Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

dimethenamid-P (ISO)

EC number: -
CAS number: 163515-14-8

CLH-O-0000003037-80-03/F

Adopted

4 June 2013

4 June 2013

CLH-O-0000003037-80-03/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: dimethenamid-P (ISO)

EC number: -

CAS number: 163515-14-8

The proposal was submitted by **Germany** and received by the RAC on **23/10/2012.**

In this opinion, all classifications are given firstly in the form of CLP hazard classes and/or categories, the majority of which are consistent with the Globally Harmonised System (GHS) and secondly, according to the notation of 67/548/EEC, the Dangerous Substances Directive (DSD).

PROCESS FOR ADOPTION OF THE OPINION

Germany has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation*** on **23/10/2012**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **7/12/2012**.

ADOPTION OF THE OPINION OF THE RAC

Rapporteur, appointed by RAC: **Thomasina Barron**

Co-rapporteur, appointed by RAC: **Benjamin Piña**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation.

The RAC opinion on the proposed harmonised classification and labelling was reached on **4 June 2013** and the comments received are compiled in Annex 2.

The RAC Opinion was adopted by **consensus**.

OPINION OF THE RAC

The RAC adopted the opinion that dimethenamid-P (ISO) should be classified and labelled as follows:

Classification and labelling in accordance with the CLP Regulation

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors
					Hazard Class and Category Code(s)	Hazard state-ment Code	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard state-ment Code(s)	
Current Annex VI entry	-	-	-	-	-	-	-	-	-	-
Dossier submitter's proposal	616-215-00-3	dimethenamid-P (ISO); 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide	-	163515-14-8	Acute Tox. 4 Skin Sens. 1B Aquatic Acute 1 Aquatic Chronic 1	H302 H317 H400 H410	GHS07 GHS09 Wng	H302 H317 H410		*M=10* *M=10*
RAC opinion	616-215-00-3	dimethenamid-P (ISO); 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide	-	163515-14-8	Acute Tox. 4 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H302 H317 H400 H410	GHS07 GHS09 Wng	H302 H317 H410		*M=10* *M=10*
Resulting Annex VI entry if agreed by COM	616-215-00-3	dimethenamid-P (ISO); 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide	-	163515-14-8	Acute Tox. 4 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H302 H317 H400 H410	GHS07 GHS09 Wng	H302 H317 H410		*M=10* *M=10*

Classification and labelling in accordance with DSD

	Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits
Current Annex VI entry	-	-	-	-	-	-	-
Dossier submitter's proposal	616-215-00-3	dimethenamid-P (ISO); 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide	-	163515-14-8	Xn; R22 Xi; R43 N; R50-53	Xn; N R: 22-43-50/53 S: 60-61	N; R50-53: C ≥ 2,5 % N; R51-53: 0,25 % ≤ C < 2,5 % R52-53: 0,025 % ≤ C < 0,25 %
RAC opinion	616-215-00-3	dimethenamid-P (ISO); 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide	-	163515-14-8	Xn; R22 R43 N; R50-53	Xn; N R: 22-43-50/53 S: (2-)24-37-60-61	N; R50-53: C ≥ 2,5 % N; R51-53: 0,25 % ≤ C < 2,5 % R52-53: 0,025 % ≤ C < 0,25 %
Resulting Annex VI entry if agreed by COM	616-215-00-3	dimethenamid-P (ISO); 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxypropan-2-yl]acetamide	-	163515-14-8	Xn; R22 R43 N; R50-53	Xn; N R: 22-43-50/53 S: (2-)24-37-60-61	N; R50-53: C ≥ 2,5 % N; R51-53: 0,25 % ≤ C < 2,5 % R52-53: 0,025 % ≤ C < 0,25 %

SCIENTIFIC GROUNDS FOR THE OPINION

RAC general comment

The hazard classes evaluated by the RAC and documented in this opinion are: acute toxicity, skin sensitisation, carcinogenicity, reproductive toxicity and environmental hazards. The Committee did not evaluate any other hazard class related to this substance

RAC evaluation of acute toxicity

Summary of the Dossier submitter's proposal

The dossier submitter (DS) proposed classification for Acute toxicity Category 4 H302: Harmful if swallowed (Xn; R22 according to DSD). Acute toxicity classification via the inhalation or dermal route was not proposed.

The DS's proposal on acute toxicity was based on the following information.

Acute toxicity oral:
Dimethenamid-P was tested for acute oral toxicity in rats and the LD_{50} (males) was 429 mg/kg bw. Clinical signs seen on the day after dosing with dimethenamid-P included: decreased activity, lacrimation, excessive salivation, yellow ano-genital staining, black and/or brown staining on the snout, oral area, buccal area and/or extremities, lethargy, decreased food consumption and decreased faecal volume. All surviving animals were free of clinical signs by day 5 after dosing. Similar signs were seen with the racemic dimethenamid, but were more pronounced at the (higher) top dose of 600 mg/kg bw (LD_{50} = (males) 371 mg/kg bw).

Acute toxicity inhalation:
Dimethenamid-P and racemic dimethenamid showed low toxicity after inhalation exposure. The acute inhalation toxicity of dimethenamid-P was determined in the limit test according to EPA Guidelines (> 2 mg/l) which differs from the OECD/EU requirement (> 5 mg/l). No mortality was observed after 4-h inhalation (nose-only) exposure of rats to a dimethenamid-P aerosol at a concentration of 2.2 mg/l air *(MMAD = approximately 3.4 µm, GSD = 2.0, approximately 4% of particles were ≤ 1.0 µm, approximately 58% were ≤ 4.9 µm and 94% were ≤ 10.0 µm)*. In the study with dimethenamid-P, clinical signs were observed for up to 2 d in some animals and included secretory (lacrimation, chromodacryorrhea, red and clear nasal discharge and dried red facial material) and respiratory (laboured breathing and moist rales) responses. Although an exposure of 2.2 mg/l was below the 5 mg/l limit required by OECD 403, no mortality and only transient clinical signs clearly indicated low inhalation toxicity.

Acute toxicity dermal:
Dimethenamid-P and racemic dimethenamid showed low toxicity after single dermal exposure. The rabbit dermal LD_{50} was > 2000 mg/kg bw for both dimethenamid-P and racemic dimethenamid.

Comments received during public consultation

Comments were received from two member states, both supporting the DS's classification proposal for acute toxicity.

Assessment and comparison with the classification criteria

The studies provided to support the classification proposal of the DS are considered reliable and sufficient to assess the classification proposal.

The acute oral toxicity of dimethenamid-P meets the DSD and CLP criteria. Based on the calculated LD_{50} of 429 mg/kg bw, dimethenamid-P should be classified as Acute toxicity, Cat. 4; H302 according to Annex VI of Regulation (EC) No. 1272/2008 (criteria: 300 >ATE < 2000) and R22 'Harmful if swallowed' according to Annex I of Council Directive 67/548/EEC (criteria: 200 < LD_{50} ≤ 2000 mg/kg).

The results of the acute inhalation toxicity studies do not meet the DSD and CLP criteria for classification. The acute inhalation toxicity was determined in a limit test and no mortality was observed after 4-h inhalation exposure of rats to a dimethenamid-P aerosol at a concentration of 2.2 mg/l air or to an aerosol of racemic dimethenamid at a concentration of 4.99 mg/l air (maximum attainable concentration under the exposure conditions). Classification and labelling of dimethenamid-P for acute inhalation is not required.

The results of the acute dermal toxicity studies do not meet the DSD and CLP criteria for classification as there were no mortalities following exposure to 2000 mg/kg bw (dimethenamid-P or dimethenamid). Classification and labelling of dimethenamid-P for acute dermal toxicity is not required.

RAC evaluation of skin sensitisation

Summary of the Dossier submitter's proposal

The DS's proposal was Skin sensitisation Category 1B H317 according to CLP (Xi;R43 according to DSD). The proposal was based on two tests: a Buehler test where Guinea pigs were exposed to dimethenamid-P and a Magnusson and Kligman test where Guinea pigs were exposed to racemic (R,S)-dimethenamid.

Dimethenamid-P tested positive in a Buehler assay. The induction dose of aqueous 91.1% dimethenamid-P caused irritation which increased in incidence and severity during the induction phase. When challenged with undiluted test substance, 17/20 test animals (85%) exhibited clear dermal responses compared to 0/10 in the controls.

Racemic dimethenamid gave a strong positive test result in a Magnusson-Kligman test. 5% in DMSO was used for the intradermal and topical inductions and for challenge. All treated animals (100%) had very slight to well defined erythema (grade 2; 16/20, grade 1; 3/20 (1 mortality)) at the 24 hour reading, and 15/19 (79%) still showed a skin reaction (grade 2; 4/20, grade 1; 11/20, grade 0; 4/20) at 48 hours. No positive reactions were observed in the control group.

The DS concluded that dimethenamid-P was a skin sensitiser (1B) on the basis of the Buehler test and should be classified accordingly. The DS also concluded that the positive maximization test (Magnusson and Kligman) carried out with the racemic dimethenamid confirms the result of the Buehler test and supports the proposed classification.

Comments received during public consultation

Two member states supported the DS's proposal for classification as Skin sens. 1B (H317).

Assessment and comparison with the classification criteria

Two studies summarised in the CLH report were evaluated by the RAC.

The first study, a guideline-compliant Buehler test (Blaszcak, 1996) on dimethenamid-P, showed a strong positive dermal sensitising potential with 85% of the animals tested giving a positive response to undiluted test substance in both induction and challenge phases.

The second study, a maximation test according to Magnusson and Kligman (GPMT), was reported as acceptable. In this study in guinea pigs, 5% racemic (R,S)-dimethenamid was used for intradermal induction and 100% for topical induction. The challenge was performed with undiluted test substance. Slight to well defined erythema was seen in 100% of the guinea pigs at the 24 hour observation and in 79% at 48 hours.

CLP Criteria: According to the 2nd ATP CLP, classification in Cat 1 is appropriate where data are not sufficient for sub-categorisation into Cat 1A or Cat 1B. Sub-categorisation into either Cat 1A or 1B is on the basis of either frequency of occurrence in humans and/or degree of potency in animal studies as follows.

Classification into Cat 1 is based on a ≥ 30% positive response in an adjuvant type test such as the M&K test or a ≥15% positive response in a non-adjuvant test such as a Buehler test.

Sub-categorisation is based on the following:

Guinea pig maximisation test
Category 1A:
≥ 30 % responding at ≤ 0.1 % intradermal induction dose or
≥ 60 % responding at > 0.1 % to ≤ 1 % intradermal induction dose
Categrory 1B:
≥ 30 % to < 60 % responding at > 0.1 % to ≤ 1 % intradermal induction dose or
≥ 30 % responding at > 1 % intradermal induction dose
Buehler assay
Category 1A:
≥ 15 % responding at ≤ 0.2 % topical induction dose or
≥ 60 % responding at > 0.2 % to ≤ 20 % topical induction dose
Categrory 1B:
≥ 15 % to < 60 % responding at > 0.2 % to ≤ 20 % topical induction dose or
≥ 15 % responding at > 20 % topical induction dose

Given that there was a high level of responders after intradermal induction with 5% racemic dimethenamid in the GPMT, there is a strong possibility that a slightly lower intradermal induction concentration of 1% would still result in a high level of responders. As intradermal induction concentrations lower than 5% were not tested, the data are in principle insufficient to decide on the appropriate subcategory.

Accordingly, it is not possible to use the data presented for dimethenamid-P to sub-categorise, as the only dose tested in the induction phases was in excess of the limits described above and positive responses were between 79 and 100% in both tests.

RAC concluded that classification of dimethenamide-P as Skin Sens. 1 is therefore warranted.

According to the DSD criteria (≥ 30% positive in an M&K test, ≥15% positive in a Buehler test), classification as R43 is supported.

RAC evaluation of carcinogenicity

Summary of the Dossier submitter's proposal

The DS did not propose classification for carcinogenicity.

Chronic toxicity and oncogenicity studies were only conducted with racemic (R,S)-dimethenamid.

The results of a 2-yr chronic/oncogenicity study in rats indicated that the high dose of 1500 ppm (ca. 80 mg/kg bw/d males; 109 mg/kg bw/d females) was a maximum tolerated dose This is demonstrated by a body weight gain depression for the first 80 wk of treatment (15% in males and 23% in females). The liver was a target organ for the racemic dimethenamid in the rat. Observations included an increase in serum γ-glutamyltransferase and cholesterol, an increase in liver weight and liver pathology including altered eosinophilic hepatocytes, bile duct hyperplasia and cystically dilated bile ducts. Other effects noted in high dose males were an increase in epithelial hyperplasia of the limiting ridge of the stomach, posterior lenticular opacity, and hyperplasia in the parathyroid. There was no evidence of a treatment-related increase in neoplasms.

A carcinogenicity study in mice was conducted up to the maximum tolerated dose as evidenced by significant body weight gain depression. As with the rat, the liver was the apparent target organ in mice. Liver weights were increased, and hepatocyte enlargement was observed at the two highest doses. In addition, hyperkeratosis of the limiting ridge of the stomach was observed in high-dose animals at the interim sacrifice time-point only. Increased kidney weights observed in mid- and high-dose females were not accompanied by corresponding histopathological findings

and were therefore regarded to be of equivocal toxicological significance. There was also no evidence of a treatment-related increase in neoplasms.

The overall combined (males and females) NOAELs obtained in long-term studies were:

Rats: 5 mg/kg bw/d
Mice: 40 mg/kg bw/d.

In summary, long-term feeding studies with the racemic dimethenamid in rats and mice demonstrated that the primary target organ was the liver. No treatment related increases in neoplasms were noted in mice or rats. It was concluded that the racemic dimethenamid has no carcinogenic potential.

Comments received during public consultation

There were no comments on carcinogenicity.

Assessment and comparison with the classification criteria

Rat study (Ruckman, 1990)

Liver adenoma: In addition to the findings addressed above, a slight increase in liver tumours was noted at the high dose in male rats only. The incidence of carcinomas was not statistically different from controls and was within the historical control range. The incidence of adenomas was also not statistically different from controls but was just slightly outside of historical control range at the conducting laboratory. The slight increase in adenomas in males was most likely due to a considerably increased survival at the high dose compared to control (36% in controls vs 62% at 1500 ppm). The increased survival allowed a larger number of older age animals to develop the spontaneously occurring adenoma which increases in incidence with age. The incidence for the racemic dimethenamid in high dose males was slightly outside the HRC historical control range but well within the historical control range for Sprague-Dawley rats as compiled by the Registry of Industry Toxicology Animals (RITA).
Overall, the slight increase in the benign liver tumour in high-dose males does not indicate that the racemic dimethenamid is carcinogenic. The increase was not statistically significant, was within historical control range for Sprague-Dawley rats and was most likely due to the considerable increase in survival at that dose.

Ovarian tubular adenoma: The original report indicated a slight increase in ovarian tubular adenomas. In view of the borderline nature of the ovarian findings, and of recent advances in diagnostic criteria for rodent ovarian neoplasia, a pathology peer review was conducted following the issue of the final report. The original and peer review analyses for ovarian tumours and hyperplasia are tabulated below. Between the original review and the peer review, pathology terminology had changed. Lesions originally diagnosed as ovarian tubular adenomas or hyperplasia were rediagnosed as sertoliform tubular adenoma or hyperplasia. This change in terminology reflects a change from the original classification of these neoplasms as epithelial in nature (tubular adenoma) to their current grouping with the other sex cord-stromal neoplasms. Neoplasms diagnosed by the original pathologist as "tubular adenomas" were reclassified by the reviewers as "Sertoliform tubular adenomas". They consist of tubular structures lined by Sertoli-like cells. They differ from true Sertoli cell tumours in that the tubular cells lack basal nuclei and vertically oriented cytoplasm.

In general, the differentiation between Sertoliform tubular hyperplasia and adenoma is difficult and subjective because of the diffuse nature of the lesion. There is a biological continuum from hyperplasia to adenoma. In the original report pathologists diagnosed adenoma when at least 50% of the ovary was involved. Lesions below this threshold size were diagnosed as hyperplasia. The reviewers used similar criteria, but also considered compression of surrounding ovarian stroma to be indicative of neoplasia rather than hyperplasia.

The peer review found (relative to the original pathology report) 1 additional tumour in the control group, 2 additional tumours in the low and mid dose groups and 1 less tumour at the high dose.

The final analysis demonstrated that there is no statistical or biologically significant incidence of ovarian tumours. The incidence at the high dose is within historical control range, and the difference in incidence from control is not statistically significant.
When incidences of adenoma and hyperplasia were combined for analysis, there was only a minimal difference between the control group and the high dose group. The organ weights of the ovaries of the high dose group were not increased in comparison with the controls.
Sertoliform tubular hyperplasia and adenoma are mainly found in the Sprague-Dawley (SD) rat. These lesions are rarely found in other strains of rat.

There is also information available on sertoliform tubular adenoma in the literature(Boorman and Everitt 2006; Dixon *et al*. 1999; Gregson *et al.* 1984) that support the conclusion of the DS that these adenomas are more common in SD rats and support the discussion on reclassification of the original tumours. Boorman and Everitt (2006) state that sertifoliform tubular adenomas comprise the majority of sex cord/stromal adenomas in SD rats (Gregson et al. 1984), and gives the incidence of tubular ademonas (a definition which now includes the sertoliform tubular adenoma) in SD rats (5903 SD rats from 1978-1984) as approx 74% in long-term studies. Sertoliform tubular adenoma differs from sertoli cell tumour in that the tubular cells lack a basement nuclei and vertically oriented cytoplasm. These were more commonly seen in SD rats than other strains and were previously classified with epithelial tumours and described as tubular adenomas (Dixon et al 1999).

In conclusion, the possible increase in ovarian tubular hyperplasia and adenoma is not likely to be treatment-related.

RAC concluded that classification for carcinogenicity is not required for dimethenamid–P, as there was no increase in tumours which was considered related to treatment in the long-term studies in rats with the racemic dimethenamid. In addition, RAC agreed with the DS that there was no evidence that the racemic dimethenamid produced a carcinogenic effect in mice.

RAC evaluation of reproductive toxicity

Summary of the Dossier submitter's proposal

The DS did not propose classification for reproductive toxicity.

Fertility:
Reproductive function was not affected in the 2-generation study (Suter et al, 1989) and therefore the NOAEL for reproductive function is the highest dose tested (2000 ppm, ca. 150 mg/kg bw/d). The NOAEL for systemic toxicity in the parental animals in the 2-generation study was 500 ppm (ca. 50 mg/kg bw/d). The only pup effect noted was decreased body weight gain during lactation at the high dose. The NOAEL for developmental toxicity in the F1 and F2 litters was 500 ppm (ca. 50 mg/kg bw/d).

Development:
In the prenatal toxicity study in rats using dimethenamid-P, developmental toxicity was observed at the two highest doses tested. The developmental effects included reduced foetal weights and an increase in delayed ossifications. These variations have been shown to be reversible delays in development associated with slower growth in smaller fetuses. Further evaluation demonstrated that the increases in delayed ossifications were due to unusually low control values and were not related to treatment. Maternal toxicity was observed in all dose groups. The NOAEL for developmental toxicity was 25 mg/kg bw/d and the NOAEL for maternal toxicity was <25 mg/kg bw/d.

In the prenatal toxicity study in rats using racemic dimethenamid, the NOAELs for maternal toxicity and developmental toxicity were 50 mg/kg bw/d. The different NOAELs in the studies with racemic dimethenamid and dimethenamid-P are partly explained by the different dose levels used in these studies. The different maternally toxic dose levels between the studies could also be attributed to normal inter-study differences. The study with racemic dimethenamid was performed in 1987 and the study with dimethenamid-P in 1996. However, the submitted repeated dose toxicity studies show that there is no significant difference in the short term toxicity between racemic dimethenamid and dimethenamid-P. Due to the compatible findings in the repeated dose

studies conducted with racemic dimethenamid and dimethenamid-P the submitted studies on developmental toxicity in rats are nevertheless acceptable as part of the bridging concept.

In the rabbit prenatal toxicity study, significant maternal toxicity was observed at the high dose and less severe effects were noted at the mid dose. Abortions in 2 high-dose animals were considered treatment-related, but must be seen in with the context of clear evidence for maternal toxicity at that dose. The NOAEL for maternal toxicity in rabbits was 37.5 mg/kg bw/d and the developmental toxicity NOAEL was 75 mg/kg bw/d. The lowest NOAEL for developmental toxicity was 25 mg/kg bw/d (rat prenatal toxicity study, dimethenamid-P).

In summary, dimethenamid-P does not show any adverse effects on sexual function and fertility in adult males and females or developmental toxicity in the offspring. Classification of dimethenamid-P as a reproductive toxicant is not warranted.

Comments received during public consultation

None

Assessment and comparison with the classification criteria

Overall Assessment

In the rat multigeneration study (7.5-151 mg/kg bw/d) there were no effects on reproductive function or offspring and parental toxicity was demonstrated at the high dose. The first rat developmental study (York, 1996) (25-300 mg/kg bw/d) showed clear maternal toxicity at 300 mg/kg and some toxicity at 150 mg/kg bw/d. In this study, the very marginal reductions in mean foetal weight and some reduced ossification were not considered to be significant or biologically relevant. In the 2nd rat developmental study (Lochry, 1987) (50-425 mg/kg bw), the mid- and high-doses were maternally toxic and a significant increase in early resorptions occurred from the mid-dose. The mean resorption incidence was outside the historical controls although not statistically significant. In general, treatment-related increased early resorptions is infrequently observed. It may be associated with a very specific targeting of the foetus early in development and are not regarded as general non-specific developmental retardation/systemic toxicity, such as may be linked to severe maternal toxicity or generally retarded foetal development. This effect was not seen in the multigeneration study (litter size not affected) and also was not seen in the later rat study (York, 1996). In addition, there was no adverse effect on the developing embryo/foetus in the rabbit study. Therefore, the finding is inconsistent with the other data presented.

The RAC concludes that the findings in Lochry (1987) do not represent sufficient grounds for a classification proposal for Repr. 2; H361 (CLP)/Cat 3; R63 (DSD), as the finding has no support from the other data presented.

RAC evaluation of environmental hazards

Summary of the Dossier submitter's proposal

The DS proposed Aquatic Acute 1 with an M-factor 10 and Aquatic Acute 1 with an M-factor 10 (according to DSD N; R50-53 with the specific concentration limits as given below).

A ready biodegradability test was not available. Based on the findings from water/sediment simulation tests, dimethenamid-P appears to be susceptible to primary degradation and not to ultimate mineralisation. Considering the levels of mineralisation in the simulation studies, dimethenamid-P is considered not rapidly (readily according to DSD) biodegradable (a degradation >70 % within 28 days) for purposes of classification and labelling.

Dimethenamid-P has an experimentally measured log K_{ow} of 1.89. The experimentally derived steady state BCF value of 58 l/kg ww (without lipid normalization) for dimethenamid is below the trigger of 100 (criterion for bioaccumulating potential conform Directive 67/548/EEC) for not rapidly biodegradable substances and is also below the trigger of 500 (criterion for bioaccumulating potential conform Regulation EC 1272/2008) for not rapidly biodegradable substances.

All the reported LC_{50}, EC_{50} or NOEC values for aquatic species were based on the mean measured concentrations. The acute LC_{50} value for fish (*Oncorhynchus mykiss*) was 6.3 mg/l and the EC_{50} value for invertebrates (*Daphnia magna*) was 12 mg/l. The reported acute ErC50 value was 0.0378 mg/l for algae (*Pseudokirchneriella subcapitata*) and 0.031 mg/l for an aquatic plant (*Lemna gibba*). There are no chronic toxicity data for fish and invertebrates available.

Classification according to CLP. The DS concluded that dimethenamid-P fulfils the criteria for classification for short-term aquatic hazard as Aquatic Acute 1 (H400) with an M-factor 10 based on the data for the algae *S. capricornutum* (ErC50 = 0.0378 mg/l) in a 120-h static study. The conclusion on long-term aquatic hazard was Aquatic Chronic 1 (H410) with an M-factor 10 based on not proven rapid degradation and the chronic toxicity in the duckweed (*L. gibba*, NOEC = 0.0012 mg/l) in a 14-d semistatic study.

Classification according to DSD. Based on the toxicity data for the algae *P. subcapitata* (ErC_{50} = 0.0378 mg/l) in a 120-h static study and for the aquatic plant *Lemna gibba* (ErC_{50} = 0.0311 mg/l) in a 14-d semistatic study and not being readily degradable, dimethenamid-P fulfils the criteria for classification with N; R50-53 in DSD the following specific concentration limits should be applied: N; R50-53 C ≥ 2.5%, N; R51-53 when 0.25% ≤ C < 2.5% and R52-53 when 0.025% ≤ C < 0.25%.

Comments received during public consultation

The environmental hazard classification was supported by three MSCAs. Supplementary data on batches used for the different tests and aerobic biodegradation of dimethenamid-P were provided during the PC by the DS. The latter confirmed that the substance is not rapidly (CLP) or readily (DSD) biodegradable.

Assessment and comparison with the classification criteria

RAC agrees that the substance is not rapidly (CLP) or readily (DSD) degradable (a degradation >70 % within 28 days), either in water/sediment systems or aerobic biodegradation in soil.

Dimethenamid-P has a log K_{ow} of 1.89. Experimental BCF_{ss} in bluegill (*Lepomis macrochirus*) was calculated as 58 l/kg w.w. Both values are below the reference values for bioaccumulative substances (log K_{ow} >4 and BCF > 500 in CLP; log K_{ow}>3 and BCF > 100 in DSD). The substance is slightly surface active (surface tension, 53 mN/m), a circumstance that may underestimate its bioaccumulative capacity (IR/CSA R.7C). In fact, the calculated K_{ow} is clearly below the predicted XlogP value, 2.6 (http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=13633097). However, as even this predicted higher value is below the guidance criteria, RAC considers the substance not meeting the criteria for a potential to bioaccumulate.

RAC agrees with the public consultation comment that 72h ErC_{50} values for algae should be used to conclude on short-term aquatic hazard instead of the 120 h values. The most sensitive species in the reported acute studies is the algae *P. subcapitata* (ErC_{50} = 0.030 mg/l, 72-h static study). RAC agrees also that dimethenamid-P should be considered as not rapidly degradable and that the long-term aquatic hazard classification should be based on the chronic toxicity in the duckweed (*L. gibba*, NOEC (14-d) = 0.0012 mg/l). The resulting classification for dimethenamid-P is Aquatic Acute 1 (H400) with an M-factor 10 and Aquatic Chronic 1 (H410) with an M-factor 10.

Based on the classification and labelling criteria in accordance with DSD, the LC_{50} for the most sensitive species *P. subcapitata* ErC_{50} (72-h) equals to 0.030 mg/l. As the substance is not readily degradable, dimethenamid-P should be classified as N, R50-53 with specific concentration limits N; R50-53: C ≥ 2.5%, N; R51-53: 0.25% ≤ C < 2.5% and R52-53: 0.025% ≤ C < 0.25%.

References

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ANNEXES:

Annex 1 Background Document (BD) gives the detailed scientific grounds for the opinion. It is based on the CLH report prepared by the dossier submitter; the evaluation performed by the RAC is contained in RAC boxes.

Annex 2 Comments received on the CLH report, response to comments provided by the dossier submitter and the RAC (excl. confidential information).