Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

Fenpyrazamine

EC number: NA
CAS number: 473798-59-3

CLH-O-0000001412-86-55/F

Adopted

12 March 2015

12 March 2015

CLH-O-0000001412-86-5/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 harmonized classification and labelling (CLH) of:

Chemicals name: **Fenpyrazamine**

EC number: **NA**

CAS number: **473798-59-3**

The proposal was submitted by **Austria** and received by the RAC on **04 June 2014.**
All classifications are given in the form of CLP hazard classes and/or categories, the majority of which are consistent with the Globally Harmonized System (GHS); the notation of 67/548/EEC, the Dangerous Substances Directive (DSD) is no longer given.

PROCESS FOR ADOPTION OF THE OPINION

Austria 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 **08 July 2014**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **22 August 2014.**

ADOPTION OF THE OPINION OF THE RAC

Rapporteur, appointed by the RAC: **Stephen Dungey**

Co-rapporteur, appointed by the RAC: **Zilvinas Uzomeckas**

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 harmonized classification and labelling was reached on **12 March 2015** and the comments received are compiled in Annex 2.

The opinion was adopted by consensus.

OPINION OF THE RAC

The RAC adopted the opinion on Fenpyrazamine that should be classified and labelled as follows:

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	613-3180 0-5	fenpyrazamine (ISO); S-allyl 5-amino-2-isopropyl-4 -(2-methylphenyl)-3-o xo-2,3-dihydropyrazol e-1-carbothioate	-	473798 -59-3	Aquatic Chronic 2	H411	GHS09	H411			
Dossier submitters proposal	613-3180 0-5	fenpyrazamine (ISO); S-allyl 5-amino-2-isopropyl-4 -(2-methylphenyl)-3-o xo-2,3-dihydropyrazol e-1-carbothioate	-	473798 -59-3	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=10 M=10	
RAC opinion	613-3180 0-5	fenpyrazamine (ISO); S-allyl 5-amino-2-isopropyl-4 -(2-methylphenyl)-3-o xo-2,3-dihydropyrazol e-1-carbothioate	-	473798 -59-3	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=10 M=1	
Resulting Annex VI entry if agreed by COM	613-3180 0-5	fenpyrazamine (ISO); S-allyl 5-amino-2-isopropyl-4 -(2-methylphenyl)-3-o xo-2,3-dihydropyrazol e-1-carbothioate	-	473798 -59-3	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=10 M=1	

ENVIRONMENTAL HAZARD ASSESSMENT

RAC evaluation of environmental hazards

Summary of the Dossier submitter's proposal

Fenpyrazamine is currently approved to be used as an active substance in plant protection products. In November 2012 RAC adopted an opinion that fenpyrazamine should be classified as Aquatic Chronic 2; H411. However, this was not considered as an existing entry in Annex VI by the dossier submitter (DS) at the time when the new CLH dossier was submitted to ECHA on 4 June 2014. The 6th Adaptation to Technical Progress (ATP) to the CLP Regulation was published in the Official Journal of the European Union on 6 June 2014, meaning it is currently listed in Annex VI of the CLP Regulation. Additional ecotoxicity data made available since the original opinion was adopted led to the submission of an updated CLH report to revise the environmental classification. The (revised) classification and labelling of fenpyrazamine is based on its high acute and chronic toxicity to aquatic invertebrates (marine), bivalves and algae (marine and freshwater diatoms) and the fact that the active substance is not rapidly degradable.

The DS proposed to classify fenpyrazamine as Aquatic Acute 1 (H400) with an M-factor of 10 and Aquatic Chronic 1 (H410) with an M-factor of 10, based on the lowest acute EC_{50} of 0.034 mg/L for growth rate of the alga *Skeletonema costatum* and the lowest chronic NOEC of 0.0049 mg/L based on yield for the alga *Navicula pelliculosa*.

Degradation

Fenpyrazamine is hydrolytically stable at 20°C at pH 4 and 7, but is rapidly hydrolysed at pH 9, with a half-life of 24 days. Aqueous photolysis is rapid with extensive breakdown after 30 days' incubation and an estimated half-life of 1.7 days at pH 7 and 25°C under natural summer sunlight conditions, although photolysis is not relevant for classification.

The substance was degraded by an average of 1% after 28 days in a ready biodegradation test (OECD TG 301B). Simulation tests in two aerobic water-sediment systems using radio-labelled substance indicated primary degradation and formation of non-extractable residues, with first order degradation DT_{50} values for the whole system of 18 – 68 days (geometric mean 35.5 days), and relatively little mineralisation over 100 days (3.1 – 8.5% of applied radioactivity (AR)). Aerobic degradation in soils followed a similar pattern, with limited mineralisation after 120 days (5.2 – 8.5% of AR) and DT_{50} values of 24 – 40 days.
Based on the lack of ready biodegradation, limited mineralisation and primary degradation half-lives exceeding 16 days in an aquatic simulation study, fenpyrazamine does not meet the criteria for being rapidly degradable in the environment.

Bioaccumulation

The n-octanol/water partition coefficient (log K_{ow}) of fenpyrazamine is 3.5 at 25 °C and pH 7.2. The experimentally derived steady state bioconcentration factor (BCF) for the parent substance was between 8 and 9 L/kg wet weight (ww) for fish with an average lipid content of about 1.9% (w/w). This is equivalent to a BCF of up to 24 L/kg ww after normalisation to 5% lipid content. The parent substance was extensively metabolised in fish, and the steady-state BCF based on total radio-active residues (TRR) was 283 – 289 L/kg ww (equivalent to a BCF of up to 760 L/kg ww after normalisation to 5% lipid content). The major residues were the metabolite S-2188-DC and its glucuronic acid conjugate (at concentrations in whole fish of 8.0 – 18.8% and 16.1 – 33.3% TRR, respectively). More than 95% of the ^{14}C residues were eliminated during the depuration phase (within 14 days), and the depuration half-life was less than one day.

S-2188-DC is also one of the main products of photolysis, alkaline hydrolysis and mammalian metabolism. It forms through loss of the S-2-propen-1-yl carbothioic-acid ester group from the parent substance. No data are presented about the aquatic degradability of S-2188-DC (too few data were available in the water-sediment study to estimate a DT_{50}). In the DAR a log K_{ow} of 0.23 is reported (estimated using KOWWIN, version not stated). It is not stated whether this substance

falls within the applicability domain of the model, but it appears to have a lower bioaccumulation potential than the parent. Aquatic acute toxicity tests for fish, *Daphnia* and algae are summarised in the DAR, and it is an order of magnitude less acutely toxic than the parent substance (all acute L(E)C_{50}s were above 82 mg/L; the 72-h NOEC for algae was 2.7 mg/L). Based on this evidence, fish metabolites do not need to be taken into account in defining the BCF for fenpyrazamine.

In summary the BCF for the parent substance is below 500 L/kg for the purposes of classification and labelling.

Aquatic Toxicity

Reliable acute and chronic aquatic toxicity data are available for the three trophic levels fish, aquatic invertebrates and algae. Based on the test with one of most sensitive algae *Skeletonema costatum*, RAC notes that despite the potential for photolysis, the concentration in the algal study was well maintained. The most sensitive organisms for both acute and chronic tests are as follows (the key study results are highlighted in bold):

Test organism	Short-term	Long-term
Oncorhynchus mykiss	96-h LC_{50} = 5.2 mg/L	90-d NOEC = 0.37 mg/L
Cyprinodon variegatus Sheepshead minnow	96-h LC_{50} > 3.9 mg/L	**33-d NOEC = 0.062 mg/L**
Daphnia magna	48-h EC_{50} = 5.5 mg/L	21-d NOEC = 0.34 mg/L
Americamysis bahia Mysid	**96-h EC_{50} = 0.83 mg/L**	**28-d NOEC = 0.024 mg/L**
Crassostrea virginica Oyster	**96-h EC_{50} = 0.66 mg/L**	
Pseudokirchneriella subcapitata	72-h E_rC_{50} > 0.9 mg/L	72-h NOE_rC = 0.22 mg/L
Navicula pelliculosa Freshwater diatom	**96-h E_rC_{50} = 0.202 mg/L**	**96-h NOE_rC = 0.074 mg/L** **96-h NOEC = 0.0049 mg/L (Yield)**
Skeletonema costatum Marine diatom	**96-h E_rC_{50} = 0.034 mg/L**	**96-h NOE_rC = 0.011 mg/L**

Acute toxicity

The DS proposed to classify fenpyrazamine as Aquatic Acute 1 (H400) based on acute toxicity to:

- the aquatic invertebrates *Americamysis bahia* (96-h LC_{50} = 0.83 mg/L based on immobility) and *Crassostrea virginica* (96-h EC_{50} = 0.66 mg/L based on shell deposition); and
- the algae *Navicula pelliculosa* (96-h E_rC_{50} = 0.202 mg/L) and *Skeletonema costatum* (96-h E_rC_{50} = 0.034 mg/L).

Chronic toxicity

The DS proposed to classify fenpyrazamine as Aquatic Chronic 1 (H410) based on long-term toxicity to:

- the fish *Cyprinodon variegatus* (33-d NOEC = 0.062 mg/L based on growth); the aquatic invertebrate *Americamysis bahia* (28-d NOEC = 0.024 mg/L based on growth); and the algae *Navicula pelliculosa* (96-h NOEC = 0.0049 mg/L based on yield and 0.074 mg/L based on growth rate).

Comments received during public consultation

Comments were received from four Member States (MS), who all supported the DS's proposal to classify fenpyrazamine as Aquatic Acute 1 and Aquatic Chronic 1, as well as the proposed acute M-factor of 10. Two MS queried the basis for the chronic M-factor (see below).

One commenter noted that the dossier did not include some additional valid data, but pointed out that this had no influence on the proposal. The DS replied that the study with the freshwater algae *Anabaena flos-aquae* was not included because it was not considered valid. The study for the sediment organism *Chironomus riparius* was included in the CLH report for the first submission of fenpyrazamine and was accidentally deleted for the revised submission.

One MS disagreed with the proposed chronic M-factor of 10 and suggested to use the 96-h NOE_rC of 0.011 mg/L for *Skeletonema costatum* as the most sensitive algal result instead of the 96-h NOEC of 0.0049 mg/L for *Navicula pelliculosa* based on cell density, as growth rate is the preferred endpoint for classification because it is independent of test design. Another MS asked for an explanation of why the yield endpoint should be used when a NOE_rC was available from the same study. In reply, the DS was of the opinion that the most sensitive endpoint should be used for chronic classification.

The CLP guidance (and the CLP Regulation), however, state that the classification shall be based on the ErC50, which also applies for the NOEC. RAC considers that the yield endpoint (based on biomass measurement) suffers from similar statistical drawbacks as the biomass endpoint. The growth rate endpoint is therefore preferred when available. This is consistent with the CLP guidance for acute endpoints and also EFSA Guidance for plant protection products.

Assessment and comparison with the classification criteria

Degradation

RAC agrees with the DS's proposal to consider fenpyrazamine as not rapidly degradable, based on hydrolytic stability at pH 4 and 7, 1% degradation in a ready biodegradation test, and limited primary degradation (mean DT50 35.5 d) with minimal mineralisation in a water-sediment simulation study.

Bioaccumulation

RAC agrees with the DS's proposal that fenpyrazamine does not meet the CLP criteria for bioaccumulation, based on a parent BCF of 8-9 L/kg (up to 24 L/kg ww after normalisation to 5% lipid content).

Aquatic Toxicity

RAC notes that there are reliable acute and chronic aquatic toxicity data for fish, aquatic invertebrates and algae. The marine diatom *Skeletonema costatum* is the most sensitive species in both acute and chronic tests.

Based on the available information, RAC is of the opinion that fenpyrazamine should be classified as:

Aquatic Acute 1 based on a 96-h E_rC_{50} of 0.034 mg/L for *S. costatum*. As this value is above 0.01 mg/L but ≤ 0.1 mg/L, the **acute M-factor is 10**.

Aquatic Chronic 1 based on a 96-h NOE_rC of 0.011 mg/L for *S. costatum*. As this value is above 0.01 mg/L but ≤ 0.1 mg/L, and the substance is not rapidly degradable, the **chronic M-factor is 1**. RAC disagrees with the DS's proposed chronic M-factor of 10 based on a yield NOEC of 0.0049 mg/L for *N. pelliculosa*.

Conclusion on Classification

RAC agrees with the DS's proposal with the exception of the chronic M-factor. This classification was based on the substance being not rapidly degradable, non-bioaccumulative and very toxic to aquatic organisms.

Fenpyrazamine should be classified as Aquatic Acute 1 (H400), M=10 and Aquatic Chronic 1 (H410), M=1.

ANNEXES:

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

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and rapporteurs' comments (excl. confidential information).