HAZARD ASSESSMENT

OUTCOME DOCUMENT

for

EC/List number	CAS number	Substance name
403-080-9	92484-48-5	Sodium 3-(2H-benzotriazol-2-yl)-5-sec-butyl-4-hydroxybenzenesulfonate

Member State(s): Spain

Dated: 23 January 2023

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1. HAZARD SUBJECT TO ASSESSMENT

The substance covered in this document (EC 403-080-9) was selected for hazard assessment in order to clarify suspected hazard properties:

PBT/vPvB

2. OUTCOME OF HAZARD ASSESSMENT

The available information on the substance and the hazard assessment conducted has led the assessing Authority to the following considerations, as summarised in the table below.

Hazard Assessment Outcome	**Tick box**
According to the authority's assessment the substance does not have PBT/vPvB properties based on the currently available information.	X
According to the authority's assessment the substance has PBT/vPvB properties.	
According to the authority's assessment further information would be needed to confirm the PBT/vPvB properties but follow-up work is not relevant or carried out at present.	

This outcome is based on the REACH and CLP data as well as other available relevant information.

3. BASIS FOR REASONING[1]

The Substance EC 403-080-9 is a sodium salt of 3-(2H-benzotriazol-2-yl)-5-sec-butyl-4-hydroxybenzenesulfonic acid. The Substance is reported to have a pKa value of 7.93 and three functional groups that are eligible for ionisation: sulfonic acid, phenolic group (acid) and aza-group (base). Having the sulfonic acid group affects ionisation of the Substance. The salt is expected to dissociate when in contact with water, and hence, the PBT assessment has been performed on the free acid form of the Substance.

Additionally, the Substance has slight surface-active properties (surface tension < 60 mN/m). Due to ionisation of the Substance the surface tension could vary with different the pH values, which could result in some uncertainty in the measured log Kow value, as well as, in the QSAR predictions on log Kow and log D. Nevertheless, due to ionisation, log Kow and log D values are not very good predictors of the environmental behaviour of the Substance.

Structurally related substance (Metabolite M1)

The assessment is also supported by the structurally related substance 3-[3-(2H-Benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propionic acid (EC 630-348-4), referred to as M1 in this document.

M1 is similar to the free acid form of the Substance; only differing in the acid group (propionic acid instead of sulfonic acid) and in the branching of the butyl substitution group. Sulfonic acids are analogous to carboxylic acids, resulting in similar properties. However, sulfonic acids are much stronger acids than their corresponding carboxylic acids.

PBT concerns on M1 (3-[3-(2H-Benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propionic acid;

[1] Assessments of PBT properties are based on Annex XIII to the REACH Regulation.

EC 630-348-4) have been removed. The metabolite M1 meets the criteria for P and vP according to Annex XIII of REACH but based on the available information, it has limited bioaccumulation potential and does not meet the criteria for B/vB. In conclusion, the metabolite M1 is not PBT/vPvB according to Annex XIII of REACH.

Persistence

In the available OECD TG 111 study, the Substance is considered hydrolytically stable with a half-life of more than one year at 25 ºC and pH of 4, 7 and 9.

In a ready biodegradability screening test (OECD TG 301A, 1981), based on DOC removal, no degradation of the Substance was observed after 28 days. Additionally, in a supporting BOD5/COD study following EU Method C.5 (Degradation: Biochemical Oxygen Demand) no or negligible biodegradation of the Substance was observed after 5 days. Both studies are available in the registration dossier of the Substance.

Furthermore, the results of the QSAR models BIOWIN 2, 3 and 6 indicate that the free acid form of the Substance should be considered as a borderline case for meeting the screening criteria for P/vP included in ECHA Guidance R.11. It is noted that the triazole group is not included as a fragment in the BIOWIN models, which adds uncertainty to the predictions. In addition, based on the CATALOGIC 301C QSAR model prediction, the acid form of the substance is likely to be persistent.

Hence, the Substance screens for P/vP.

No simulation studies are available for the Substance. However, information on the structurally related substance M1 (EC 630-348-4) (see above information on the structural similarity of M1 and the Substance) is available from an OECD 308 study with another phenolic benzotriazole substance (EC 407-000-3). In this study M1 was identified as a major degradation product. M1 was formed in the water phase and dissipated rapidly in a few days to the sediment compartment. In the sediment, M1 is persistent with calculated disappearance half-lives up to 238 and 248 days (at 20 °C) in pond sediment under aerobic and anaerobic conditions. As the disappearance in this case has to be faster than the degradation of M1, DegT50-values in turn have to be higher than the DT50-values. Moreover, the DT50 values are expected to be even higher if converted to environmentally more relevant temperature of 12°C. This study and the results recalculated for the degradation product M1 by the German CA were discussed and accepted by the Member State Committee during the SVHC identification of the UV-320 (EC 223-346-6), UV-327 (EC 223-383-8), UV-328 (EC 247-384-8) and UV-350 (EC 253-037-1) substances. In conclusion, the structurally related substance M1 fulfils the criteria for P and vP according to Annex XIII of REACH.

It is noted that the sec-butyl group in the Substance can be more easily degraded than the tert-butyl group in M1. Based on BIOWIN QSARs and EAWAG-BBD predictions, the sulfonic acid (in the Substance) group may be more difficult to degrade than the propionic acid (in M1). However, all in all, the screening test results and the QSAR models suggest that the degradation of the free acid form of the Substance is slow and similar to that of M1. Therefore, as the DT50 values determined for M1 were well above the vP criterion in sediment, it can be concluded that the 3-(benzotriazol-2-yl)-5-butan-2-yl-4-hydroxybenzenesulfonic acid is also likely P/vP.

Bioaccumulation

Based on the predicted and measured log Kow values, the Substance is expected to have very low bioaccumulation potential and it does not screen for B/vB. The BCFBAF (v3.01) regression based QSAR model predicts low BCF value (3.16 L/kg) for the Substance based on the predicted log Kow of 1.24 (KOWWIN) and the Substance being ionisable. The model recognises all fragments of the Substance, including the sulfonic acid/salt with aromatic attach fragment.

However, the distribution coefficient log Dow at neutral pH has been considered more relevant for predicting bioaccumulation potential of ionisable substances than the log Kow of the neutral form. A log D of -2.62 at pH 7 is predicted for the free acid form of the Substance, which indicates low bioaccumulation. Recent studies have shown that octanol-water partitioning coefficients (log Kow and log D) may not be good predictors of the bioaccumulation potential of ionisable substances (e.g. Mueller et al 2020). Other processes than lipophilicity may affect the uptake and accumulation of ionisable substances in organisms, e.g. sorption to membranes or protein binding. No alert was found in the QSAR Toolbox for the Substance, i.e. the Substance does not match the structural criteria specified in the boundaries of the profiler regarding protein binding based on OECD criteria. However, it is noted that the model neither shows alerts for PFOS, which are known to bioaccumulate by protein binding.

There is no experimental data on the bioaccumulation of the Substance. However, in a dietary OECD 305 study with structurally related substance M1 (Schlechtriem et al 2020), a tentative BCF of 203 and a BMF of 0.037 were calculated. These results indicate low bioaccumulation and biomagnification potential for M1. The OECD 305 test shows that the $t_{1/2}$ of M1 in fish liver is 0.703 days with a depuration rate k_{2g} of 0.99, which indicate that high biotransformation of M1 is expected in fish. Based on the measured and predicted water solubility and log Kow and log D values, the Substance (both the neutral and ionised forms) seems to be more water soluble and less lipophilic than M1. Therefore, the Substance could have even lower bioaccumulation potential than M1. The difference in the acid group could lead to differences in the sorption and bioaccumulation behaviour of M1 and the free acid. However, based on the BCFBAF predictions on biotransformation half-life and information on other anionic substances assessed in the OECD 305 studies by Schlechtriem et al (2020), biotransformation of the free acid of the Substance can be expected, which likely leads to formation of metabolites that are more easily excreted than the parent substance.

No toxicokinetic data is available on the Substance nor on the similar substance M1. However, in the available mammalian toxicokinetic study on EC 400-820-2 and another structurally similar substance (CAS 84268-08-6), M1 was observed as major metabolite. In these studies, most of the radioactivity was eliminated rapidly and only minimal amounts remained in the test animals after 48-168 hours. This could suggest that M1 is rapidly eliminated in mammals.

The metabolism behaviour of the free acid was predicted in Meteor Nexus (Lhasa Nexus v.3.1.0) by ECHA. Based on the model prediction, it seems that the free acid is eligible to undergo hydroxylation of the butyl-group and subsequent glucuronidation or oxidation of the OH-groups in the aliphatic alcohol. The model did not predict any reactions in the sulfonic acid moiety. It is noted that for M1, Meteor Nexus predicts glucuronidation of the carboxylic acid and phenolic-OH but no hydroxylation of the tert-butyl group. Hence, although the metabolism pathways of the free acid and M1 may differ, according to the model predictions, glucuronidation leads to formation of metabolites which can be quickly excreted for both substances.

In conclusion, based on the available information M1 has low bioaccumulation potential and does not fulfil the B/vB criteria according to Annex XIII of REACH. As a consequence, based on the structural similarity to M1, predicted biotransformation of the Substance in fish and mammals, and the Substance being more water soluble and less lipophilic than M1, similar low bioaccumulation potential in fish and in mammals as for M1 is expected for the Substance (both the neutral and ionised form of the free acid).

Toxicity

The substances have no harmonised classifications for Carc. 1A/1B, Mut 1A/1B, Repr. 1A/1B/2 or STOT RE 1/2.

No data are available for long-term toxicity studies on fish nor invertebrates. ECOSAR predicts low chronic toxicity in fish (ChV values 123-206 mg/L) and daphnia (ChV values 58-101 mg/L) for baseline toxicity, benzotriazoles-acid and phenols-acid classes.

An algal toxicity test performed according to EU method C.3 and OECD guideline 201 (version 1993) is available for the Substance with the green algae *Pseudokirchnerella subcapitata.* showing a 72h-NOErC of 4.3 mg/L (nominal concentration). No detailed information on the results are given in the registration dossier and hence it is not possible to assess whether the validity criteria of OECD TG 201 were met (e.g. regarding constant exponential growth in the controls).

There is no experimental information available on the aquatic toxicity of the structurally related substance M1. Based on the available QSAR predictions for aquatic toxicity, the metabolite M1 is not likely to meet the criterion for T. However, no firm conclusion can be drawn. Based on the available information on toxicity, there does not seem to be a concern on possible T properties for human health.

Based on the available ecotoxicity data, not possible to conclude on toxicity, however the substance is not likely to meet the criterion for T.

Overall conclusion:

Overall, based on the available information, the Substance (free acid form) is concluded to be likely P/vP but not B/vB, and therefore, it does not fulfil the PBT/vPvB criteria of REACH annex XIII.

The Substance is currently under Substance Evaluation to clarify concern for PMT/vPvM concern.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

Indication of a tentative plan is not viewed as a commitment by the authority. Any commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Follow-up action	Date for intention	Actor
SEv	03/2023	Spain

REFERENCES

Schlechtriem, C; Ebersbach,I; Müller, C.; Kühr, S; Goss, K-U; Trapp, S.; Polesel, F (2020). Bioaccumulation of ionic compounds - Deriving of alternative screening criteria from experimental studies. Final report. TEXTE 00/2019. UBA, German Environment Agency. Dessau-Roßlau, November 2020.