Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

pyridaben (ISO)

EC number: 405-700-3
CAS number: 96489-71-3

CLH-O-0000002480-82-02/F

Adopted

23 August 2013

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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: pyridaben (ISO)

EC number: 405-700-3

CAS number: 96489-71-3

The proposal was submitted by **the Netherlands** and received by the RAC on **18 December 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

The Netherlands 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 **18 December 2012**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **1 February 2013**.

ADOPTION OF THE OPINION OF THE RAC

Rapporteur, appointed by RAC: **Bogusław Barański**

Co-rapporteur, appointed by RAC: **Stephen Dungey**

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 **23 August 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 **pyridaben (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 statement Code(s)	Pictogram Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard state-ment Code	
Current Annex VI entry	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	Acute Tox. 3* Acute Tox. 3* Aquatic Acute 1 Aquatic Chronic 1	H331 H301 H400 H410	GHS06 GHS09 Dgr	H331 H301 H410		
Dossier submitters proposal	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	Removal of * from Acute Tox. 3					Addition of an acute M-factor of 1000 Addition of a chronic M-factor of 1000
RAC opinion	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	Acute Tox. 3 Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H301 H400 H410	GHS06 GHS09 Dgr	H331 H301 H410		Addition of an acute M-factor of 1000 Addition of a chronic M-factor of 1000
Resulting Annex VI entry if agreed by COM	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	Acute Tox. 3 Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H301 H400 H410	GHS06 GHS09 Dgr	H331 H301 H410		M = 1000 M = 1000

Classification and labelling in accordance with the DSD

	Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits
Current Annex VI entry	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	T; R23/25 N; R50-53	T; N R: 23/25-50/53 S: (1/2-)36/37-45-60-61	
Dossier submitters proposal	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	T; R23/25 N; R50-53		SCL: N; R50-53: C ≥ 0.025% N; R51-53: 0.0025% ≤C <0.025% R52-53:0.00025% ≤ C < 0.0025%
RAC opinion	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	T; R23/25 N; R50-53		SCL: N; R50-53: C≥ 0.025% N; R51-53: 0.0025% ≤ C < 0.025% R52-53:0.00025% ≤ C < 0.0025%
Resulting Annex VI entry if agreed by COM	613-149-00-7	pyridaben (ISO); 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one	405-700-3	96489-71-3	T; R23/25 N; R50-53	T; N R: 23/25-50/53 S: (1/2-)36/37-45-60-61	N; R50-53: C≥0.025% N; R51-53: 0.0025% ≤ C < 0.025% R52-53:0.00025% ≤ C < 0.0025%

SCIENTIFIC GROUNDS FOR THE OPINION

RAC general comment

The only hazard classes considered by RAC were those of acute toxicity and the environment.

Please note that references cited here can be found in the CLH report and/or the background document to the opinion; references not quoted in the above documents are however included at the end of this opinion for the sake of convenience.

HUMAN HEALTH HAZARD ASSESSMENT

RAC evaluation of acute toxicity

Summary of the Dossier submitter's proposal

Pyridaben has currently the harmonized classification of acute oral and inhalation toxicity in the Annex VI to CLP Regulation: Acute Tox. 3* (H301) and Acute Tox. 3* (H331); and T; R23/25

The Dossier Submitter provided the following data on oral and inhalation toxicity of pyridaben indicating that the "*" could be removed:

Method	Results	Remarks	Reference
Oral toxicity			
OECD 401 OECD 401 OECD 401 OECD 401 OECD 401 OECD 401	**LD_{50} male: 161 mg/kg bw** LD_{50} female: 181 mg/kg bw LD_{50} female: 205 mg/kg bw LD_{50} male: 253 mg/kg bw LD_{50} female: 383 mg/kg bw LD_{50} male: 424 mg/kg bw LD_{50} female: 570 mg/kg bw LD_{50} male: 1100 mg/kg bw LD_{50} female: 820 mg/kg bw LD_{50} male: 1350 mg/kg bw	Rat, CD strain Mouse, Crj:CD-1 (ICR), females Mouse, Crj:CD-1 (ICR), males Mouse, Crj:CD-1 (ICR) Rat, Crj:CD (SD) Rat, CD strain	DAR 2007, Vol 3 B 6 DAR 2007, Vol 3 B 6 DAR 2007, Vol 3 B 6 DAR 2007, Vol 3 B 6 DAR 2007, Vol 3 B 6 DAR 2007, Vol 3 B 6
Inhalation toxicity			
OECD 403	**LC_{50} female: 0.62 mg/L** LC_{50} male: 0.66 mg/L	Rat, Fischer (F344/Ducrj)	DAR 2007, Vol 3 B 6

Based on these data the Dossier Submitter concluded that according to the CLP pyridaben should be classified as Acute Tox. category 3 for the oral route because the lowest LD_{50} is within the limits, 50 < ATE ≤ 300 (oral, mg/kg bw) and Acute Tox. category 3 for the inhalation route because the LC_{50} is within the limits, 0.5 < ATE ≤ 1.0 (dusts and mists (mg/L)). Pyridaben is classified as such already in Annex VI, table 3.1. Therefore, the minimum classification Acute Tox Cat 3* is considered no longer necessary and consequentially the * can be removed. [Font]The current classification according to 67/548/EEC should remain unchanged.

Comments received during public consultation

Three MSCAs expressed support for the classification of pyridaben as acute tox. 3 (H301 and H331) based on the data provided.

Assessment and comparison with the classification criteria

The lowest acute oral LD_{50} of pyridaben was found in rats to be 161 mg/kg bw in male and 181 mg/kg bw in female rats and 205 mg/kg bw for female and 253 for male mice.
Since the acute oral median lethal dose (LD_{50}) of pyridaben to rats and mice is within the range of 50 < ATE ≤ 300 (oral, mg/kg bw), this substance meets CLP classification criteria for category Acute Tox 3 with hazard statement H301.

The acute (4 hours exposure) median lethal concentration LC_{50} for inhalation of pyridaben (as an aerosol) was found in rats to be 0.62 mg/L in males and 0.66 mg/L in females.
Since the acute median lethal concentration (LC_{50}) for inhalation of pyridaben for rats is within the range 0.5 < ATE ≤ 1.0 (dusts and Mists, mg/L), this substance meets CLP classification criteria for category Acute Tox 3 with hazard statement H331.

ENVIRONMENTAL HAZARD ASSESSMENT

RAC evaluation of environmental hazards

Summary of the Dossier submitter's proposal

Pyridaben is already classified in Annex VI of the CLP Regulation as Aquatic Acute 1 (H400) and Aquatic Chronic 1 (H410), but without harmonized M-factors. The Dossier Submitter proposed to set an M-factor of 1,000 for both acute and chronic hazard in accordance with CLP (with equivalent specific concentration limits under the DSD). This proposal was based on short- and long-term marine invertebrate toxicity results (96-h LC_{50} of 0.67 µg/L and 35-d NOEC of 0.047 µg/L, respectively), together with the fact that the substance is not rapidly degradable (or readily biodegradable).

Comments received during public consultation

Five EU Member States indicated support for the proposal, and no further information was submitted.

Assessment and comparison with the classification criteria

Degradability:

Pyridaben is hydrolytically stable in water at pH 5, 7 and 9 at 25°C. It failed a test for ready biodegradation (achieving at most 3% mineralization in 29 days). Simulation tests in two aerobic water-sediment systems using radio-labeled substance indicated primary degradation, with a half-life of approximately 20.5 days for the total water/sediment system (results were averaged for the two test systems as well as differently radio-labelled test substance; this is not considered important for classification purposes in this case). A maximum of 6.2% mineralization occurred over 120 days.

On this basis, pyridaben does not meet the criteria for being rapidly degradable (or readily biodegradable) in the environment.

***Bioaccumulation*:**

The log n-octanol-water partition coefficient (K_{ow}) of pyridaben is >6.37 at 23°C. It therefore has a potential for bioaccumulation. However, in view of the degradability conclusion this end point does not influence the determination of an M-factor or the specific concentration limits, so was not considered further.

Ecotoxicity:

The lowest reliable ecotoxicity results were as follows (the key studies are highlighted in bold):

Trophic level	Species	Short-term result	Long-term result
Fish	*Oncorhynchus mykiss*	96-h LC_{50} = 0.73 µg/L	-
	Pimephales promelas	-	301-d NOEC = 0.28 µg/L
Aquatic invertebrates	*Daphnia magna*	48-h LC_{50} = 1.0 µg/L	21-d NOEC = 0.086 µg/L

	*Americamysis bahia**	**96-h LC_{50} = 0.67 µg/L**	**35-d NOEC = 0.047 µg/L**
Aquatic algae and plants	*Four species*	Acute E_rC_{50} > 13 µg/L	-

* The CLH report uses the former name *Mysidopsis bahia*

All toxicity values are based on mean measured concentrations, with the exception of the aquatic algal toxicity studies. The DAR (2007; but not the CLH report) indicates that test substance concentrations in the algal tests dropped below the analytical detection limit after 5 days (due to light instability), so initial measured concentrations were used (the same nominal concentration was used for each species). Only one of the tested species (*Skeletonema costatum*) experienced a significant level of growth inhibition (20% after 120 hours), so failure to maintain test concentration and lack of information on algal EC_{10}/NOECs is not considered to be relevant to the classification.

A long-term result is not available for the most acutely sensitive fish species, and there appear to be no acute data for the only species for which long-term data are available. The acute sensitivity for three species presented in the CLH report varies over an order of magnitude. The reported long-term NOEC was very similar to the reported acute LC_{50}. It is therefore relevant to consider the surrogate approach for fish.

The *Americamysis* studies were considered to provide the key data. The long-term result was obtained from a slightly longer duration than the usual 28-day test. Reproduction among dilution water control organisms did not reach the minimum requirement of the test guideline after 28 days. The study was therefore extended to 35 days, but there was no improvement in the dilution water control. All other validity criteria were satisfied, so overall the test was considered to be acceptable.

The substance is an insecticide and acaricide but no aquatic insects were included in the data set presented by the dossier submitter. RAC noted that the DAR included a long-term toxicity study with one insect species (*Chironomus riparius*), but this involved sediment as well as aqueous exposure. The NOEC in this study (based on the concentration in the aqueous phase) was two orders of magnitude higher than the NOEC obtained for *Americamysis bahia*, so it was not considered further for the classification of pyridaben.

Classification according to CLP

Acute aquatic hazard:
Acute toxicity data were available for all three trophic levels. The lowest reliable short-term aquatic toxicity result was a 96-h LC_{50} of 0.67 µg/L for the marine invertebrate *Americamysis bahia*. This result was very similar to acute toxicity values for both fish and other invertebrates. Pyridaben was therefore classified as Aquatic Acute 1 (H400), with an M-factor of 1,000 (0.0001 < $L(E)C_{50}$ < 0.001 mg/L).

Chronic aquatic hazard:
Pyridaben was not considered to be rapidly degradable. Although the CLH report indicated that long-term toxicity data were available for all three trophic levels, no information was provided for algae, and it is not clear whether the result for fish was from the most acutely sensitive species. Algae appear to be significantly less sensitive than fish and invertebrates. The lowest reported value was a 35-d NOEC of 0.047 µg/L for the marine invertebrate *Americamysis bahia*. This is supported by a similar value for *Daphnia*. These concentrations are below the threshold value of 0.1 mg/L for non-rapidly degradable substances, leading to classification as Aquatic Chronic 1 (H410) with an M-factor of 1,000 (0.00001 < NOEC < 0.0001 mg/L).

The surrogate approach was considered for fish since it was not clear what the chronic toxicity would be for the most acutely sensitive species. However, based on the lowest acute LC_{50} of 0.73 µg/L combined with the substance's lack of rapid degradability, a more stringent M-factor was not necessary.

In summary, pyridaben classification as Aquatic Chronic 1 (H410), with an M-factor of 1,000 is justified.

Classification according to DSD

The lack of ready biodegradation and a 96-h LC_{50} of 0.67 µg/L for invertebrates (with a similar value for fish) mean that pyridaben fulfils the criteria for classification with N; R50-53. The following specific concentration limits are therefore applicable:

Concentration of pyridaben in the mixture, C (w/w)	Classification of the mixture
C ≥ 0.025%	N; R50-53
0.0025% ≤ C < 0.025%	N; R51-53
0.00025% ≤ C < 0.0025%	R52-53

In summary, the RAC agreed with the original proposal of the Dossier Submitter.

ANNEXES:

Annex 1 The Background Document (BD) provides 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 the RAC boxes.

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