Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

dodemorph acetate

EC number: 250-778-2
CAS number: 31717-87-0

CLH-O-0000002169-72-02/A2

Adopted

13 September 2013

ANNEX 1 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON DODEMORPH ACETATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

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

ECHA accepts no responsibility or liability for the content of this table.

Last data extracted on 04.02.2013

Substance name: Dodemorph acetate
EC number: 250-778-2
CAS number: 31717-87-0

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	1
Comment received				
The German CA supports the harmonised classification and labelling for dodemorph acetate, which is an active ingredient in plant protection products. Furthermore could you please clarify whether there are any special reasons to classify Dodemorph acetate just as Skin Corr. 1 without the possible subcategories A,B,C.?				
Dossier Submitter's Response				
Thank you for the support. With regard to skin corrosion: The available data do not allow to assign a subcategory. Exposure was for 4 hours, no data are available for shorter exposure periods. Assigning a subcategory C might give the impression that shorter exposure does not result in skin corrosion, while it is not known whether that is correct. Therefore, it is chosen to classify as Skin Corr. 1, without subcategory.				
RAC's response				
RAC notes the concern expressed here, but was advised by ECHA that this was not an option under the framework provided at present by the CLP Regulation. Accordingly, using the available criteria, RAC's opinion is that the appropriate classification would be Skin Corr. 1C.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium	BASF SE	BehalfOfAnOrganisation	2
Comment received				
CLH-Report Dodemorph acetate – Comments from BASF Page 6, point, 1.1, table 1 and page 15, point 1.2 (minimum a.i. content in TK) BASF agree with the specification for the dry technical material (TC) for dodemorph acetate: 950 g/kg. However, regarding the TK (technical concentrate) the applicant was requested during the				

EU review to give a lower and an upper level since this is required acc. to the FAO manual. In addition, please note that the specification of the TK was not finalised in the EU review and new 5-batch data was requested by authorities.
Due to a formulation change of the product there are TKs in two different solvents: xylene (old formulation) and benzyl alcohol (new formulation). Additional 5-batch-studies have shown that the dodemorph content of the TK is to be set at 507-557 g/kg for the xylene TK and 726-776 g/kg for the TK in benzyl-alcohol.

The respective studies can be provided upon request.

Page 14, Table 5 (IUPAC name)

The IUPAC name is given in the dossier and EFSA conclusion as follows:
cis/trans-4-[cyclododecyl]-2,6-dimethylmorpholine acetate

ECHA proposes the following IUPAC name:
4-[cyclododecyl]-2,6-dimethylmorpholine-4-ium acetate

Since the first IUPAC name (cis/trans-4-[cyclododecyl]-2,6-dimethylmorpholine acetate) is used in all literature and the JM2 dossier submitted at EU level, BASF strongly recommend to maintain this name also for the CLH report for reasons of consistency.

Page 18, table 9 (surface tension)

Please include the surface tension data: acc. to EFSA conclusion 170, the surface tension of dodemorph acetate is:
55.1 mN/m at 20 °C (90 % saturated
solution)(98.2%); Zenide D. (2003); BASF DocID 2003/1011841

This study can be provided upon request

Page 18, table 9 (water solubility)

Please revise the endpoints for water solubility at pH 5 and pH 7 since these were not accepted in the EU review. A new study with dodemorph acetate was required acc. to the EFSA conclusion on dodemorph, which is now available and currently under evaluation by the RMS (NL) during product authorisation:

pH 5: 4760 mg/L (20°C)
pH 7: 116 mg/L (20°C)

The respective study can be provided upon request.

Dossier Submitter's Response

With regard to the technical concentrate (TK): The formulation change is noted. However, it does not influence the proposed classification, since the proposal is based on the technical material.

With regard to the IUPAC name, the correct IUPAC name should be used in all documents. However, for reasons of transparency it is suggested to include in all CLH documentation (CLH background document and RAC opinion) under substance identification that a different IUPAC name was used in the EFSA assessment namely: cis/trans-4-[cyclododecyl]-2,6-dimethylmorpholine acetate.

The NL received the studies on surface tension and water solubity and considers them

reliable and acceptable.

Update of the relevant parts of table 9

Property	**Value**	**Reference**	**Comment (e.g. measured or estimated)**
Surface tension	55.1 mN/m at 20 °C (90 % saturated solution)(98.2%)	BASF DocID 2003/1011841	
Water solubility	pH 5: 4760 mg/L (20°C) pH 7: 116 mg/L (20°C)	BASF DocID 2011/1255703	

Relevance for environmental classification
The surface tension study shows that dodemorph is considered a surface active substance (55 mN/m vs. the criterion of 60 mN/m). This can affect the interpretation of the bioaccumulation study and aquatic toxicities. However, we expect that any effect from dodemorph (acetate) will be very low. The experimental BCF value is 583-746 L/kg. These values were obtained in a BCF study conducted according to OECD 305, flow-through, 14-day exposure using 3 and 30 ug/L dodemorph acetate. Both treatments contained 1 ug/L ^{14}C-dodemorph. It appears that the solvents acetone and triethylene glycol were used as solvents but it is not stated at which concentrations. Based on the study design and low concentrations of dodemorph (acetate) used, the study is considered reliable and the obtained BCF values acceptable. Aquatic studies were considered reliable and concluded that this new information does not change our proposal for classification for the environment. Lastly, new information on water solubility for dodemorph shows that it is pH dependent. For instance, dodemorph is more water soluble in acidic condition (pH 5) and less in basic conditions (pH7). This trend was also apparent in the original values reported in the CLH report. In conclusion we consider that the information provided by BASF does not alter our proposal for classification for the environment.

RAC's response

The further information is noted.
The question of the substance name will be addressed by ECHA and the Commission when the update to Annex VI of the CLP regulation is drafted.

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2013	France		MemberState	3
Comment received				
We agree with the classification proposal.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	4
Comment received				
We support not to classify dodemorph acetate for carcinogenicity based on the data				

presented. However numbers of liver tumors in mice and in rats after the carcinogenicity phase and historical control data used to disregard these tumors should be presented. Criteria set in GD to Reg (EC) 1272/2008 for the use of historical control data should be acknowledged.
Dossier Submitter's Response
We agree that such information would be helpful. However, besides the percentage of neoplastic lesions, no data on the number of tumors or historical control data were included in the DAR. Because the original studies are not available to us, we cannot provide this information.
RAC's response
Noted.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	5
Comment received				
The German-CA supports to classify dodemorph acetate for reproductive toxicity category 2 (H361d) according to CLP / category 3 (R63) according to DSD based on the present data.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
23.01.2013	Denmark	Danish EPA	BehalfOfAnOrganisation	6
Comment received				
DK agrees the proposed classification.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	7
Comment received				
Regarding the teratogenicity studies, the findings of the developmental study on rabbits (Hellwig& Hildebrand 1994) are relevant for classification for reprotoxicity. The incidences of the sternebra (irregular shape) observed in the fetuses increased at high dose and are statically significant (10.9 foetuses/litter). Those effects occurred in the absence of maternal toxicity: no mortality is observed, the food consumption was not affected and body weight and body weight gain were not statically different at this dosage. Furthermore, other effects are observed : cleft palate in one foetus and open eye in 4 foetus, which support the adverse effect on the development of the foetus. Following the guidance, we agree that there is some evidence from experimental animal of an adverse effect, statically significant and supplemented with other information. We support the classification cat. Rep.2 H361d				
Dossier Submitter's Response				
Thank you for the support.				

RAC's response
Noted.

RESPIRATORY SENSITISATION

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	8
Comment received				
We also agree not to classify R37 based on absence of the data.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted (although R37 related to irritancy, not sensitisation).				

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	9
Comment received				
The dermal irritation study (Hutchinson 2002) is relevant for the classification of corrosive property. Due to the dark necrotic area observed in one rabbit study after exposure up to a 4 hour duration, we agree with the corrosive property of dodemorph acetate and therefore we support the classification cat.1. The DS proposed the classification C R34 according to the DSD criteria. In order to be consistent, we suggest to classify Skin Corr 1B H314 according to the CLP criteria as defined in the guidance. Besides the labeling EUH 071, we suggest to add the precautionary statement P260: "Do not breathe dust/fume/gas/mist/vapour/spray."				
Dossier Submitter's Response				
The criteria for skin corrosion in the DSD and CLP are different. Classification under CLP as Skin Corr. 1B would not be correct, since this suggests that skin corrosion would occur after an exposure period of > 3 minutes - ≤ 1 hour. Since this is not known, and only data are available for an exposure period of 4 hours, we prefer to classify as Skin Corr. 1, without subcategory. The determination of precautionary statements under CLP is not relevant for the CLH dossier as precautionary statements are not included in Annex VI. Therefore, no precautionary statements are proposed in the dossier.				
RAC's response				
The data presented show that an exposure period of 4 hours (skin contact, semi-occlusive) gives a corrosive response on rabbit skin. Using these data, RAC's opinion is that the criteria for classification Skin Corr 1C are met. RAC agrees that EUH071 should be applied. However, there is no scope for specifying P-statements in Annex VI of the CLP Regulation.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	10
Comment received				
Furthermore, as the classification Skin Corr.1, H314 covers the eye damage, we support not to classify as Eye damage 1.				

Dossier Submitter's Response
Thank you for the support.
RAC's response
Agreed.

OTHER HAZARDS AND ENDPOINTS – Skin Sensitation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	11
Comment received				
The German-CA supports to classify dodemorph acetate as skin irritant cat 1 (H314). In this context the proposed labelling with EUH071 is supported as well as C (R34) according to DSD. We furthermore support to classify dodemorph acetate as a skin sensitizer cat. 1 (H317). The data presented are convincing that these classifications are needed.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	12
Comment received				
Regarding the GPMT test, we agree with the classification Skin Sens 1A: H317 as at least 60% of the animals showed a sensitizing reaction after intradermal induction with 1%. Therefore the criteria for sub category 1A are fulfilled.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Agreed.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	13
Comment received				
Wording: On p 37, you mentioned that dodemorph acetate is already classified for the corrosive properties and it is written Skin Corr C; H 314. We assume that this is a phrasing mistake.				
Dossier Submitter's Response				
This is indeed a phrasing mistake. This should be replaced with Skin Corr. 1; H314				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2013	Spain		MemberState	14

Comment received
We agree with the environmental classification and labelling proposal.
Dossier Submitter's Response
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2013	Sweden		MemberState	15
Comment received				
SE supports the environmental classification of Dodemorph actetate(Cas No 31717-87-0) as specified in the proposal. SE agrees with the rationale for classification into proposed hazard classes and differentiations. The lowest L(E)C50 obtained for dodemorph actetate is 1.1 mg/l in algae. Dodemorph acetate therefore does not fulfill the criteria for classification as Aquatic Acute Cat.1. Dodemorph acetate is considered not rapidly degradable and has a high potential to bioaccumulate. NOEC values for dodemorph are available for all trophic levels. A NOErC of 0.059 mg/l and a NOEC of 0.10 mg/l were obtained in algae, Daphnia and fish respectively. Dodemorph acetate therefor fulfills criteria for Classification as Aquatic Chronic Cat 1. An M-factor of 1 for chronic toxicity is proposed based on NOEC values 0.01<NOEC≤0.1 mg/l and the fact that dodemorph acetate is not rapidly degradable.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	16
Comment received				
The German-CA supports the proposed aquatic chronic classification and the proposed M-factor. Section 5, p. 53ff.: Please also include real references for the studies listed, i.e. Author, year, Report No. This information can also be taken from the respective DAR.				
Dossier Submitter's Response				
Thank your for your support. The summaries included in this proposal are partly copied from the DAR volume 3, annex B. In section 6 of the CLH report, we refer the reader to the DAR for more information. For the time being, we prefer to keep the CLH report in its current form. However, for future proposals NL will include individual references on relevant information and key studies.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	17
Comment received				

Based on the results of the aquatic toxicity tests (Pseudokirchneriella subcapitata with 72hErC50 dodemorph acetate= 1.1 mg/l , 72hNOErC dodemorph acetate=0.059 mg/l) and the fact that the substance is not rapidly degradable, it is justified to classify, following the classification criteria of the 2nd ATP, as Aquatic Chronic1, H410.

In view of the proposed classification and the toxicity band for chronic toxicity between 0.01mg/l and 0.1mg/l, an M-factor for chronic toxicity of 1could be assigned for this not rapidly degradable substance.

Based on the classification and labelling criteria in accordance with dir. 67/548/EEC, Pseudokirchneriella subcapitata 72hErC50 dodemorph acetate= 1. 1 mg/l(mm), log Kow=4.6>3, Dodemorph acetate should be classified as N, R51/53.

In conclusion : we support the environmental classification proposed by the NL MSCA provided that the reported ErC50 value is based on the geometric mean concentration (see comments).

Some editorial or/and minor comments:
- Please give the reference for each indicated test.
- Algae study : please mention the species used
- Did biomass in the control cultures increase exponentially by a factor of at least 16 within the 72-hour test period?
If deviation from the nominal or measured initial concentration is not within the range of ± 20 %, the ErC50 value should be based on the geometric mean concentration during exposure as recommended by OECD guideline 201? Is the given ErC50 value expressed as mean measured concentration or geometric mean?
If the given ErC50 is not based on the geometric mean, this will influence the above proposed classification as ErC50 is close to 1mg/l.

Dossier Submitter's Response

Thank you for your comments. With regard to editorial and minor comments:

-The summaries included in this proposal are partly copied from the DAR volume 3, annex B. In section 6 of the CLH report, we refer the reader to the DAR for more information. For the time being, we prefer to keep the CLH report in its current form. However, for future proposals NL will include individual references on relevant information and key studies.

-The species used in the algae study was the *Pseudokirchneriella subcapitata*. This information is presented in Table 28 of the report, section 5.4.

-We do not have access to the raw data of the algae study. According to the DAR the validity criteria was met for test guideline OECD 201;EEC92/69. One of the criteria a test should meet in order to be valid is that the biomass concentration in the control cultures should have increased by a factor of at least 16 within the test period. From this information we can conclude that the control cultures increased by a factor of 16.

-With regard to the last point, the statistical analysis that resulted in a NOE_rC of 0.059 mg/L and E_rC50 of 1.1 mg/L were based on geometric mean measured concentrations of dodemorph.

RAC's response

Noted.