Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

isoxaflutole

EC number: -
CAS number: 14111-29-0

CLH-O-0000002522-82-03/F

Adopted

08 March 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: Isoxaflutole

EC number: -

CAS number: 14111-29-0

The proposal was submitted by the **Netherlands** and received by the RAC on **14 May 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 **14 May 2012.** Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **28 June 2012**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by the RAC: **Hans-Christian Stolzenberg.**

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 **8 March 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 **isoxaflutole** should be classified and labelled as follows:

Classification and labelling in accordance with CLP

	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(s)	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard state-ment Code	
Current Annex VI entry	606-054-00-7	isoxaflutole (ISO); (5-Cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl] methanone	-	141112-29-0	Repr. 2 Aquatic Acute 1 Aquatic Chronic 1	H361d*** H400 H410	GHS08 GHS09 Wng	H361d*** H410		
Dossier submitter's proposal	606-054-00-7	isoxaflutole (ISO); (5-Cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl] methanone	-	141112-29-0						Addition of M=10 (acute) M=100 (chronic)
RAC opinion	606-054-00-7	isoxaflutole (ISO); (5-Cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl] methanone	-	141112-29-0						Addition of M=10 (acute) M=100 (chronic)
Resulting Annex VI entry if agreed by COM	606-054-00-7	isoxaflutole (ISO); (5-Cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl] methanone	-	141112-29-0	Repr. 2 Aquatic Acute 1 Aquatic Chronic 1	H361d*** H400 H410	GHS08 GHS09 Wng	H361d*** H410		 M = 10 M = 100

Classification and labelling in accordance with DSD

	Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits
Current Annex VI entry	606-054-00-7	isoxaflutole (ISO); (5-cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl]methanone	-	141112-29-0	Repr. Cat. 3; R63 N; R50-53	Xn; N R:50/53-63 S:(2-)36/37-60-61	
Dossier submitter's proposal	606-054-00-7	isoxaflutole (ISO); (5-cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl]methanone	-	141112-29-0			Addition of: N; R50-53: C ≥ 2,5 % N; R51-53: 0,25 % ≤ C < 2,5 % R52-53: 0,025 % ≤ C < 0,25 %
RAC opinion	606-054-00-7	isoxaflutole (ISO); (5-cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl]methanone	-	141112-29-0			Addition of: 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	606-054-00-7	isoxaflutole (ISO); (5-cyclopropyl-1,2-oxazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl]methanone	-	141112-29-0	Repr. Cat. 3; R63 N; R50-53	Xn; N R:50/53-63 S:(2-)36/37-60-61	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 evaluation of environmental hazards

Summary of the Dossier submitter's proposal

Isoxaflutole has an existing environmental classification in Annex VI to the CLP Regulation: Aquatic Acute 1 and Aquatic Chronic 1 (CLP Regulation) and N; R50-53 (DSD). The dossier submitter (DS) has reviewed the environmental hazard data and concluded that no change to the environmental classification is necessary but proposed to update the Annex VI entry by including an acute M-factor of 10 and a separate chronic M-factor of 100 based on available chronic toxicity data.

Similarly, the following Specific Concentration Limits (SCL) according to DSD are proposed:
N; R50-53: C ≥ 2,5%
N; R51-53: 0,25% ≤ C < 2,5%
R52-53: 0,025% ≤ C < 0,25%

No other changes to the existing harmonised environmental classification are proposed.

The proposal for setting an acute M-factor is based on the acute toxicity data from test results for all three trophic levels, i.e. two fish species (*Lepomis macrochirus* and *Onchorhynchus mykiss*), one species of crustacean (*Daphnia magna*), one species of algae (*Selenastrum capricornutum*) and two tests with the duckweed *Lemna gibba*. In addition, chronic test results are available for fish (*Onchorhynchus mykiss*) and *Daphnia magna* which enable a separate chronic M-factor to be set.

The available data show that the aquatic plant *Lemna gibba* is the most sensitive aquatic species with an **EC_{50}** and an **EC_{10}** of **0.0219 mg/l** and **0.0004 mg/l**, respectively. Data on *Lemna gibba* were, therefore, considered the most appropriate for the derivation of both acute and chronic M-factors, and for SCLs according to DSD criteria.

One particular study performed with *Lemna gibba* was selected as the key study for deriving M-factors and SCLs. This study was in conformity with the relevant EPA test guidelines (U.S. EPA FIFRA Test Guidelines 122-2 and 123-2) and the exposure lasted for 14 days. The examination of the growth rate over time in this study showed that the control cultures were no longer in an exponential growth phase on days 9, 12 and 14. Any deviations from exponential growth in the controls can skew the results. For this reason, the ErC_{50} and ErC_{10} were re-calculated using measurements for days 0 to 6. This 6-day exposure time is considered to be sufficiently close to the 7-day exposure recommended in OECD guideline 221.

Regarding degradation, isoxaflutole undergoes rapid primary degradation in water through hydrolysis. However, data on primary degradation may be used for classification purposes only when it can be satisfactorily demonstrated that the degradation products formed do not meet the criteria for environmental classification. For one of the degradation products (RPA202248) an EC_{50} < 1 mg/l and a chronic NOEC of < 0.1 mg/l (*Lemna gibba*) was determined which would result in a classification as hazardous to the aquatic environment. Biodegradability of isoxaflutole was tested in an enhanced ready biodegradability study and in a water/sediment simulation test. In the enhanced ready biodegradability study, only 11% degradation was observed. In the water/sediment study, isoxaflutole disappears rapidly from the system with a DT_{50} of < 1 day. However, in the water/sediment study three degradation products were formed. For one degradation product, the DT_{50} could not be determined, while for the other two degradation products DT_{50} values of 52-97 days and 255-700 days were established.

In conclusion, while isoxaflutole hydrolysed at all pH levels tested, the degradation products do not degrade rapidly. Furthermore, tests also show that negligible mineralisation occurs. For this reason isoxaflutole is considered **not rapidly degradable**.

The above findings allow an acute M-factor of 10 ($0.01 < EC_{50} \leq 0.1$) and a chronic M-factor of 100 (non-rapidly degradable and $0.0001 < EC_{10} \leq 0.001$) to be determined according to CLP and SCLs according to DSD of:

N; R50-53: C ≥ 2,5%
N; R51-53: 0,25% ≤ C <2,5%
R52-53: 0,025% ≤ C < 0,25%

Comments received during public consultation

Two comments on the environmental classification were submitted during the public consultation by MSCAs. One MS agreed with the proposed M-Factors and SCLs. The other MS requested further clarification on the relevance of re-calculating the toxicity for *Lemna gibba* after 6 days of test duration in the context of the 14-days EPA test guidelines used i.e. U.S. EPA FIFRA Test Guidelines 122-2 and 123-2 (compared to the OECD test guideline) as this would influence the value of the proposed chronic M-factor.

Assessment and comparison with the classification criteria

Degradation
The RAC confirms the DS's conclusion that isoxaflutole is non-rapidly degradable. In spite of rapid primary hydrolytic degradation, mineralisation rates were far below the cut-off criterion of 70% within 28 days, both in an enhanced ready biodegradability test and in a water/sediment simulation study. While the RAC notes that results from tests on inherent biodegradability (e.g. OECD 302) would not be appropriate to confirm rapid degradability for classification purposes, the Committee considers the low mineralisation rate (11%) as supporting evidence for the non-rapid degradation of isoxaflutole. Moreover, in the water/sediment study, one degradation product of isoxaflutole is classifiable and two others showed high DT50 values.

Aquatic Toxicity
The particularly high sensitivity of duckweed to isoxaflutole is consistent with the substance's herbicidal mode of action. As micro-algae are about two orders of magnitude less sensitive according to the available test, it is appropriate to use the key study with *Lemna* for deriving both the acute and chronic M factors. The Committee supported the DS's argumentation for the recalculation of the study data to derive 6d ErC_{50} and ErC_{10} values, i.e. sufficiently in line with the 7d requirement of the OECD 221 guideline.

The recalculated 6-day EC_{50} of 0.0219 mg/l is well below the 1 mg/l criterion for CLP Category Aquatic Acute 1, and the corresponding acute M-factor for 0.01 < 0.0219 ≤ 0.1 mg/l is 10.

The recalculated 6-day EC_{10} of 0.0004 mg/l is well below the ≤ 0.1 mg/l criterion for CLP Category Aquatic Chronic 1 (non-rapidly degradable substances), and the corresponding chronic M-factor for 0.0001 < 0.0004 ≤ 0.001 mg/l is 100.

Conclusion on classification

Isoxaflutole is **non-rapidly degradable**. Based on a measured log Kow of 2.32, its bioaccumulation potential is low.

The RAC agrees with the DS that adequate M-factors for the existing classification of isoxaflutole's aquatic toxicity should be based on recalculated 6-day EC-values from the key study with duckweed, and that the appropriate classification are CLP Categories **Aquatic Acute 1 (H400) with M = 10** and **Aquatic Chronic 1 (H410) with M = 100.**

RAC also agrees with the proposed SCLs according to DSD:
N; R50-53: C ≥ 2,5%
N; R51-53: 0,25% ≤ C <2,5%
R52-53: 0,025% ≤ C < 0,25%

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 RAC is contained in RAC boxes.

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