COMPILED COMMENTS ON CLH CONSULTATION

Comments provided during consultation are made available in the table below as submitted through the web form. Please note that the comments displayed below may have been accompanied by attachments which are listed in this table and included in a zip file if non-confidential. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Last data extracted on 26.10.2022

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

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

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				

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				

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				

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

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				

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				

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				

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				

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

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.				

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.				

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]