HAZARD ASSESSMENT

OUTCOME DOCUMENT

for

EC/List number	CAS number	Substance name
407-000-3	127519-17-9	A mixture of branched and linear C7-C9 alkyl 3-[3-(2H-benzotriazol-2-yl)-5-(1,1-dimethylethyl)-4-hydroxyphenyl]propionates
400-830-7	-	A mixture of: α-3-(3-(2H-benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl)propionyl-ω-hydroxypoly(oxyethylene); α-3-(3-(2H-benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl)propionyl-ω-3-(3-(2H-benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl)propionyloxypoly(oxyethylene)
400-820-2	84268-33-7	methyl 3-[3-(2H-1,2,3-benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propanoate
630-348-4	84268-36-0	3-[3-(2H-Benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propionic acid

Member State(s): Spain

Dated: 28 January 2022

Disclaimer:

The information and views set out in this document are those of the evaluating authority and do not necessarily reflect the position or opinion of the other Member States or ECHA. Neither ECHA nor the evaluating authority nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any formal regulatory activities that ECHA or the Member States may initiate at a later stage. Hazard assessments and their outcomes are compiled on the basis of information available by the date of the publication of the document.

1. HAZARD SUBJECT TO ASSESSMENT

The three substances covered in this document (EC 407-000-3, EC 400-830-7 and EC 400-820-2) were originally 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 parent substances EC 407-000-3, EC 400-830-7 and EC 400-820-2 and their major metabolite M1 (3-[3-(2H-Benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propionic acid; EC 630-348-4) belong to a group of phenolic benzotriazoles, which are used as ultraviolet-light absorbers. The parent substances covered in this document are very similar. They contain a benzotriazole central moiety with a 2-phenol attached at the 2-position. Substituents on the phenol are a tert-butyl at position 3 and an ester at position 5 of the phenyl ring. The only structural difference is the side chain connected to the carboxylic moiety at position 5 of the phenyl ring. In EC 400-830-7, at position 5 of the phenyl ring a CH2-CH2-COO group is connected to a (C2H4O)n group (n is typically in the range of 2 to 10). In EC 407-000-3 branched or linear C7-C9 alkyl chains and in EC 400-820-2 a methyl group is connected to the CH2-CH2-COO group. The metabolite M1 is a degradation product formed through the cleavage of the ester bond in the parent substances.

Persistence

Parent substances

In the available OECD 111 test with EC 400-830-7 slow hydrolysis was observed at pH 7 and 9 while at pH 4 a half-life of 7.54 days was reported. No tests on abiotic degradation of the other two parent substances are available but the constituents of the substances have an ester functional group in one of the side chains of the phenol group, which is expected to be susceptible to hydrolysis. The other functional groups of the constituents are expected to resist hydrolytical degradation.

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

In the ready biodegradability screening tests with EC 407-000-3, EC 400-830-7 and EC 400-820-2 slow degradation (ranging from < 10% to 24 %) was observed after 28 days, and thus, the substances screen P/vP.

The parent substances EC 407-000-3 and EC 400-830-7 are UVCB substances and thus the PBT assessment should take into account all relevant constituents. Based on BIOWIN QSAR models, which are not fully reliable for benzotriazole substances, all the constituents of these substances meet the screening criteria for persistence or are borderline cases for meeting the criteria.

However, in the available water-sediment simulation studies (OECD 308) with EC 407-000-3, the parent substance disappeared rapidly (whole system DT50 5.2-6.5 d under aerobic conditions and 15.2 d under anaerobic conditions) and a major degradation product was formed. Hence, it seems that rapid primary degradation through hydrolysis of the ester bond in the side chain of the phenol ring occurs. As all the constituents of the parent substance have an ester bond in the same position, and they only differ in the length and branching of the side chain connected to the ester bond, a similar degradation pathway can be expected for all of them. In conclusion, it seems that the constituents of the parent substance do not fulfil the criteria for P/vP according to Annex XIII of REACH.

No simulation studies are available for the other two substances, EC 400-830-7 and EC 400-820-2. The registrants of EC 400-830-7 have used read across from the simulation study with EC 407-000-3. All three substances are very similar and have an ester bond in the same position. Therefore, similar primary degradation leading to formation of M1 as major degradation product is expected for them. The degradation pathway predictions made for the substances also support this conclusion.

In conclusion, the constituents of the parent substances do not seem to fulfil the criteria for P/vP according to the Annex XIII of REACH.

Metabolite M1

There are no ready biodegradability tests available on the metabolite M1. Based on the BIOWIN QSAR predictions, which are not fully reliable, the metabolite is a borderline case for meeting the screening criteria for P/vP. The similar substances UV-320, UV 327 and UV-328 showed no or very little degradation in OECD 301 C and B tests.

In the OECD 308 studies with the parent substance EC 407-000-3, metabolite 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 metabolite M1 by the German CA were discussed and accepted by the Member State Committee during the SVHC identification of the UV-320, UV-327, UV-328 and UV-350 substances. In conclusion, the metabolite M1 fulfils the criteria for P and vP according to Annex XIII of REACH.

Bioaccumulation

Parent substances

Based on the predicted and measured log Kow values, the constituents of the three substances screen B/vB. However, the available experimental BCF values in fish for the whole substances

EC 407-000-3 and EC 400-830-7 are low although it is noted that the studies are not fully reliable. The BCFBAF QSAR models predict high BCFs for some of the branched constituents of EC 407-000-3 when using the regression model but low bioaccumulation potential is predicted by the Arnot-Gobas model for all the constituents of the substance when taking into account biotransformation estimations. For EC 400-830-7 and EC 400-820-2 the predicted BCF values are low. The available toxicokinetic data on mammals available for EC 400-820-2 and other similar substances suggest that the constituents of the parent substances may be susceptible to biotransformation through enzymatic hydrolysis of the ester bond, which may lead to low bioaccumulation of the parent substances. The apparent half-life was less than 12 hours and minimal amount remained 48 hours after dosing. However, it is noted that the metabolism may differ between mammals and fish.

In conclusion, the constituents of the parent substances are not likely to meet the criteria for B/vB according to Annex XIII of REACH.

Metabolite M1

Low BMF (0.037) and high depuration rate (1.29 day^{-1}) were determined in a dietary OECD 305 study with metabolite M1 and a tentative BCF of 203 was calculated. These results indicate low bioaccumulation potential.

The predicted log Kow values of the metabolite are in the range of 3.0-5.15 depending on the QSAR model used. The BCFBAF (v3.01) regression based QSAR model predicts low BCF value (3.16 L/kg) for the metabolite M1 based on the predicted log Kow of 3.3 (KOWWIN) and the metabolite being ionisable.

M1 is mainly present in the ionised form at environmentally relevant pHs and therefore log Dow is considered a better predictor of the bioaccumulation potential of M1 than the log Kow of the neutral form. The predicted log Dow values of M1 at pH 7 are in the range of 1.58-3.32, which also indicate limited bioaccumulation potential.

As the substance is ionisable, also other processes than lipophilicity may affect the uptake and accumulation in organisms, e.g. membrane sorption and protein binding. However, the phospholipid-water partition coefficient predicted for M1 using COSMOmic model does not indicate concern for bioaccumulation via membrane sorption either.

Regarding protein binding potency, no alert for M1 has been found in the QSARToolbox. M1 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 bioaccumulated by protein binding.

In the available mammalian toxicokinetic studies on EC 400-820-2 and another similar substance (CAS 84268-08-6), the metabolite 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 the metabolite M1 is rapidly eliminated in mammals. Similarly, the available information from the OECD 305 test shows that the $t_{1/2}$ in fish liver is 0.703 days with a depuration rate k_{2g} of 0.99, which indicate that high metabolization is expected in fish.

The metabolism behaviour of M1 was predicted in Meteor Nexus. Based on the model prediction, it seems that M1 may go immediately into phase II metabolism that may lead to quick conjugation (glucuronidation) and excretion.

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.

Toxicity

Parent substances

The substances have no harmonised classifications for Carc. 1A/1B, Mut 1A/1B, Repr. 1A/1B/2 or STOT RE 1/2. However, it is noted that two of the registrants of EC 407-000-3 have self-classified the substance as STOT RE 2 and for EC 400-830-7 classification as STOT RE 1 is reported in the C&L inventory.

Based on the available ecotoxicity data, the substances are not likely to meet the criterion for T. However, no firm conclusion can be drawn since for EC 400-820-2 no long-term aquatic toxicity studies are available, and for EC 407-000-3 and EC 400-830-7 no long-term tests with fish are available.

Metabolite M1

There is no experimental information available on the aquatic toxicity. 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.

Overall conclusion:

Overall, based on the available information, the parent substances EC 407-000-3, EC 400-830-7 and EC 400-820-2 themselves do not fulfil the PBT/vPvB criteria of REACH annex XIII.

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

It is noted that if/when the criteria for PMT/vPvM substances under REACH are defined, it should be assessed whether M1 could be considered vPvM as it is very persistent, and the ionised form is expected to have high water solubility and low log Koc.