

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

EC number: 216-474-9
CAS number: 1593-77-7

CLH-O-0000002170-89-02/A2

Adopted
13 September 2013

ANNEX 1 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DODEMORPH

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.

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Last data extracted on 04.02.2013

Substance name: Dodemorph

EC number: 216-474-9

CAS number: 1593-77-7

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2013	Spain		MemberState	1
Comment received				
We are in agreement with the proposed classification and labelling for the environment.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	2
Comment received				
The German-CA supports to harmonise classification and labelling for dodemorph, which is an active ingredient in plant protection products.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

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.				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium	BASF SE	BehalfOfAnOrganisation	4
Comment received				

CLH-Report Dodemorph – Comments from BASF

Page 6, point, 1.1, table 1 and page 15, point 1.2
(minimum a.i. content in technical concentrate (TK))

BASF agree with the specification for the dry technical material (TC) for dodemorph: 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 17, 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

Page 17, table 9 and page 25, point 4.4.1.3 (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.

The NL received the studies on surface tension and water solubility 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	

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Water solubility	pH 5: 4760 mg/L (20°C) pH 7: 116 mg/L (20°C)	BASF DocID 2011/1255703	
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Consequently, in paragraph 4.4.1.3 , the sentence 'The solubility of dodemorph acetate is 2.29 mg/L at pH 9 to 736 mg/L at pH 5 at 25 °C (Table 9)' should be replaced with 'The solubility of dodemorph acetate is 4760 mg/L at pH 7 to 116 mg/L at pH 5 at 20 °C (Table 9)'.

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 ¹⁴C-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

Environment:

We agree with DS.

Health: noted but no impact on classification;

Date	Country	Organisation	Type of Organisation	Comment number
23.01.2013	Denmark		MemberState	5

Comment received

Agree to the proposal for dodemorph (acetate).

DK don't agree to remove the classification for corrosive properties for dodemorph. I understand the rationale presented in section 4.4.1.5., however as both forms of dodemorph and dodemorph acetat exist in aqueous solutions at pH 6,5-10,5.

It is not possible at the moment to conclude what form of dodemorph, the data material for corrosive effects had been made with. The reason for the lack of data should not exempt classification for dodemorph.

Dossier Submitter's Response

The substance used in the study is dodemorph acetate. Since the study is performed in circumstances where only little water is available, the solubility, pH of the solution and the form in which dodemorph is present will affect the effect on the skin in a way that is difficult to predict. Therefore, read across to dodemorph is not possible. With the conclusion 'no classification due to lack of data' we do not indicate that dodemorph itself has no corrosive properties, but that we do not know whether it does or not. We do not agree that a substance should be classified, when there is a lack of data.

RAC's response

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Irritation/corrosion studies were performed on dodemorph acetate and not on dodemorph.

In presence of water, dodemorph will dissociate into dodemorph-H⁺ and OH⁻ that may result in an increase of the pH. Besides, there is a 300-fold difference in solubility between pH 9 (2.29 mg/l) and pH 5 (736 mg/l). These differences in solubility and/or pH introduce an uncertainty and question whether local behaviour of dodemorph and dodemorph acetate will be similar.

Therefore, local effects of dodemorph may differ from local effects of dodemorph acetate and do not support the use of dodemorph acetate data for dodemorph for local effects.

No classification due to lack of data is therefore supported.

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	6
Comment received				
We support not to classify dodemorph 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	Belgium		MemberState	7
Comment received				
We support the classification Repro Cat.2: H361d.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	8
Comment received				
The German-CA supports to classify dodemorph for reproductive toxicity category 2 (H361d) according to CLP / category 3 (R63) according to DSD based on the present data.				

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

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	9
Comment received				
Due to the lack of data and the uncertainties of the irritation/ corrosivity and eye irritation properties of Dodemorph, we support the removal of the classification Skin Irrit.2; H315 and Eye irrit.2; H319.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitization Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	10
Comment received				
Due to the lack of data and the uncertainties of the irritation/ corrosivity and eye irritation properties of Dodemorph, we support the removal of the classification Skin Irrit.2; H315 and Eye irrit.2; H319.				
Dossier Submitter's Response				
Thank you for the support. (the comment is on skin/eye irritation, same as above. We assume this comment should be on skin sensitization).				
RAC's response				
Noted				

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	11
Comment received				
We do not support to delete the existing classification for skin and eye irritation category 2. Based on data presented for the acetic salt of dodemorph there is sufficient evidence for classification and labelling of dodemorph with at least skin irrit cat. 2 (H315) and eye irrit. Cat. 2 (H319). Since dodemorph acetate is considered for being classified as corrosive (skin irrit cat. 1, H314), dodemorph should also be considered for a similar classification (as argued by the RMS in the DAR). Since dodemorph acetate was also shown to have an extreme sensitizing potential, this should be discussed for dodemorph as well and classification and labelling of the substance as skin sensitizer cat 1 (H317) should be considered, since it is not very likely that the acetate moiety of the molecule is responsible for the extreme reaction observed in a GPMT.				
Dossier Submitter's Response				
We agree that it is not likely that the acetate moiety of dodemorph acetate that causes the irritation and sensitization. We hypothesize that the effects are caused by the formation of the quaternary ammonium ion, which is present in solutions with dodemorph acetate at				

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pH<10,5. In circumstances with only little water like in skin irritation and sensitisation studies, dodemorph (which already has a poor solubility) will increase the pH (due to the formation of dodemorph-H⁺ and OH⁻), which will reduce the solubility even further, and thereby reduce the formation of the quaternary ammonium ion. In circumstances with little water, the formation of the quaternary ammonium ion is therefore not similar for dodemorph and dodemorph acetate. Effects like skin irritation/corrosion and sensitisation depend on the amount of substance that can penetrate and/or react with the skin. As less dodemorph will be in solution the amount that penetrates and/or reacts is reduced. Therefore the effect will be lower. Given that there is a 40-fold difference in solubility between pH 7 and pH 5, the difference in skin effect are also expected to be large. Thus, no read across is possible and thus, there are no data available for dodemorph. For that reason, we propose no classification due to lack of data.

RAC's response

The formation of a quaternary ammonium from dodemorph acetate in amounts sufficient to induce local effects is not confirmed by available data on hydrolysis and photodegradation (see environment part).

However, in presence of water, dodemorph will dissociate into dodemorph-H⁺ and OH⁻ that may result in an increase of the pH. Besides, there is a 300-fold difference in solubility between pH 9 (2.29 mg/l) and pH 5 (736 mg/l). These differences in solubility and/or pH introduce an uncertainty and question whether local behaviour of dodemorph and dodemorph acetate will be similar.

Therefore, local effects of dodemorph may differ from local effects of dodemorph acetate and do not support the use of dodemorph acetate data for dodemorph for local effects.

No classification due to lack of data is therefore supported.

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	12
Comment received				
We agree to remove the classification STOT SE cat.3 H335 as there is no repeated inhalation toxicity tests providing useful information in terms of clinical signs of toxicity (dyspnoea, rhinitis,...) and histopathology (hyperemia, edema, minimal inflammation, thickened mucous layer).				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Belgium		MemberState	13
Comment received				
Based on the results of the aquatic toxicity tests (Pseudokirchneriella subcapitata with 72hErC50 dodemorph= 0.91 mg/l , 72hNOErC dodemorph=0.05 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 Acute1, H400 and Aquatic Chronic1, H410.				
In view of the proposed classification and the toxicity band for acute toxicity between 0.1mg/l and 1mg/l, an M-factor for acute toxicity of 1 could be assigned, and for chronic				

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toxicity an M-factor of 1 (not rapidly degradable substance and $0.01 < \text{NOEC} \leq 0.1 \text{ mg/l}$).

Based on the classification and labelling criteria in accordance with dir. 67/548/EEC, *Pseudokirchneriella subcapitata* 72hErC50 dodemorph= 0.91 mg/l, $\log K_{ow}=4.6 > 3$, Dodemorph should be classified as N, R50/53.

SCL :

N, R50/53 $C \geq 25\%$

N, R51/53 $2.5\% \leq C < 25\%$

R52/53 $0.25\% \leq C < 2.5\%$

In conclusion : we support the environmental classification proposed by the NL MSCA

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 $\pm 20\%$, 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?

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 NOEC of 0.05 mg/L and ErC50 of 0.91 mg/L were based on geometric mean measured concentrations of dodemorph.

RAC's response

Noted.

Editorial and minor comments:

We agree with DS.

Date	Country	Organisation	Type of Organisation	Comment number
31.01.2013	Germany		MemberState	14
Comment received				
The German-CA supports the proposed classification for Aquatic Acute and chronic category 1 and the proposed M factors of 1.				

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Section 5, p. 52ff.: 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 you 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
01.02.2013	Sweden		MemberState	15
Comment received				
SE supports the environmental classification of Dodemorph (Cas No 1593-77-7) as specified in the proposal. SE agrees with the rationale for classification into proposed hazard classes and differentiations.				
Dodemorph fulfills the criteria for classification as aquatic environmental hazard acute category 1, H400 with the M-factor 1 and aquatic environmental hazard chronic category 1: H410 with the M factor of 1. The acute M-factor is 1, based on the acute toxicity data for the algae <i>Pseudokirchneriella subcapitata</i> (ErC50=0.91 mg/l) in a 72 h static study. Based on the L(E)C50 value of 0.91 mg/l an acute M-factor of 1 is proposed (0.1 mg/l < L(E)C50 ≤ 1 mg/l).				
Dodemorph 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 0.08 mg/l and 0.10 mg/l were obtained in algae, Daphnia and fish respectively. Dodemorph therefore 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 is not rapidly degradable.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted.				