus causative for death. So please assure that mortality in the repeated dose studies did not occur within the first study days and can thus be excluded as an acute toxic effect.<br><br>As supportive study for classification "R48/STOT RE", we think that the 90-day-study in rats by Malley (1997) is more convincing than the 28-day-study in mice by Reynolds (1993b) in terms of species sensitivity, study duration, mortality rate, and substance concentration causing death. | occurrence have been provided, where available. These data show that mortality did not occur within the first few days. The earliest mortalities were observed in the 28 day study in mice (Reynolds, 1993b), in which mice in the highest dose groups were sacrificed in extremis after 7 days.<br><br>We agree. Therefore, we have based our conclusion on the 90 day study by Malley (1997), supported by the data from the 28 day study by Reynolds (1993b). | |
| 08/10/2010 | Spain / Member State | p. 28 Summary and discussion of acute toxicity | | |

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| | | Acute oral<br>The Spanish CA supports the proposed classification of Indoxacarb (pure S enantiomer) as T, R25: Toxic if swallowed according to Directive 67/548/EC and as Acute Tox 3 (oral) (H301: Toxic if swallowed) according to Regulation EC 1272/2008. This classification is due to the LD50 value in female (LD50 =179 mg/kg bw day) obtained in the oral toxicity study with indoxacarb (pure S enantiomer).<br>The proposed classification of Indoxacarb (enantiomeric reaction mass 75:25 S:R) is Xn, R22 (Harmful if swallowed) according to Directive 67/548/EC and Acute Tox 3 (oral) (H301: Toxic if swallowed) according to Regulation EC 1272/2008. This classification is due to the LD50 value in female (LD50 =268 mg/kg bw day) obtained in the oral toxicity study with indoxacarb (enantiomeric reaction mass 75:25 S: R).<br><br>Acute inhalation<br>The Spanish CA supports the proposed classification of Indoxacarb (pure S enantiomer) and Indoxacarb (enantiomeric reaction mass 75:25 S: R) as Xn; R20 (Harmful by inhalation) according to Directive 67/548/EC and as Acute Tox. 4 (inhalation) (H332: Harmful if inhaled) according to Regulation EC 1272/2008.<br>The classification for both Indoxacarb (pure S enantiomer & enantiomeric reaction mass 75:25 S: R) is based on the LD50 value in female (LC50=4.2 mg/kg bw day) obtained in the inhalation toxicity study with Indoxacarb (racemic mixture 50:50 S: R)<br>This is justified because there is no data available neither for Indoxacarb (pure S enantiomer) nor for Indoxacarb (enantiomeric reaction mass 75:25 S:R) and because the study performed with Indoxacarb (enantiomeric reaction mass 75:25 S: R)-MUP can not be considered due to the low purity (70.7%). | Thank you for the support | Noted |

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| | | p. 32 Summary and discussion of sensitisation<br>The Spanish CA supports the proposed classification of Indoxacarb (pure S enantiomer) and Indoxacarb (enantiomeric reaction mass 75:25 S:R) as skin sensitizer; R43 (May cause sensitisation by skin contact) according to Directive 67/548/EC and as Skin Sens. 1 (H317: May cause an allergic skin reaction) according to Regulation EC 1272/2008. This classification is based on the positive response obtained in more than 30% of the animals in the guinea pig maximisation test with Indoxacarb (enantiomeric reaction mass 75:25 S:R).<br><br>p. 39 Summary and discussion of repeated dose toxicity<br>The Spanish CA is in agreement with the proposed classification of Indoxacarb (pure S enantiomer) and Indoxacarb (enantiomeric reaction mass 75:25 S: R) as Xn; R48/22 (Harmful: danger of serious damage to health by prolonged exposure if swallowed) based on Directive 67/548/EEC and as STOT Rep.1- (H373: May cause damage to organs through prolonged or repeated exposure) according to Regulation EC 1272/2008.<br>Studies have been conducted with Indoxacarb (pure S enantiomer), Indoxacarb (enantiomeric reaction mass 75:25 S: R) and Indoxacarb (racemic mixture 50:50 S:R). The results of the different studies demonstrate that Indoxacarb (pure S enantiomer), Indoxacarb (enantiomeric reaction mass 75:25 S: R) and Indoxacarb (racemic mixture 50:50 S:R) show similar dose-response characteristics. The results of the studies with Indoxacarb (racemic mixture 50:50 S:R) are relevant for the prediction of the toxicity and classification of Indoxacarb (pure S enantiomer) and Indoxacarb (enantiomeric reaction mass 75:25 S: R).<br>Mortality was observed in several studies in rats. In the 90 day study in rats, 5/10 female died at dose of 8.94 mg/kg bw/day. In the 28-day study in rats 2/5 and 3/5 female died at dose of 235 ppm (3.5 mg/kg bw/day) and 400 ppm respectively. In the 2 years rat studies, it was | | |

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| | | observed an increased mortality at 7.83 mg/kg bw/day during the first year.<br>Anaemia haemolytic was consistently evident across the species (rats, mice and dogs, with the dog being more sensitive than the rat, and both being more sensitive than the mouse) in the different studies:<br>In a 90-day study in rats performed with Indoxacarb (pure S enantiomer), a decrease in Hb>10% from 4.1 mg/kg bw/day for females associated with increased methaemoglobin concentration (4%) was seen. Furthermore histopathology findings indicative of blood breakdown were seen, including increased pigment (haemosiderin) deposit in the liver and spleen at ≥ 1.7 mg/kg bw/day in female as well as splenic erythrocytic at doses 3.2 and 4.1 mg/kg bw day in male and female respectively.<br>In a 90-day study in rats performed with Indoxacarb (enantiomeric reaction mass 75:25 S: R) a decrease was observed in Hb ≈ 10% at 15 and 8.94 mg/kg bw /day for males and females respectively associated with increased haemosiderin deposits in liver and spleen from 3.09 and 3.78 mg/kg bw/day in male and female respectively. The methaemoglobin concentration has not been determined in this study.<br>In a 90-day study in rat performed with Indoxacarb (racemic mixture 50:50 S:R) it was observed a decrease in Hb of 11% at 16 and 9.5 mg /kg bw /day for males and females respectively, associated with increased haemosiderin deposits in liver and spleen from 1.9 and 2.3 mg/kg bw/day in male and female respectively. The methaemoglobin concentration has not been determined in this study.<br>In a 2 years study in rats performed with Indoxacarb (racemic mixture 50:50 S:R), deaths in females at the dose level of 7.83 mg/kg bw/day were associated with microscopic findings of bone marrow atrophy, splenic lymphoid depletion and thymic necrosis.<br>In a 90 days study in dog performed with Indoxacarb (racemic mixture 50:50 S:R) a decrease in haemoglobin ≥ 20% at 17 mg/kg bw/day for females and a decrease in haemoglobin 10-20% from 5 mg/kg bw/day for male were observed. Furthermore increased pigment | | |

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| | | (haemosiderin) deposits were observed in liver, spleen, bone marrow and the kidney from 1 mg/kg bw/day.<br>In a 1 year study performed with Indoxacarb (racemic mixture 50:50 S:R) a decrease in haemoglobin ≥ 20% at 17.5 and 36.1 mg/kg bw/day for males and females respectively was observed. In addition there was an increase in bilirubin at ≥ 2.3 and 1.3 mg/kg bw/day for males and females respectively, increased Heinz bodies and morphological changes in erythrocytes (increased incidence of Howe-Jolly bodies, polychromasia and hypochromasia) at ≥ 33.6 and ≥ 36.1 for males and females respectively. Furthermore, secondary histopathology findings indicative of blood breakdown were seen, including increased pigment (haemosiderin) deposits in liver, spleen, bone marrow and kidney from 2.4 mg/kg bw/day.<br>All these findings appear at lower doses than the cut-off levels for classification.<br>The mechanism of action of haemolytic anaemia is proposed to be related to the formation of "aniline analog" intermediate metabolite (IN-MT 713). The results of the in vitro study with this minor metabolite suggest that the findings about red blood cell damage can be due to the oxidation of glutathione, and that humans are less sensitive than dogs, rats and mice. However, this mechanism is not clearly stablished. Therefore, it cannot be rule out that anamemia occur in humans.<br>Neurotoxicity was observed in mouse studies (28 & 90 days) from 30 mg/kg bw/day. It is characterized by weakness, head tilting and abnormal gait or mobility with inability to stand. In a lifetime (18 month) study in mouse, an increased incidence of neuronal degeneration/necrosis affecting the piriform cortex and the hippocampus occurred in the brain of both gender at dose levels ≥ 20.3 mg/kg bw/day. In addition, residual vacuolation of female brain from > 44.1 mg/kg bw/day and severe myocardial necrosis of the heart, with an associated haemorrhage in 12 /70 males at dose levels ≥ 32 mg/kg bw/day were seen. Although the results obtained in these mouse | | |

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| | | studies are not sufficient for the classification R48/22, they back the classification proposed. | | |
| 08/10/2010 | Sweden / Member State | Hazardous to the aquatic environment<br>SECA agrees with the proposed classification for the aquatic environment and would like to provide the following comments:<br>1. Since information on photolysis is not taken into account in assessment of ready biodegradability we propose to delete this section. | 1. We are not fully sure which section Sweden are referring to here. Assuming the summary in section 4.1.1, we prefer to retain the text for photodegradation. It is important to include details of any photolysis as this is relevant for the ecotoxicity test interpretation. In addition, in this section we are comparing the degradation data against the criteria "if other convincing scientific evidence is available to demonstrate that the substance can be degraded (abiotically or biotically) in the aqueous environment to a level >70% with a 28 day period" (e.g. section 4.1.3.2.3.2 of the CLP guidance). | 1. 1. Agree that information on photolysis is important especially in respect of ecotoxicity test interpretation. |
| | | 2. Section 4.1.3. Summary and discussion on persistence:<br>a. Paragraph 3: Since information on photolysis is not relevant for the assessment of biodegradability of the substance we propose to delete it from this paragraph.<br>b. Paragraph 4:: "<br>i. We propose to amend the first sentence according to:"Similarly, | 2a. Again, based on the above point, we prefer to retain the text.<br><br>2bi. As the measured products of degradation | 2a. Although photolysis is not accepted to present 'rapid degradation' in classification would prefer to keep it in the |

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| | | while the substance may quickly be adsorbed to sediment undergoes primary aerobic and anaerobic degradation, degradation products are more persistent".<br><br>ii. We propose to amend the following sentence: "Therefore, although primary degradation occurs in water and sediment fairly rapidly, dissipation of more toxic degradants does not occur rapidly" since dissipation of toxic degradation products is not relevant for the classification. In case a substance undergoes a primary degradation and forms degradation products their toxicity will decide whether the parent compound should be classified or not. Therefore the following part of the sentence "dissipation of more toxic degradants does not occur rapidly" could be changed to "toxic degradants are formed and therefore, for the purpose of classification, the S and R enantiomers are not considered readily biodegradable.<br><br>c. Paragraph 5: We propose to rephrase the last paragraph. This paragraph states that the substances are not considered to undergo significant rapid and ultimate degradation to non-toxic substances. Since ultimate degradation means mineralization ultimate degradation to something else than water and CO2 is not possible.<br><br>3. Similar changes as proposed above should be taken into account in part 7.6 where the rationale for aquatic hazard classification is summarized. | include secondary and tertiary products we prefer to retain our original text.<br><br>2bii We prefer to retain our original text. We think whether the degradants remain (or not) is an issue for classification.<br><br>c We appreciate the confusion from the wording. We propose to change the text to "…are not considered to undergo significant rapid degradation to non-toxic substances".<br><br>3 As above, we prefer to retain the text. | text. Both for ecotoxicity test validation and for background information.<br><br>2bi. Agree with the response by the dossier submitter.<br><br>2bii. Agree with the response by the dossier submitter. The issue that Sweden comments is important and is explained further in the text.<br><br>c. Noted<br><br>3. Noted |
| 08/10/2010 | Germany / Member State | Chapter 5.2 Acute toxicity and chapter 5.6 Repeated dose toxicity: The German CA would appreciate it if you could consistently give detailed dose-dependant quantitative information on the magnitude of the observed effects. This would unmistakably show the dose-response-relationship for each kind of toxic effect. | We agree that detailed dose-dependant quantitative information on the magnitude of the observed effects would be useful. However, such information would not alter | Noted |

| Date | Country/ Person/Organisation/ MSCA | Comment | Response | Rapporteur's comment |
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| | | | the proposed classification. In addition, more detailed data than described in the CLH dossier are unfortunately not included in the summaries of the DAR and CAR. | |