Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

1*H*-benzotriazole

EC Number: 202-394-1
CAS Number: 95-14-7

CLN-O-0000007150-86-01/F

Adopted

15 September 2022

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CLN-O-0000007150-86-01/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 Regulation (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: **1*H*-benzotriazole**

EC Number: **202-394-1**

CAS Number: **95-14-7**

The proposal was submitted by **Germany** and received by RAC on **20 August 2021.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

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 **8 November 2021**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **21 January 2022**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Riitta Leinonen**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **15 September 2022** by **consensus**.

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

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	1*H*-benzotriazole	202-394-1	95-14-7	Aquatic Chronic 2	H411	GHS09 Wng	H411			
RAC opinion		1*H*-benzotriazole	202-394-1	95-14-7	Aquatic Chronic 2	H411	GHS09 Wng	H411			
Resulting Annex VI entry if agreed by COM		1*H*-benzotriazole	202-394-1	95-14-7	Aquatic Chronic 2	H411	GHS09 Wng	H411			

GROUNDS FOR ADOPTION OF THE OPINION

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

1*H*-benzotriazole has no entry in Annex VI of the CLP Regulation. The Dossier Submitter (DS) proposed to classify the substance with Aquatic Chronic 2, H411 based on a 21-day EC_{10} of 0.97 mg/L for *Daphnia galeata.*

Degradation

In a ready biodegradation study performed according to the OECD TG 301 D (GLP), no degradation was observed after 28 days either with adapted of non-adapted activated sludge. In addition, no degradation after 28 days was observed in an OECD TG 301 B study (GLP) with adapted activated sludge. The DS concluded that 1*H*-benzotriazole was not readily biodegradable.

1*H*-benzotriazole was hydrolytically stable at pH4, pH 7 and pH 9 in the OECD TG 111 (GLP) study. After 5 days the concentration of the test substance was about 100 % of the starting concentrations.

In the OECD TG 302A inherent biodegradability test (GLP), 0.8% degradation was observed after 30 days.

An atmospheric half-life of 10.7 days was calculated for the reaction of 1*H*-benzotriazole with OH radicals (AOPWIN v1.91).

Regarding photo-transformation in water, two studies were available. Under acidic and neutral pH conditions clear indications of relevant photochemical processes were observed. Under basic conditions, the ionic form of 1*H*-Benzotriazole (pKa 8.4) was dominant, showing a reduced reactivity to UV light. Aniline, phenazine and supposable an oxidation product of phenazine were identified as relevant transformation products of 1*H*-Benzotriazole.

Based on all available information, the DS concluded 1*H*-benzotriazole as not being rapidly degradable.

Bioaccumulation

There was no bioconcentration study available for fish. In an OECD TG 117 study (GLP) a log P_{ow} of 1.34 was determined. The DS concluded that the log P_{ow} predicts low potential for bioaccumulation.

Aquatic toxicity

Acute

Table Summary of relevant information on acute aquatic toxicity

Species	Results [mg/L]	Test method and experimental conditions	Reliability	Reference
Fish				
Brachydanio rerio (new name: *Danio rerio*)	96h-LC_{50}= 180 (nom.)	OECD TG 203 (GLP); semi-static; no analytical monitoring, >80% assumed based on stability data of the substance	1	Registration dossier: (Anonymous, 1993a)
Brachydanio rerio (new name: Danio rerio)	96h-LC_{50}> 100 (nom.)	Verfahrensvorschlag (F.1.1) "Letale Wirkung beim Zebrabärbling Brachydario rerio" static; no analytical monitoring	2	Registration dossier: (Anonymous, 1985)
Invertebrates				
Daphnia magna	48h-EC_{50}= 137 (nom.)	OECD TG 202 (GLP); static; no analytical monitoring.	1	Registration dossier: (Anonymous, 1993b)
Daphnia magna	48h-EC_{50}= 91 (nom.)	"Bestimmung der Schwimmunfähigkeit beim Wasserfloh - Daphnia magna-" (EC0, EC50, EC100; 24 Stunden; statisches System) Verfahrensvorschlag: Umweltbundesamt Berlin, Stand Mai 1984 (GLP); static; analytical monitoring.	2	Registration dossier: (Anonymous, 1991c)
Daphnia magna	48h-EC_{50}= 107 (nom.)	OECD TG 202; static; analytical monitoring (*	1	(Seeland et al., 2012)
Daphnia galeata	48h-EC_{50}= 15.8 (nom.)	OECD TG 202; static; analytical monitoring (*	1	(Seeland et al., 2012)
Algae				
Pseudokirchneriella subcapitata (reported as Selenastrum capricornutum)	72h-E_rC_{50}= 75 (nom.)	OECD TG 201 (GLP); static; pH 8.0-8.4; no analytical monitoring	2	Registration dossier: (Anonymous, 1994c)

(*the test concentrations were analytically verified in a separate stability test. The deviation from nominal concentrations was only 6.3 to 7.0 %.

The DS presented information for fish, *Daphnia* and algae. For fish, the 96-hour LC_{50} was above 100 mg/L. The most sensitive result for invertebrates was a 48-hour EC_{50} of 15.8 mg/L for *Daphnia galeata*. For algae there was a 72-hour E_rC_{50} of 75 mg/L for *Pseudokirchneriella subcapitata*. Thus, the DS concluded that acute aquatic classification is not warranted for 1*H*-benzotriazole.

Chronic

Table Summary of relevant information on chronic aquatic toxicity

Species	Results [mg/L]	Test method and experimental conditions	Reliability	Reference
Fish				
Danio rerio	35d-NOEC= 1.07 (arithmetic mean) (post hatch survival)	OECD TG 234 (GLP), exposure duration: 63d; flow-through; analytical monitoring	1	Registration dossier: (Anonymous, 2021)
Invertebrates				
Daphnia magna	21d-NOEC= 25.9 (nom.)	"Daphnia Reproduction Test" of OECD TG 202, Part II (Draft 7/1993) (GLP); semi-static; analytical monitoring	2	Registration dossier: (Anonymous, 1995)
Daphnia magna	21d-EC_{10}> 12.8 (nom.)	OECD TG 211; semi-static; analytical monitoring	1	(Seeland et al., 2012) (*
Daphnia galeata	**21d-EC_{10}= 0.97 (nom.)** 21d-NOEC=1.0 (nom.)	OECD TG 211; semi-static; analytical monitoring	1	(Seeland et al., 2012) (*
Algae and aquatic plants				
Desmodesmus subspicatus (previous name: *Scenedesmus subspicatus*)	72h-E_rC_{10} = 1.18 (nom.)	OECD TG 201; static; analytical monitoring	1	(Seeland et al., 2012) (*
Pseudokirchneriella subcapitata (reported as Selenastrum capricornutum)	72h-E_rC_{10}= 10.5	OECD TG 201 (GLP); static; no analytical monitoring	2	Registration dossier: (Anonymous, 1994c)
Lemna minor	7d-EC_{10}= 3.94	OECD TG 221; static; analytical monitoring	1	(Seeland et al., 2012) (*

(*the test concentrations were analytically verified in a separate stability test. The deviation from nominal concentrations was only 6.3 to 7.0 %.

There were reliable chronic aquatic toxicity tests available for fish, *Daphnia*, algae and aquatic plants. The 35-day NOEC for the fish *Danio rerio* was 1.07 mg/L. The lowest value for invertebrates was a 21-day EC_{10} of 0.97 mg/L for *Daphnia galeata*. For algae and aquatic plants, the most sensitive effect values were a 72-hour E_rC_{10} of 1.18 mg/L and a 7-day EC_{10} of 3.94 mg/L for *Desmodesmus subspicatus* and *Lemna minor*, respectively. Thus, based on the EC_{10} of 0.97 mg/L to *Daphnia galeata,* the Dossier Submitter proposed to classify 1*H*-benzotriazole as **Aquatic Chronic 2, H411** for a not rapidly degradable substance (0.1 mg/L<EC_{10}≤ 1 mg/L).

Comments received during consultation

Comments were received from 3 Member States (MS) and one National Authority (NA). The Member States agreed with the DS proposal. The NA wanted more information to consider the reliability and relevance for hazard classification regarding the key study on non-validated species *Daphnia galeata* in an OECD TG 211 test design.

In addition, the NA asked for clarifications on the appropriateness of the use of data performed on *Daphnia galeata* for aquatic hazard classification. According to the NA, OECD TG 211 states: 'Other daphnids may be used provided they meet the validity criteria as appropriate (the validity criterion relating to the reproductive output in the controls should be relevant for all species)'.

- The NA asked the Dossier Submitter for a confirmation of the test protocol validity criterion regarding 'the mortality of the parent animals (female *Daphnia*) does not exceed 20% at the end of the test'.
- According to NA, the second validity criterion of the test protocol regarding 'the mean number of living offspring produced per parent animal surviving at the end of the test above 60' was not met. NA however, considered that the *Daphnia galeata* brood size may be smaller than that of *Daphnia magna* given the smaller physical size of the organism. Therefore, they were unclear whether this cut off is appropriate to assess the reproductive output of this species.
- The NA noted also that the percentage or number of dead offspring are also not reported. If this information would be available, it would be useful to calculate the coefficient of variation (CoV) of living offspring as an indicator of experimental reliability.

The DS confirmed that the *Daphnia galeata* species is smaller than *Daphnia magna*. Seeland et al 2021 describes that the difference in brood size was coherent with different body length for the species. Another publication[1] compared both species, e.g. in their life span, first brood, total number of offspring.

Table 2. Life span, first brood, total number of offspring per adult, and the number of offspring per broods of *Daphnia galeata* and *Daphnia magna*.

	Daphnia galeata[a]	*Daphnia magna*[29]
Life span (days)	28±8	50,1±10,9
First brood (days)	9±2	9,0±0,0
Total number of offspring per adult	29±23	357,8±104,7
Number of offspring per brood	4±2	13,3±3,7

[a] Data from this study

The mean number of juveniles in the control was 37 for *Daphnia galeata* in Seeland et al., 2012 in comparison with 99 for *Daphnia magna.* Taking into account the findings in Cui et al. 2016 this reproductive output of *Daphnia galeata* seems to be normal and appropriate for the assessment for toxicity testing.

In their comments, the NA argued that the NOEC might be a preferable key endpoint for *Daphnia galeata* for hazard classification regarding that the 21-day EC_{10} of 0.97 mg/L is below the 21-day

[1] Cui, R., Kwak, J.I., & An, Y. (2016). Characteristics and Toxicity Sensitivity of Korean Dominant Species Daphnia galeata for Ecotoxicity Testing: Comparative Study with Daphnia magna. Journal of Korean Society of Environmental Engineers, 38, 193-200. https://doi.org/10.4491/KSEE.2016.38.4.193

NOEC of 1 mg/L and has confidence intervals of 0.35 – 2.7 mg/L which span the CLH classification band.

The DS did not, however, consider using the NOEC value necessary, as EC_{10} values are generally preferred over NOECs.

The NA also asked if the chronic Fish Sexual Development Test (OECD TG 234) had already been reviewed under Substance evaluation and if it could be used for aquatic hazard classification. The DS informed that the study is currently reviewed under Substance Evaluation. As the post-hatch survival of the control group at 35 days post fertilization (dpf) was very high (mean: 95.8 %), the post-hatch survival of 86.7 % at 3.34 mg/L was statistically significant. Therefore, the post-hatch survival at 1.07 mg/L (95.8 %) constitutes the 35-day NOEC for this endpoint. All the post-hatch survival rates in this test were above the validity criterion of 75 % of OECD TG 234.

Assessment and comparison with the classification criteria

Degradation

RAC agrees with the DS conclusion that 1*H*-benzotriazole is not rapidly degradable based on:

- No degradation observed after 28 days in an OECD TG 301 D test with non-adapted activated sludge.
- No surface water simulation test available.
- 1*H*-benzotriazole being hydrolytically stable at pH 4, pH 7 and pH 9.

No degradation after 28 days in two ready biodegradation tests (OECD TG 301 D and OECD TG 301 B) with adapted activated sludge and 0.8% degradation in an OECD TG 302A inherent test supported the conclusion.

Bioaccumulation

RAC agrees with the DS conclusion that 1*H*-benzotriazole has low potential for bioaccumulation even in the absence of an experimental fish bioconcentration study, as the measured low Pow of 1.34 was below the classification cut-off value of 4.

Aquatic toxicity

Daphnia magna vs *Daphnia galeata*

RAC notes that regarding the use of daphnids other than *Daphnia magna* in the OECD TG 211 study, the validity criteria of the test guideline should be met. RAC recognises however that the fulfilment of the validity criteria in the control(s) 'the mortality of the parent animals (female *Daphnia*) does not exceed 20% at the end of the test' was not explicitly mentioned in the Seeland et al (2012) article available to RAC.

RAC notes also that the test protocol validity criterion 'the mean number of living offspring produced per parent animal surviving at the end of the test is > 60' was not met. RAC, however, agrees that considering the findings from Seeland et al 2021 and Cui et al 2016 articles, presented by DS, the reproductive output of *Daphnia galeata* appears to be appropriate for the assessment of aquatic toxicity.

As indicated in ECHA's CLP Guidance (v5.0, July 2017) the EC_{10} values are preferred over NOEC values for chronic toxicity studies when both are available for the same endpoint, therefore RAC agrees to use EC_{10} of 0.97 mg/L with confidence limits of 0.35 – 2.70 mg/L as a key endpoint for *Daphnia galeata* but also recognises that the NOEC of 1 mg/L would lead to a same classification.

Acute

RAC agrees with the DS in concluding that **acute aquatic classification is not warranted** for 1*H*-benzotriazole. All reliable LC/EC_{50} values (fish, *Daphnia magna*, *Daphnia galeata* and algae) were over the cut-off value of 1 mg/L for classification, the lowest value being a 48-hour EC_{50} of 15.8 mg/L for *Daphnia galeata*.

Chronic

There were reliable chronic toxicity data available for fish, *Daphnia magna*, *Daphnia galeata*, algae and aquatic plant. The lowest value is a 21-day EC_{10} of 0.97 mg/L to *Daphnia galeata* which warrants an Aquatic Chronic 2, H411 classification for a not rapidly degradable substance (0.1 mg/L<EC_{10}≤ 1 mg/L).

RAC agrees with the Dossier Submitter proposal to classify 1*H*-benzotriazole as **Aquatic Chronic 2, H411.**

Additional references

Seeland, A.; Oetken, M.; Kiss, A.; Fries, E.; Oehlmann, J. 2012. Acute and chronic toxicity of benzotriazoles to aquatic organisms; Environ Sci Pollut Res: (19) p.1781-1790

ANNEXES:

Annex 1 The 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 RAC (excluding confidential information).