Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

penconazole (ISO); 1-[2-(2,4-dichlorophenyl)pentyl]-1*H*-1,2,4-triazole

EC Number: 266-275-6
CAS Number: 66246-88-6

CLH-O-0000007383-73-01/F

Adopted

30 November 2023

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ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON PENCONAZOLE (ISO); 1-[2-(2,4-DICHLOROPHENYL)PENTYL]-1H-1,2,4-TRIAZOLE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Substance name: penconazole (ISO); 1-[2-(2,4-dichlorophenyl)pentyl]-1*H*-1,2,4-triazole
EC number: 266-275-6
CAS number: 66246-88-6
Dossier submitter: Norway

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	1
Comment received				
We support the proposal to re-discuss to what extent these three available long-term studies are sufficient to exclude a carcinogenic potential of penconazole. From our point of view, taking into account all available information, studies can be considered sufficient to conclude on classification. However, it is noted that further information is still requested for the purpose of the PPP assessment. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agreed. RAC concludes no classification for carcinogenicity.				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	2
Comment received				
Findings observed in the available in-vitro- and in-vivo-studies on genotoxicity of penconazole do not indicate a relevant genotoxic potential. Classification for mutagenicity is not warranted. However, we noted that some of the available data are not fully reliable (supplementary				

only) to conclude on clastogenicity and aneugenicity: The available in vitro assay on chromosome aberration is of limited reliability (number of scored cells too low) and because of the statistically significant increase over the concurrent negative control in one test concentration in one experiment, the result is not clearly negative when evaluated strictly according to OECD TG 473 (2016). The available in-vivo-micronucleus test in mice is of limited reliability as well because of insufficient numbers of scored cells. Nevertheless, a negative in vitro micronucleus test is available to support the in vivo result on clasto- and aneugenicity. Further confidential data generated using technical penconazole spiked with relevant impurities is considered reliable and supports the conclusion. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf
Dossier Submitter's Response
Thank you for your comment. The confidential *in vitro* micronucleus test using technical penconazole spiked with relevant impurities is available to conclude on the genotoxic potential of penconazole *in vitro* and it can support the *in vivo* result on clasto- and aneugenicity. It can be concluded that the available *in vivo* MN study is negative, but the study does not meet the acceptability criteria since the number of analysed cells is too low.
RAC's response
Noted.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	3
Comment received				
The DS' proposal for Repr. 2, H361d is supported. Justification: In a weight-of-evidence approach, the observed developmental effects should be taken into consideration to classify penconazole (Repr. 2, H361d). This is also in line with the current harmonised classification. Furthermore, other triazoles are classified for developmental effects; possible similarities could support the weight-of-evidence approach. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agreed.				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	4
Comment received				
We agree with the proposal that classification for acute oral toxicity (oral, dermal and inhalation) is required for penconazole and the existing entry in Annex VI of the CLP Regulation should be retained. The oral ATE of 971 mg/kg bw is agreed with but rounding				

to 1000 mg/kg bw may be appropriate. For acute dermal and inhalation toxicity, no classification is required. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf
Dossier Submitter's Response
Thank you for your support.
RAC's response
Agreed that the classification for acute oral toxicity is warranted. A revised oral ATE of 970 mg/kg bw is proposed based on rounding down to 2-significant figures.

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	5
Comment received				
We agree with the proposal that classification for skin corrosion/irritation is not required for penconazole. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agreed.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	6
Comment received				
Effects observed in the available eye irritation study were below the trigger for classification as an eye irritant. Thus, we agree with the proposal that classification for serious eye damage/eye irritation is not required for penconazole. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agreed.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	7
Comment received				
We agree with the proposal that based on effects observed in the available GPMT (sensitisation rate of 15%), classification for skin sensitisation is not required for penconazole.				

ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf
Dossier Submitter's Response
Thank you for your support.
RAC's response
Agreed.

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	8
Comment received				
We agree with the proposal that data are conclusive but not sufficient for classification for STOT SE. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agreed.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2022	Germany		MemberState	9
Comment received				
Please take the contributions from the uploaded document. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA_Penconazol-final.pdf				
Dossier Submitter's Response				
Thank you for yor comment. Please find the answers to your questions below: 1a) The severity grade for the necrosis incidents are not part of the original study report. However, a description of the findings is included: All dogs of the high dose group and one male of the mid dose group showed minimal, multifocal changes in the liver in the form of monocellular hepatocyte necrosis associated with minimal inflammatory cell infiltration. Additional changes were sometimes present in the form of small, circumscribed foci characterised by loss of hepatocytes haemorrhage and inflammatory cell infiltration. Two males of the high dose group showed an additional associated change in the form of vacuolization of the hepatocyte cytoplasm, this change did not show a positive reaction to staining, and was considered to be degenerative in nature. 1b) Unfortunately, no historical control data on liver necrosis in beagle dogs are available. If ECHA sees it as necessary, we can possibly ask the Applicant if they have access to further HCD. 2a) The individual raw-data do not contain information on whether the fibrosis in dogs was multi-focal or diffuse. The severity grade for fibrosis was reported as minimal to moderate inflammatory changes in association with fibrosis (inflammation with fibrosis)				

and graded in the individual animals as inflammation with fibrosis + or inflammation with fibrosis ++. Minimal to moderate inflammatory changes in association with fibrosis (inflammation with fibrosis) were present especially in the peripheral lobular region of the liver in 10/12 animals of the high dose group; minimal changes in 3/12 animals in the mid-dose group and 1/12 animals in both the low dose and control groups were also seen. Only 2 high dose females at 52 weeks showed inflammation with fibrosis ++, whereas the other positive animals (including the three animals in the mid-dose group) showed minimal changes.

According to CLP, fibrosis is relevant to support for the classification STOT-RE. However, the severity grade for fibrosis is not further specified in CLP or in the OECD test guideline of the study. In the study report it is stated that the histopathological changes noted may be concidered to be associated with the admininistration of the test compound.

Of relevant changes in biochemistry and hematology parameters, marginally higher ALP and γ-GT values were noted for mid dose males after 26 or 52 weeks of treatment (exceeding HCD). These parameters were also significantly higher in high-dose animals.

3a) Regarding open literature, the applicant submitted their searches for open literature studies concerning penconazole. However, we considered most of these studies as not relevant and/or not reliable. Of note, some of the studies reported liver findings after penconazole exposure.

RAC's response

Thank you for providing a comprehensive response during the public consulation. After reviewing both the DE comment and the response by the DS, RAC aligns with the DS proposal to classify penconazole for STOT-RE 2; H373 (liver).

A review of the data was carried out in the previous evaluation of penconazole in 2012, at that time RAC concluded that no classification was required. RAC notes that on this occasion the DS did not submit any new data to support STOT-RE 2 classification based on the finding of liver necrosis and fibrosis. RAC identified significant functional disturbances related to liver toxicity reflected in relevant changes in clinical chemistry (and histopatholgy), at the top dose level in both the 90-day and 1-year dog studies. The top dose in both cases is not so far removed from the general guidance value for STOT RE 2, the effects are potentially indicative of severe liver toxicity and CLP guidance allows for classification proposals in such circimstances (Annex I: 3.9.2.9.9). The low incidences of biologically significant histopathological changes to the liver parenchyma at dose levels below the GV for STOT RE 2 are not considered isolated findings but due to substance exposure. This is confirmed by these same effects displaying additional incidences at the next higher dose with supportive evidence from mouse and rat repeat dose toxicity tests.

Hepatic fibrosis occurred in a small number of animals (in addition to an animal in the control group) at a dose relevant for STOT RE 2 classification (i.e. 17 mg/kg bw/d) in the 1-year dog study but jumps dramatically at the top dose of (108-110 mg/kg bw/day) to affect 10/12 animals (both sexes). Incidences of hepatic necrosis likewise show a similar response in the top dose groups of both studies. RAC concludes that the effects seen in the dogs is considered biologically significant and is sufficient for classification for STOT RE 2 H373 as proposed by the DS.

Date	Country	Organisation	Type of Organisation	Comment number
20.10.2022	United Kingdom	Syngenta	Company-Manufacturer	10
Comment received				
Page 68 of CLH report, section 2.6.3.1.3. Syngenta consider that a STOT-RE classification is not required for the liver effects in dogs and rats. ECHA note – An attachment was submitted with the comment above. Refer to public attachment Penconazole STOT-RE classification rebuttal.docx				
Dossier Submitter's Response				
Thank you for the comment. We still believe that the data should be re-discussed.				
RAC's response				
See the response to comment 9 above. RAC supports STOT RE 2 H373 as proposed by the DS.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
20.10.2022	United Kingdom	Health and Safety Executive	National Authority	11
Comment received				
Aquatic Acute classification: The DS proposes to use a conservative approach using the 96-h LC50 ≤1.13 mg/L (based on initial measured concentrations and adjustment for purity) for O. mykiss (Anon., 1984 report BW-84-5-1583 in the CLH report) noting analytical verification at termination was not included and a mean measured endpoint may be <1 mg/L. We are unclear if this position is justified given i) it is unclear if test concentrations would have declined by ≥20% over the study, and ii) RAC previously noted (in the 2012 penconazole RAC Opinion ECHA/RAC/CLH-O-0000002679-61-01/F) purity corrections were not required when measured concentrations were available. Is there wider information to support the position that the 96-h LC50 of ≤1.3 mg/L (based on initial measured concentrations) is confidently expected to be <1 mg/L based on actual penconazole concentrations? Note, the study appears to have been static but s.2.9.2.2.1 of the CLH report describes it as semi-static – please can the test design be clarified as this impacts the potential loss of test substance. In addition, the RAR description includes the 96-h LC50 as 1.2 mg/L (based on initial measured concentrations and 95% C.I. 1.0-1.6) in Table 9.2.1-3 – please can the DS clarify whether the 96-h LC50 is 1.2 mg/L or 1.3 mg/L (im) and associated confidence intervals? Also, as the study employed penconazole at 87.3% purity (below the specification purity in the CLH report), is there information to consider impurity toxicity? We note a further non-GLP acute toxicity to fish (Cyprinus carpio) study (Anon., 1984a, report 840736 in the CLH report) using penconazole (99% purity) resulted in a 96-h LC50 of 3.8 mg/L (95% C.I. 2.5-5.2 mg/L) based on nominal concentrations. OECD TG 203 validity criteria were met and the study included analytical verification at termination. With the exception of the lowest treatment (76% nominal), measured concentrations were within 20% of nominal. Noting this, it would appear that an LC50 based on mean measured concentrations would be more appropriate for hazard classification (ECHA, 2017) but this is unlikely to result in a LC50 <1mg/L.				

A further (non-GLP) static, acute toxicity to O. mykiss study (Anon, 1984 report 840735 in the RAR) is available using penconazole at a higher purity (99%) and appears to be relevant for hazard classification. The quoted study 96-h LC50 was 4.3 mg/L with a NOEC of 3.2 mg/L (based on nominal concentrations). OECD TG 203 study criteria were met although >20% loss to <0.5 mg/L was observed over the study duration for all treatments (1.0-10 mg/L nominal). Following ECHA, 2017, can a LC50 based on measured concentrations using half the detection limit for LOD be calculated?

Overall, considering these three studies and given penconazole appeared stable in wider acute ecotoxicity testing (e.g. OECD TG 201 and 202), we are unclear if the penconazole acute toxicity to fish endpoint should conservatively be considered <1 mg/L.

Aquatic Chronic classification:

We note the uncertainty regarding whether the Suprenant, 1984 21-day NOEC of ≤0.069 mg/L (based on mean measured concentrations) for Daphnia magna is a true NOEC as it was the lowest treatment, or whether the true NOEC would be lower. Please can the DS confirm if the repeat study that is mentioned (due for complete in 2022) is now available along with any additional recent ecotox information?

The DS proposes to use a 21-day NOEC of 0.032 mg a.s./L / EC10 of 0.049 mg a.s./L (based on nominal a.i. concentrations) for Daphnia magna using a formulation Memmert & Knoch (1994) as supporting study. Is there any information on co-formulants to consider their potential impact on the study endpoint?

Reference: ECHA (2017) Guidance on the Application of the CLP criteria

Dossier Submitter's Response

Aquatic Acute classification

Regarding the endpoint from study with reference Anon., 1984, report no. BW-84-5-1583
We are sorry for the confusion regarding the endpoint from this study. The agreed endpoint from this study in the previous DAR (2008) was 1.13 mg a.s./$L_{initial\ measured\ (im)}$. After receiving comments on our first draft of the CLH-report, we became aware that this endpoint had been corrected for purity. In our opinion, this is not necessary as the concentrations have been measured. We thus corrected the endpoint to ≤ 1.3 mg a.s./L_{im}, however we unfortunately did not update the endpoint in all parts of the CLH-report. The relevant confidence intervals given in the study report is 1.0 - 1.6 mg/L. The 96-h endpoint of 1.2 mg a.s./L in Table 9.2.1-3 of the *Penconazole RAR 11 Volume 3CA b-9* is **a typo.** The test was performed under **static** conditions.

Regarding the question from UK on whether there is wider information to support the position that the 96-h LC50 of ≤1.3 mg/L (based on initial measured concentrations) is confidently expected to be <1 mg/L based on actual penconazole concentrations, we can add the following.

1. The formulation study with *O. mykiss* (reference: AFT-84-056) provides an a.s. endpoint below 1 mg a.s./L.
2. In four of the aquatic studies performed with technical penconazole the concentrations fell below 80% at the end of the test (see point a-d, below). In addition, the concentrations of technical penconazole fell below 80% in several of the studies with the representative formulation. Thus, there will also be an uncertainty regarding the stability of technical penconazole in the current study (BW-84-5-1583). Studies with technical penconazole were concentrations fell below 80%:
    a. **Surprenant D.C., 1984c.** The toxicity of CGA 71818 to Fathead minnow (*Pimephales promelas*) embryos and larvae.
    Design: flow-through
    Measured concentrations: ranging 34.8 – 144 % of nominal during the test (35 day exposure)
    b. **Surprenant D.C., 1984d**. The chronic toxicity of CGA 71818 to *Daphnia magna.*
    Design: flow-through
    Measured concentrations: 31% of nominal at lowest test-concentration. Other test-concentrations within ± 20% of nominal.

c. **Grade R., 1999.** Toxicity test of CGA 71818 tech. on sediment-dwelling *Chironomus riparius* (syn. *Chironomus thummi*) under static conditions.
Design: Static, Water-sediment test.
Measured concentrations: ranging 18.9-48.3 % of nominal in spiked water test.

d. **Kley A. & Wydra V., 2009.** Toxicity of Penconazole to *Pseudokirchneriella subcapitata* in an Algal Growth Inhibition Test.
Design: static.
Measured concentrations: 78% of nominal at lowest test-concentration. Other test-concentrations within ± 20% of nominal.

In addition, in the following study (considered not valid by RMS), the concentrations fell below LOQ at the end of the test.

e. **Anon, 1984.** Acute toxicity of CGA 71818 to Rainbow trout. Study reference: 840735
Design: static
Measured concentrations: below LOQ at the end of the test for all test concentrations. Please also see our comment to this study further down in this response.

Regarding the purity of penconazole in the study Anon., 1984, report no. BW-84-5-1583
UK: Also, as the study employed penconazole at 87.3% purity (below the specification purity in the CLH report), is there information to consider impurity toxicity?

The EFSA Supporting publication on recurring issues in ecotoxicology (2019) the equivalence of the batches used in the ecotoxicological studies to the reference source need to be assessed using the European Commission guidance (European Commission, 2012). The batch used in the current study (FL 830634) has been considered not equivalent to the applicants proposed reference specification in a Tier II assessment (please see Vol. 4 for details). However, a further assessment of equivalence (further than Tier II) have not been performed for the current study, as the study in question is not used in the risk assessment for penconazole. In addition, this assessment will indicate if one or more of the impurities in the ***proposed*** reference source is not good enough covered in the batch in question, however, not the other way around. Meaning it has not been done an assessment of whether the impurities in the batch FL 830634 may contribute to the toxicity observed in the study.

The final reference specification of penconazole may also be further discussed during the peer review process.

Regarding the study on *Cyprinus carpio* (Anon., 1984a, report 840736 in the CLH report)
We agree that this is a valid fish study with an endpoint clearly above 1 mg a.s./L, however we note that there are evidence from both a.s. studies and formulation studies that *O. mykiss* is more sensitive. Thus, we are of the opinion that basing the classification on the study with *C. carpio* is not sufficiently protective.

Regarding the *O. mykiss* study Anon, 1984 report 840735 in the RAR
As stated by UK, the study was not considered valid as concentrations fell below the detection limit at the end of the test. Please see an overview of the measured concentrations in the study:

Table 9.2.1-10: Nominal concentrations, initial measured concentrations and 96h measured concentrations

Nominal concentrations (mg a.s./L)	Initial measured concentrations (mg a.s./L)	Measured concentrations 96h (mg a.s./L)*
10.0	9.37	< 0.5
5.8	5.67	< 0.5
3.2	3.6	< 0.5
1.8	1.44	< 0.5
1.0	1.08	< 0.5
Control	< 0.5	< 0.5

* In the study report it is stated that "No CGA71818 (< 0.5 mg/l) were detected after 4 days".

UK propose to calculate the endpoint based on mean measured concentrations using half the detection limit for LOD. However, RMS will note that as only two measurements are performed (at the beginning and at the end of the test), it cannot be known if the decline of the test substance occurred short after the start of the study or towards the end. Thus, such an endpoint will be highly uncertain. We would vote against such an calculation.

PS!

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON PENCONAZOLE (ISO); 1-[2-(2,4-DICHLOROPHENYL)PENTYL]-1H-1,2,4-TRIAZOLE

We note that after receiving comments on the RAR in the EFSA peer review process of the pesticide active substance penconazole,we have proposed that a new study with technical penconazole and *O. mykiss* should be provided (as the data requirements for pesticides currently is not addressed for fish (a valid study with *O. mykiss* and technical penconazole is required according to the data requirements Commission Regulation (EU) No. 283/2013).

EFSA have proposed the following way foreward in the Reporting table:
Data requirement.
The applicant to provide a new valid study with O. mykiss and technical penconazole, in order to fulfil the data requirement 8.2.1 of Commission Regulation 283/2013 or in case the study is not available to provide the clear and valid justification on why the acute study with Carp and the technical penconazole is suitable as a substitute for the study with Rainbow trout.

We do not know whether the applicant have started an acute study with *O. mykiss*, and whether it will be provided during the Stop-the-clock-period (1st quarter of 2023) or not.

Aquatic chronic classification.

The peer review process of penconazole as an active substance is currently undergoing. The applicant have provided the following information in the Reporting table:
Applicant: A new GLP compliant study to determine the effects of penconazole on reproduction to Daphnia magna, according to OECD TG 211 is now available; ***the new study can be submitted on request.***

EFSA have made the following requirement:
Data Requirement
Applicant to provide a new chronic study with Daphnia magna and technical penconazole to fulfil data requirement.
Applicant should also provide a study summary which can be added to the applicant M-II document. In addition, the applicant should provide a statistical re-evaluation of the study by Suprenant 1984d.

We expect the applicant to provide the study during the Stop-the-clock (1st quarter of 2023).

Regarding the co-formulants of the study by Memmert & Knoch (1994)
The co-formulants are given in Table C.1.5.1.2-1 of Vol. 4 for Syngenta in the RAR. One co-formulant is classified with H412, the remaining co-formulants have no classification with regard to the aquatic environment. Please see RAR Vol 4 for details.

RAC's response

Thank you for your comment. Noted.

During the preparation of the first draft opinion the new toxicity studies with penconazole on algae *Desmodesmus subspicatus*, aquatic plant *Lemna gibba* and invertebrate *Daphnia magna* were provided by applicant to EFSA/ECHA (see additional key elements in draft opinion). In addition, statistical re-analaysis of the chronic toxicity to *D. magna* (Suprenant, 1984) was also provided. RAC evaluated additional studies and data for penconazole and considers them adequate. Therefore it is appropriate to consider them relevant for classification of the substance.

RAC notes that the EC_{50} value from new acute toxicity study with *L. gibba* (7d E_rC_{50} = 0.755 mg/L) and EC_{10} value from new chronic daphnia study (21 d EC_{10} = 0.016 mg/L) are lower that the key values used for classification of the substance for acute and chronic hazard by DS (96 h $LC_{50} \leq 1.3$ mg/L for *Oncorhynchus mykiss* and 21 d NOEC ≤ 0.069 mg/L for *Daphnia magna*). However, the new study on *Lemna gibba* has no impact on the acute classification of penconazole as proposed by the DS but the new chronic daphnia study leads to a higher M factor for the chronic classification of penconazole as proposed by DS.

Overall, RAC is of the view that penconazole should be classified as Aquatic Acute 1 (H400) with M-factor of 1 and Aquatic Chronic 1 with M-factor of 10.

Date	Country	Organisation	Type of Organisation	Comment number
20.10.2022	France		MemberState	12
Comment received				
FR agrees with the acute classification, the acute M factor and the corresponding assessment proposed in the CLH report. FR agrees with the chronic classification and the chronic M factor proposal pending the submission of statistical re-evaluation of Surprenant, 1984d or the new chronic study with D.magna.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you for your comment. Noted. During the preparation of the first draft opinion the new toxicity studies with penconazole on algae *Desmodesmus subspicatus*, aquatic plant *Lemna gibba* and invertebrate *Daphnia magna* were provided by applicant to EFSA/ECHA (see additional key elements in draft opinion). In addition, statistical re-analaysis of the chronic toxicity to *D. magna* (Suprenant, 1984) was also provided. RAC evaluated additional studies and data for penconazole and considers them adequate. Therefore it is appropriate to consider them relevant for classification of the substance. RAC notes that the EC_{50} value from new acute toxicity study with *L. gibba* (7d E_rC_{50} = 0.755 mg/L) and EC_{10} value from new chronic daphnia study (21 d EC10 = 0.016 mg/L) are lower that the key values used for classification of the substance for acute and chronic hazard by DS (96 h LC_{50} ≤ 1.3 mg/L for *Oncorhynchus mykiss* and 21 d NOEC ≤ 0.069 mg/L for *Daphnia magna*). However, the new study on *Lemna gibba* has no impact on the acute classification of penconazole as proposed by the DS but the new chronic daphnia study leads to a higher M factor for the chronic classification of penconazole as proposed by DS. Overall, RAC is of the view that penconazole should be classified as Aquatic Acute 1 (H400) with M-factor of 1 and Aquatic Chronic 1 with M-factor of 10.				

OTHER HAZARDS AND ENDPOINTS – Physical Hazards

Date	Country	Organisation	Type of Organisation	Comment number
20.10.2022	France		MemberState	13
Comment received				
FR: for corrosive properties, the proposed waiver is not an acceptable waiver. Please re-considered the waiver based on criteria for corrosive to metals described in the section 2.16 of Annex I to the CLP Regulation. Note that the active substance is a solid, no adequate corrosive to metal test is available.				
Dossier Submitter's Response				
Thank you for your remark. We are of the opinion that the waiver is in line with the guideline(s) in "*Guidance on the Application of the CLP Criteria*" (version 5.0; 04.07.2017; Section 2.16); Quoating:				

"There is no reference in the definition (CLP Annex I, 2.16.1) to the physical state of the substances or mixtures that need consideration for potential classification in this hazard class. (…). According to the classification criteria only substances and mixtures for which the application of the UN Test C.1 (described in part III, *Section 37.4.1.1 of the UN-MTC) is relevant and needs to be considered. Application of classification criteria in the UN-MTC, Section 37.4 excludes solids, while 'liquids and solids that may become liquids (during transport)', have to be considered for such a classification.* *The wording 'solids that may become liquids' was developed for UN RTDG Model Regulations classification purposes, and needs further explanation. Solids may become liquids by melting (due to increase in temperature). Solids having a melting point lower than 55 °C (which is the test temperature required in UN Test C.1) must then be taken into consideration (…).* *Non-testing data* *Following parameters are helpful to evaluate corrosive properties before testing:* - *melting points for solids (…)"*
RAC's response
Noted.

PUBLIC ATTACHMENTS
1. DE-CA_Penconazol-final.pdf [Please refer to comment No. 1, 2, 3, 4, 5, 6, 7, 8, 9]
2. Penconazole STOT-RE classification rebuttal.docx [Please refer to comment No. 10]