COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

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Last data extracted on 15.10.2019

Substance name: 4,4'-oxydi(benzenesulphonohydrazide)
CAS number: 80-51-3
EC number: 201-286-1
Dossier submitter: Germany

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
24.09.2019	Finland		MemberState	1

Comment received

FI CA do not support the proposed classification of no acute classification and Aquatic Chronic 1 with M-factor of 1 for 4,4'Oxybi(benzenesulphonohydrazide).

The lowest acute value EC50 of 0.69 mg/L was obtained from the study with Daphnia magna (OECD 202, 48 h, static), based on mean measured concentrations. In our opinion this result is relevant and it would warrant the Aquatic Acute Category 1, with M-factor of 1 classification for 4,4'Oxybi(benzenesulphonohydrazide). However, the Dossier Submitter is proposing to use the test result of EC50 15 mg/L based on nominal concentrations from that study. Reasoning for this is the discovered low recovery rate (3.43 – 16.7 %) of the test substance, most likely caused by hydrolysis and the assumed toxic hydrolysis product.

Based on the available OECD 111 hydrolysis test 4,4'Oxybi(benzenesulphonohydrazide) hydrolyses fast at the temperature of 25 °C in all three pHs 4,7 and 9 (5.8 h, 7.9 h, 9.2 h, respectively). Transformation products were not identified in the test but based on chemical structure it was assumed in the CLH dossier that hydrazine and 4,4'oxybis(benzenesulfonic acid) are expected degradation products. Hydrazine has harmonised classification of Aquatic Acute 1 and Aquatic Chronic 1.

As no degradation products were identified in the hydrolysis test and no rate for transformation could be derived the Dossier Submitter is suggesting to base the classification of 4,4'Oxybi(benzenesulphonohydrazide) on data of the substance itself. FI CA do not agree with this proposal and the reasoning behind it. In our opinion the lack of identification of hydrolysis product(s) do not justify leaving them out from consideration and using nominal/initial measured concentrations in this case.

Based on the available analytical measurements it can be noted that in static and semi-static tests test concentrations did not remain 80-120 % of nominal. Therefore, the test results which are based on nominal or initial measured concentrations may be considered as invalid for classification purposes as in the absence of analytically measured concentrations at least at the start and end of test, no valid interpretation can be made. In addition, a data gap for acute toxicity to fish is identified as there is only one fish test available with measured concentration, which is a limit test.

When measured concentrations are available (e.g. algae studies) results should be based on

geometric mean measured concentrations, and where concentrations at the end of test are below the analytical detection limit, such concentrations shall be considered to be half that detection limit. In case of semi-static tests it should be clarified whether the geometric mean for each renewal period has been calculated, and if the mean exposure over the whole exposure period has calculated from these data. Recalculating algae studies' test results according to the recommendations in the CLP-guidance could affect also to the proposed long-term aquatic hazard classification.

Regarding hydrolysis test it was mentioned on p. 12 that the test was performed at 25 °C temperature, but on p. 17 temperature of 20 °C was mentioned instead. Would you please clarify the correct temperature.

In addition, in our opinion the studies presented in the CLH dossier should be described more in detail e.g. based on available information it is not possible to assess properly whether validation criteria of test guidelines are fulfilled or have tests conducted in compliance with GLP.

Date	Country	Organisation	Type of Organisation	Comment number
11.10.2019	United Kingdom		MemberState	2

Comment received

4,4'-oxydi(benzenesulphonohydrazide) (EC: 201-286-1; CAS: 80-51-3)

Data:
The DS has referred to the REACH Registration dossier accessed in July 2018 (ECHA, 2018 in the CLH report) for relevant environmental endpoints. The reliability of the data is therefore described in the REACH registration without study reports being reviewed by the DS. We note that some study summaries do not include all the information to support the reliability score e.g. details of all validity criteria in ecotox tests, control and raw data, and all relevant endpoints (see below comment for chronic toxicity to fish).

Hydrolysis:
The substance undergoes significant hydrolysis at 25oC with DT50 values <12 hours. The degradation products were not identified although the DS considers that hydrazine and 4,4'-oxybis(benzenesulfonic acid) are expected hydrolysis products based on parent structure. Hydrazine has a harmonised classification of Aquatic Acute 1 and Aquatic Chronic 1 (index number: 007-008-00-3) (ECHA, 2019).

There is uncertainty regarding the toxicity of these potential degradants because these products were neither identified in the hydrolysis test, nor in aquatic ecotoxicity tests. In addition, no information on the toxicity of the expected degradation product 4,4'-oxybis(benzenesulfonic acid) is provided. It is therefore unclear whether the parent compound or the degradation products are inducing toxicity.

ECHA guidance considers that for 'substances where the degradation half-life (DT50) is less than 12 hours, environmental effects are likely to be attributed to the hydrolysis products rather than to the parent substance itself'. However it is unclear at what temperature this relates to for hydrolysis DT50s. For example, it is unclear if DT50s should be temperature corrected to 12oC, similar to the process for biodegradation endpoints. We note that such a temperature correction involves uncertainty due to extrapolation but consider that some form of consistency is required.

As mentioned above where hydrolysis DT50 values are <12 hours, it is then appropriate to base the results from static and semi-static toxicity tests on initial measured or nominal concentrations in order to account for this rapid hydrolysis and the toxicity of the degradation product (although measured concentrations of the toxic degrades are desirable). It is also practice to use mean measured concentrations if the toxicity is driven by the parent compound and actual concentrations are not within 80-120% of the nominal.

Dependant on the appropriate temperature for the hydrolysis DT50s, we are unclear whether endpoints should be based on initial measured or mean measured parent concentrations.
This is relevant for some endpoints to consider the appropriate acute classification. For example, the Daphnia magna 48 h EC50 for immobilisation is 15 mg/L based on nominal concentrations and 0.69 mg/L measured concentrations. The later would result in an Aquatic Acute 1 classification with an M-factor of 1. We note this classification mirrors the acute classification for hydrazine. Algal ErC50 values based on mean measured concentrations are not provided in the CLH report or in the online registration dossier so it is unclear if they are in the same concentration range resulting in Aquatic Acute 1 classification.

Overall, we think the DS should consider if the hydrolysis DT50 should be temperature corrected and based on this justify whether nominal/initial measured or mean measured ecotoxicity endpoints are appropriate.

Chronic toxicity to fish:
The REACH registration summary does not include endpoints for length and weight. As this is the key chronic study, these should be presented to conclude if they are or are not more sensitive.

ECHA, (2019). Summary of classification and labelling. Available: https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/13707. Last accessed 26/09/2019.

Date	Country	Organisation	Type of Organisation	Comment number
11.10.2019	France		MemberState	3

Comment received

ANSES would like to thank the German competent authority for his work and proposal.
ANSES agrees on the proposed classification for 4,4'-oxydi(benzenesulphonohydrazide) as Aquatic Chronic 1 M-factor of 1. However, ANSES is of the opinion that a classification for aquatic acute hazard 1 is suitable and could be proposed. As expressed in the classification dossier, fast hydrolysis occur and no degradation products were identified. Nevertheless, as detailed in the dossier, considering the chemical structure of the substance, the hydrolysis is expected to lead to hydrazine and 4,4’-oxybis(benzenesulfonic acid) and hydrazine as a harmonized classification as Aquatic Acute 1 and Aquatic Chronic 1 (Index number 007-008-00-3). Moreover, the Daphnia magna test used for the proposed classification show a 48hEC50 = 0.69 mg/L based on measured concentration, but the recovery rate of the parent substance was low and the degradation products were not identified. It could be assumed that it has been hydrazine that engendered this low 48hEC50. In order to ensure the maximum protection for environment, and due to the expected degradation product, already classified, ANSES is of the opinion that a classification as Aquatic Acute 1 in addition to Aquatic Chronic 1 could be proposed for 4,4'-oxydi(benzenesulphonohydrazide)

Date	Country	Organisation	Type of Organisation	Comment

				number
11.10.2019	Belgium		MemberState	4
Comment received				

Degradation
We support the conclusion that OBSH is not rapidly degradable. Although it is demonstrated that the substance degrades abiotically via hydrolysis with a half-life <16h it is not demonstrated that hydrolysis products don't fulfil the classification criteria as hazardous to the aquatic environment. Moreover, one of the expected (but not identified) hydrolysis products, hydrazine, has a harmonised classification for the environment: aquatic acute 1, H400 and aquatic Chronic 1, H410.

Bioaccumulation
A BCF study was performed, but values were below the LOD. Due to the very quick hydrolysis, OSBH is not expected to meet the bioaccumulation criterion for classification. This is confirmed in a valid QSAR estimation of log Kow (log Kow = 0.08)

Aquatic toxicity

• Acute
Fish:
Concerning the first fish study with Oryzias latipes we consider the 96h LC50 of 74 mg/l, based on nominal concentrations, invalid. No analytical monitoring was performed in this study and, although a solvent is used, it is not clear what concentrations were tested.

Invertebrates:
We agree that due to quick hydrolyzation of OBSH (half-life of 7.9h at pH7 and 25°C <12h) the toxicity observed in the first study with Daphnia magna (48h EC50 = 15 mg/L-nom) are more likely due to the hydrolysis products, The recovery rate of OBSH in this study was 3.43 to 16.7 % of the nominal concentrations.
Although degradation products were not identified in the hydrolysis study hydrazine and 4,4'-oxybis(benzenesulfonic acid) can be expected as hydrolysis degradants based on the chemical structure of OBSH.

In the registration dossier of hydrazine a mean 48hEC50 of 0.175 mg/L for Daphnia magna is reported, which is in the same order of magnitude as the measured EC50 of 0.69 mg/L of the OBSH Daphnia study.

Algae;
Following CLP guidance I.4.1. a) half of the detection limit should be used when concentrations at the end of the test are below the analytical detection limit.

The result of the first algae study is expressed as nominal concentrations while result of analytical monitoring showed that OBSH was not detected in all samples at the end of the test (72 hrs).
The second study with Pseudokirchniriella subcapitata 72hErC50= 0.7 mg/L is based on initial measured concentrations as at the end of the test no test material could be determined analytically. Measured concentrations at 72h were below 0.01 mg/L, thus resulting in a EC50 of 0.005 mg/L

• Chronic aquatic toxicity:
Algae: see acute toxicity: same remark for the chronic values.