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 22.05.2023

Substance name: pyriproxyfen (ISO); 2-(1-methyl-2-(4-phenoxyphenoxy)ethoxy)pyridine; 4-phenoxyphenyl (RS)-2-(2-pyridyloxy) propyl ether
CAS number: 95737-68-1
EC number: 429-800-1
Dossier submitter: The Netherlands

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
12.05.2023	Belgium		MemberState	1
Comment received				
Based on the results of the aquatic toxicity test on the most sensitive species (invertebrates: Mysidopsis Bahia with 96h LC50 = 0.065 mg/L, invertebrates: Daphnia magna with 21d NOEC = 0.0000088 mg/L), the fact that the substance is considered as not rapidly degradable it is justified to classify, following the classification criteria of regulation 1272/2008, as Aquatic acute 1, H400 and Aquatic Chronic 1, H410. In view of the proposed classification and toxicity band for acute toxicity between 0.01mg/l and 0.1 mg/l, an M-factor for acute toxicity of 10 can be assigned and an M-factor for chronic toxicity of 10 000 (not rapidly degradable substance and 0.000001 mg/L <NOEC ≤0.00001 mg/L) The proposed environmental classification is supported.				

Date	Country	Organisation	Type of Organisation	Comment number
11.05.2023	United Kingdom	Health and Safety Executive	National Authority	2
Comment received				
Pyriproxyfen (ISO) (EC: 429-800-1; CAS: 95737-68-1). The key study for aquatic chronic classification is the Daphnia magna reproduction study by Blakemore et al 1992 (with additional statistical analysis by Lewis et al, 2016). The GLP study is well reported following US EPA Pesticide Assessment Guidelines, 72-4(b) and broadly follows OECD TG 211. However, details of DMF solvent concentrations are not included in the CLH report and the RAR indicates that solvent concentrations in treatments may have exceeded the solvent control concentration…'The concentration of DMF in the vehicle control was a factor of 17 lower than in the 20 ng/L test concentration' While this comment appears to relate to Test 2, please can the DS provide details of solvent concentrations in controls and treatments for both Test 1 and 2. This information				

is important to consider the potential impact of the solvent and aid interpretation of the statistically significant Test 2 NOEC of 0.00002 mg/L (mm) when comparing treatments to the solvent control only.
The CLH report considers that the study 21-day NOEC is 0.000015 mg/L (mm) from Test 1. We are unclear of the basis of this endpoint given no statistically significant effects were observed in Test 1 when treatments were compared to pooled or solvent controls. The RAR states that '… while not significant, young / adult reproduction days was slightly reduced at the mean measured concentration of 0.000031 mg a.s./L' indicating this is the basis of the NOEC at the 0.000015 mg/L (mm) treatment below it. On this basis, we would consider a statistically significant NOEC should take precedence – this would result in a 21-day NOEC ≥0.000031 mg/L (mm) from Test 1.
The quoted 21-day EC10(reproduction) of 0.0000088 mg/L (mm) is derived from effects observed at all treatments in Test 2. It is below the lowest treatment (0.00002 mg/L mm) and therefore outside of the model. OECD and ECHA guidance (ECHA, 2010) recognise that estimated ECx values outside the concentration-response modelling are subject to great deal of uncertainty. In addition, the 95% CIs of 0.0000026 to 0.000016 mg/L span 2 hazard classification bands. While preference is to use an EC10 in place of a NOEC if available, we recognise the uncertainty with the extrapolated EC10 and consider a NOEC may be more statistically reliable in this instance. Alternatively, we note a 21-day EC20(reproduction) of 0.000018 mg/L is also available – this is just below the lowest Test 2 treatment of 0.00002 mg/L which represents the Test 2 NOEC if comparing to the solvent control.
Considering the long-term NOEC, EC10 and EC20 endpoints from the Blakemore et al 1992 study, the Test 2 EC10(reproduction) is the most stringent (resulting in a chronic M-factor of 10000) and is the only endpoint in the 0.000001<NOEC/ECx≤0.00001 mg/L range. However, it is the endpoint with the highest degree of uncertainty. We note the DS calculated a Test 2 EC10(reproduction) of 0.0000123 mg/L which would result in an M-factor of 1000. Given the Test 1 NOEC, the ECx endpoint with less uncertainty (EC20), and potential Test 2 NOEC (when comparing to the solvent control) lie in the 0.00001<NOEC/ECx≤0.0001 mg/L range, it appears that a weight of evidence supports a chronic M-factor of 1000.

ECHA (2010) Guidance on information requirements and chemical safety assessment Chapter R.10: Characterisation of dose [concentration]-response for environment

Date	Country	Organisation	Type of Organisation	Comment number
11.05.2023	France		MemberState	3

Comment received

Thank you for giving us the opportunity to comment this CLH proposal.
We had a look to the data in the CAR of pyriproxyfen (NL, 21 September 2012) and have the following comments:

In the CAR, there are mesocosm studies (R.P.A van Wijngaarden, 2004) which are considered key acute studies and from which a LOECcommunity of 5 µga.s./L was derived (Ri=2). This study was used to calculate a PNEC (acute) in the CAR dossier. We do not have access to the Doc IIIA to check if an EC50 is available for this study. As it is the lowest endpoint for acute studies, we ask ourselves whether this endpoint needs to be checked to determine if it should appear in section 11.5 of the CLH report. In this case, the acute M factor could be increased (100). Moreover, the BPR dossier contains an efficacy test on Aedes aegypti from which EC50 (6h) of 21.4 ng/L is derived. This

endpoint was not used in the BPR dossier because it is a target species. But as this target species is not claimed in the PPPR dossier, we wonder if this endpoint on Aedes should be taken into account for the acute classification.

Please also note that Koc value in the CLH report is different from the BPR endpoint. In the frame of the one substance/one health assessment, a harmonization of the endpoint would be valuable.
Please also note that the BPR dossier seems to contain an additional fish bioaccumulation study. However it will not change the conclusion.

We also have typo comments:
In Table 69: replace "HC biphasic model" by "HS biphasic model".
In Table 72: the data from the first line of the table (acute toxicity to fish) does not appear.
In Table 73: there is the same problem with the amphibian data.

Date	Country	Organisation	Type of Organisation	Comment number
08.05.2023	Germany		MemberState	4

Comment received

11.1 Rapid degradability of organic substances
We agree with the conclusion that pyriproxifen is not rapidly degradable based on the available data. However, with respect to the water sediment degradation study (Lewis, 2000a) the DT50 values reported in the CLH-report (Pond = 22.12 d, Lake = 27.8 d at 20°C) differ from those reported in the CAR of 2012 (Pond = 5.4 d, Lake = 7.8 d at 20°C). Could you please check and explain this difference?

11.4 Bioaccumulation:
Please note that the study on fish bioconcentration in C. carpio was judged as “not reliable” during evaluation for the renewal assessment report for pyriproxyfen (e.g. no kinetic BCF calculated, not enough consecutive analyses within ±20 % to derive a steady state, only two fish analysed per concentration). It would therefore be more appropriate to classify this study as supportive information only, and not as key study. Furthermore, according to our data the study is dated from 1998 and not 1993. Please check and correct the date, if necessary.
We agree with the overall conclusion that the substance pyriproxyfen is classified as bioaccumulative for CLH-purposes (BCF > 500), primarily based on the bioconcentration study on L. macrochirus.

Classification:
We agree with the classifications as aquatic acute 1, M = 10 based on the EC50 of 0.065 mg/L for A. bahia and aquatic chronic 1, M = 10000 based on the EC10 of 0.0000088 mg/L for D. magna.