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Helsinki, 15 August 2019

Registered substancesubject to this decision, hereafter 'the Substance': Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides
EC number: 264-120-7
CAS number: 63393-96-4
Date of latest submission(s) considered: 3 August 2018
Decision/annotation number: Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXXX-XX-XX/F)
Addressee(s): Registrant(s)[1] of Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides.

DECISION ON SUBSTANCE EVALUATION

In accordance with Article 46(1) of the REACH Regulation (Regulation (EC) No 1907/2006), you must submit the following information on the Substance:

1. Solubility in pure n-octanol at 20°C; CIPAC method MT 181 (Solubility in Organic Solvents)[2] can be used for testing. Alternatively, for solubilities below 10 g/L or for higher precision, OECD Test Guideline 105 (Water Solubility) may also be adapted.
   Concurrently, critical micelle concentration in water (CMC) at 20°C; OECD Test Guideline 115 must be used for surface tension measurements, as specified in Appendix 1.

2. Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water - simulation biodegradation test,
   EU C.25/OECD 309, including the identification of relevant degradation products at a temperature of 12°C, as specified in Appendix 1.

3. Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, by using aqueous exposure, with measurements of the BCF in whole body and inedible portions, as specified in Appendix 1.

You must provide an update of the registration dossier(s) containing the requested information, including robust study summaries and, where relevant, an update of the chemical safety report by timelines as further defined below.

Tiered testing strategy:

Request 1: Solubility in pure n-octanol at 20°C must be determined for the registered

[1] The terms registrant(s), dossier(s) or registration(s) are used throughout the decision, irrespective of the number of registrants addressed by the decision.

[2] Collaborative International Pesticide Analytical Council. Published in CIPAC Handbook H. http://www.cipac.org/index.php/methods-publications/handbooks/handbook-h

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substance (applying the "whole substance" approach), in order to estimate the Kow as the ratio of solubility in pure n-octanol and solubility in water measured under the same temperature conditions. The water solubility is already available in the IUCLID dossier for the registered substance. Additionally, the CMC of the registered substance (applying the "whole substance" approach) must be determined and used to re-calculate the Kow instead of water solubility, so to check that the first Kow calculation is not unrealistically low.

The information required according to point 1 above must be generated and provided by **15 August 2020**. The deadline takes into account the time that you, the Registrant(s), may need to agree on who is to perform any required tests. Three months is allocated for this.

If the logKow value proves to be higher than the trigger value of 4.5 for B assessment, request 2 must be fulfilled, as foreseen by the PBT assessment strategy (ECHA guidance IR/CSA, Chapter R11: PBT Assessment, version 3.0, June 2017).

Request 2: When applicable, the information required according to point 2 above must be generated and provided by **15 February 2023**.

If the results from request 2 above show that the registered substance does not fulfil the criteria for persistence according to REACH Annex XIII Section 1.1.1 (degradation half-life in fresh or estuarine water > 40 days), no further testing is required. Otherwise, request 3 must be provided.

Request 3: When applicable, the information required according to point 3 above must be generated and provided by **15 November 2023**.

Table 1: Summary of the tiered testing strategy

Test requested	**Conditions when to perform test**	**Time**
1. Solubility in pure n-octanol at 20°C: CIPAC method MT 181 (solubility in Organic Solvents) or OECD Test Guideline 105 (Water Solubility) and Critical micelle concentration in water (CMC) at 20°C. OECD Test Guideline 115 for surface tension measurements	Unconditionally	12 months (including 3 months to decide who will perform the required testing)
2. Simulation study: OECD 309	Results from tests 1 yield an estimated logKow	30 months (including 12 months for preparation of radiolabelled test

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	higher than 4.5	material)
3. Bioaccumulation in Fish: Aqueous and Dietary Exposure: OECD 305 test	Results from test 2 show that the registered substance fulfils the criteria for P or vP according to REACH Annex XIII (degradation half-life in fresh or estuarine water > 40 days)	9 months (taking into account that 12 months for preparation of radiolabelled test material are already included in the request 2)

In addition to the robust study summaries, you must submit the full study report by the same deadline for:

Request 2.Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/OECD 309;

Request 3. Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, aqueous exposure with the registered substance.

The reasons of this decision and any further test specifications of the requirements are set out in Appendix 1. The procedural history is described in Appendix 2. Further information, observations and technical guidance as appropriate are provided in Appendix 3. Appendix 4 contains a list of registration numbers for the addressees of this decision. This appendix is confidential and not included in the public version of this decision.

Who performs the testing?

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all registrant(s) within 90 days. Instructions on how to do this are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has a suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals

Authorised[3] by Christel Schilliger-Musset, Director of Hazard Assessment

[3] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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Appendix 1: Reasons

Based on the evaluation of all relevant information submitted on Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides and other relevant available information, ECHA concludes that further information is required to enable the evaluating Member State competent authority (MSCA) to complete the evaluation of whether the substance constitutes a risk to the environment.

The evaluating MSCA will subsequently review the information submitted by you and evaluate if further information should be requested to clarify the concern for the substance being PBT/vPvB in the follow up process.

The potential risk

The identification of a potential risk is based on a combination of exposure and hazard information.

According to information in the registration dossier and in the chemical safety report the Substance is used in pH regulators and water treatment products. Industrial use results in manufacture of another substance. At the workplace, (closed) batch processing in synthesis or formulation and mixing in open batch processes are reported. Significant exposure to the environment cannot be excluded.

Based on information in the registration dossier and information from the published literature as detailed below, there is a concern that the Substance may be a PBT or vPvB substance as defined in REACH Annex XIII.

As stated in Annex I, Section 4 of REACH, conventional hazard assessment of the long-term effects and the estimation of the long-term exposure cannot be carried out with sufficient reliability for the purpose of assessing the safety of substances satisfying the PBT and vPvB criteria in Annex XIII.

Based on this exposure and hazard information, there is a potential risk for the environment. As the available information is not sufficient to conclude on potential PBT/vPvB properties, further information is needed to clarify the risk.

The possible improved risk management measures

If the obtained data from Requests 1, 2, and 3 are sufficient to confirm the suspected PBT/vPvB properties as defined in REACH Annex XIII, the evaluating MSCA will assess the need for further regulatory risk management in the form of identification as a substance of very high concern (SVHC) under Article 57 of REACH and subsequent authorisation or restriction of the Substance.

PBT assessment approach and testing strategy

The substance is registered by you as a multi-constituent substance, with four main constituents and one impurity relevant for PBT assessment. The substance is a cationic surfactant, with a water solubility value of 1023 mg/L.

The four main constituents are structurally related and only differ by the lengths of the alkyl chains (C8 or C10). Therefore, they are expected to have similar behaviour and PBT properties, so a 'whole substance' approach is used for the PBT assessment, according to REACH Guidance R.11, 2017, Section R.11.4.2.2.2.

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The P screening criterion is met, and the substance is deemed very persistent by you based on the prolonged OECD 301 D screening test result.

ECHA considers that there is sufficient information available to assess toxicity based on reprotoxic effects and therefore further testing on toxicity of the substance is not considered necessary to clarify the concern of PBT properties.

In the last dossier update (3rd August 2018) you included a PBT evaluation of three side impurities (octanol CAS: 111-87-5; decanol CAS 112-30-1; Amines, tri-C8-10-alkyl CAS: 68814-95-9) listed in the composition. None of the impurities resulted in a concern for PBT or vPvB.

Nevertheless based on the available information, there is still a concern that the substance itself may have PBT/vPvB properties.

If the outcome of the Request 1 as screening information allows to clearly exclude B property, no further testing is needed for P assessment and, consequently, for B. Otherwise the Request 2 (Simulation testing on ultimate degradation in surface water) must be performed to conclusively clarify the P/vP property. If the outcome of the Request 2 confirms the P/vP property, the Request 3 (BCF study) must be performed. This testing strategy is considered to be an efficient way to clarify the concern for P and B properties. Request 1 involves simple physicochemical tests which can be used to check whether the screening B criterion is fulfilled. If the screening B criterion is not fulfilled, then there would be no need for an expensive simulation test (Request 2) or for a vertebrate test (BCF study Request 3).

Consideration of your comments on the original draft decision

In your comments on the draft decision, you indicate that the information requests and the reasons fail to take into account the identified uses and thus do not identify the impact of the requested information on the risk assessment. This, in your view, results in lack of proportionality as the additional studies will only generate cost and data but will not lead to improved risk management measures. As indicated above ("The potential risk"), ECHA considers that there is potential for exposure to the environment. Furthermore, we explain above under "The possible improved risk management measures" which measures may result if the PBT/vPvB properties are confirmed.

In your comments you also indicate your opinion that the tiered testing strategy is not proportionate and is not in accordance with the general regulatory concept as given in REACH Article 46. In your view, you are still obliged to perform the tiered testing scheme should you decide to cease manufacture after receiving results of the first tests. This would result in unnecessary expenditure in your view. Furthermore, even if you cease manufacture after receiving the results of tier 1 or tier 2 in the testing scheme, you would be obliged to perform the final bioaccumulation test with vertebrate animals. This would, in your view, be a violation of Article 25 of REACH.

It is clear from the first section of this decision that the scheme of testing is conditional and the conditions when to perform the required tests are specified in Table 1: *Summary of the tiered testing strategy*. From the table it is clear that tests 2 and 3 do not have to be performed unconditionally.

Furthermore, the tiered testing strategy was followed in spite of the fact that this does

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potentially delay the time period to receive all relevant information to assess the PBT/ vPvB properties of the Substance, in order to avoid unnecessary animal testing.

On the cease manufacture, ECHA notes that this is a hypothetical argument as long as you do not substantiate your intention to cease manufacture at a specified date in the future. Moreover, it is an incorrect assumption that the studies which aim to assess the potential PBT/vPvB properties of a substance are no longer needed after a cease of manufacture. Thus, Article 50(4) REACH envisages the possibility to request under Article 46 REACH for further information from registrants that have ceased manufacture where there is, for example, a potential long-term risk to human health or the environment justifying the need for further information and/or where the exposure to the substance contributes significantly to that risk.

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1. Solubility in pure n-octanol to derive Kow and Critical micelle concentration in water (CMC)

The concern(s) identified and why new information is needed

The available information is not sufficient to conclude on the B or vB properties, as described in detail below.

The n-octanol/water partition coefficient (Kow) is the first step to clarify the B property of the substance (ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment, Version 3.0, June 2017). No experimental results are available, since neither the Shake Flask Method nor the HPLC Method are applicable to surface-active materials, such as Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides (surface tension: 27.0 mN/m at 20°C, determined according to OECD Test Guideline 115 by the ring method at 90% of saturation in water, i.e. 993 mg/L). According to EC test method A.8 (Partition Coefficient), corresponding partly to OECD Test Guideline 107 and partly to OECD Test Guideline 117, "*The shake-flask method applies only to essentially pure substances soluble in water and n-octanol. It is not applicable to surface active materials (for which a calculated value or an estimate based on the individual n-octanol and water solubilities should be provided). [...] The HPLC method is not applicable to strong acids and bases, metal complexes, surface-active materials or substances which react with the eluent. For these materials, a calculated value or an estimate based on individual n-octanol and water solubilities should be provided.*" Likewise, OECD Test Guideline 123 (Slow-Stirring Method) cannot be used for substances that display significant interfacial activity, either.

Consideration of logKow prediction by KOWWIN

As an alternative to experimental testing, logKow has been covered by you by QSAR calculations, performed by KOWWIN (v1.68) of EPI Suite v.4.11. The logKow values of the individual quaternary ammonium constituents are in the range 6.1 to 9.1, based on calculated values of water solubility (in the range 0.0016–0.000015 mg/L for the individual quaternary ammonium constituents). A second estimation was also carried out by you, using the experimental water solubility value of the substance (1023 mg/L at 20°C, determined according to OECD 105 by the Flask Method). The re-calculated logKow values submitted by you proved to be very different, in the range from -0.094 to 0.52.

Nevertheless, ECHA considers that the logKow prediction by KOWWIN should be regarded as inaccurate due to the lack of reference substances similar to the substance of interest (surfactants) for validation purposes.

In your comments on the draft decision, you agreed that the logKow prediction by KOWWIN should be regarded as inaccurate for surface active substances, and also concluded that the logKow can be calculated from measured solubility in water and measured solubility in octanol.

However, you provided a further estimation of the logKow to support the potential low bioaccumulation for the registered substance, by an equation correlating logKow and water solubility ("one step model")

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$$\text{Log S(mol/l)} = 0.796 - 0.854\text{LogKow} - 0.00728\text{MW} + \Sigma\text{Corrections}\ ^{4}$$

A logKow value of 0.224 was predicted from the experimental water solubility as in the IUCLID dossier (1.023 g/L at 20°C) and the mean molecular weight of [redacted] g/mol (calculated as $\Sigma MW_i/4$, i.e. without taking into account the actual alkyl chain lengths distribution of the substance constituents).

You described the above-mentioned equation as an 'experimentally-validated equation between logKow and water solubility'. However, no evidence has been provided by you that it can be applied reliably to surface-active substances, such as the registered substance.

Consideration of data from other related quaternary ammonium compounds

The estimations and considerations you provided for other quaternary ammonium compounds, such as Dimethyldioctadecylammonium chloride (EC 203-508-2), Methyltrioctylammonium chloride (EC 225-896-2) and Tributylmethylammonium chloride (EC 260-135-8), do not clarify the doubts about the reliability of the proposed approach when applied to the registered substance and, more in general to surfactants, either.

For the physical-chemical end-points, the read-across to data of comparable quaternary ammonium compounds is not justified. Dimethyldioctadecylammonium chloride is characterized by two C8 alkyl chains and two methyl groups. In contrast, the constituents of Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides are expected to be more lipophilic, owing to three C8-C10 alkyl chains bonded to the quaternary ammonium. Dimethyldioctadecylammonium chloride does not stand as a 'worst-case' for Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides, so the logKow of Dimethyldioctadecylammonium chloride is considered of limited value to draw any conclusion on the registered substance of interest.

For Methyltrioctylammonium chloride, a logKow of 4.59 by HPLC is reported in the registration dossier. The HPLC method is not applicable to surfactants and the given experimental logKow is questionable.

In consideration of its structure (three C4 alkyl chains bonded to the quaternary ammonium), Tributylmethylammonium chloride does not stand as a representative/ worst-case for Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides. In addition, the submitted data on Tributylmethylammonium chloride highlight a discrepancy between the experimental logKow and logKow estimated by the EPIWIN-model.

On the whole, the information presented by you on other quaternary ammonium compounds are considered neither particularly relevant nor conclusive as regards Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides.

Consideration of OECD TG 123

In your comments on Proposals for amendment (PfAs) to the draft decision, you refer to the conclusions from ERASM (Hodges *et al.*, 2019), that the OECD Test Guideline 123 (Slow-Stirring Method) would be the most precise and recommended method to

[4] Equation 19 from Meylan and Howard (1994a) cited in WSKOWWIN
NB: No corrections reported for quaternary ammonium salts.

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determine the Kow for surfactants. However, you did not clarify which surfactants had been considered in the investigations and you did not provide any sound argumentations to justify why the ERASM conclusions for those surfactants should be extended to the registered substance. As clearly stated under "*Applicability of the test*" para. 11 of OECD Test Guideline 123, the method applies to pure substances that do not display significant interfacial activity. Therefore, ECHA considers the guideline not applicable to the registered substance, with a surface tension of 27 mN/m at 20°C for a 90% saturated solution (OECD Guideline 115).

Consideration on estimating Kow based on measured n-octanol and water solubilities

In light of the above, ECHA believes that the best way-forward for a realistic Kow estimation is the calculation based on the ratio of solubility in pure n-octanol (to be determined) and solubility in water (already available in IUCLID dossier) measured under the same temperature conditions. The Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance (Version 6.0, July 2017) considers a Kow calculation based on the measured n-octanol and water solubilities as the first choice for surfactants. The Guidance also suggests it might be prudent to take the critical micelle concentration in water (CMC) as a solubility limit, in order to avoid the artefact of unrealistically low Kow values.

Once the solubility in octanol and the CMC have been measured for the registered substance ("whole substance" approach), you must derive the ratio of the octanol solubility:water solubility in order to estimate the Kow. You must compare this Kow result with the B/vB screening criterion of logKow > 4.5 (ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment, Version 3.0, June 2017). If the screening criterion is met, Simulation testing on ultimate degradation in surface water is needed (request 2) in order to clarify whether the P/vP criterion of REACH Annex XIII is met.

Considerations on the test method and testing strategy

For the purpose of the Kow estimation, the experimental determination of the solubility of the substance in pure n-octanol at 20°C is required. CIPAC method MT 181[5] can be used for testing. Alternatively, for solubilities below 10 g/L or for higher precision, OECD Test Guideline 105 (Water Solubility) may also be adapted.

Additionally, the CMC of the substance must be determined and used to re-calculate the Kow instead of water solubility, so to check that the first calculation is not unrealistically low. For surface tension measurements, OECD Test Guideline 115 can be used.

Deadline for provision of the study

Regarding the timeline, in the commenting phase you requested 12 months instead of 9 from the date of decision to provide the data. ECHA agrees with you that no OECD protocol is available for CMC determination. Although no new technique is actually needed (CMC is to be derived by a series of surface tension measurements according to *OECD Test Guideline 115*), nonetheless ECHA can understand your concerns regarding the experimental approach to CMC since the technique is new for you. Also in

[5] Collaborative International Pesticide Analytical Council. Published in CIPAC Handbook H. http://www.cipac.org/index.php/methods-publications/handbooks/handbook-h

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consideration that the results are crucial for triggering the subsequent requirements in the decision tiered testing strategy, ECHA agrees that the information under request 1 must be generated and provided within 12 (instead of 9) months.

Consideration of alternative approaches

The request for measuring solubility in octanol and CMC is suitable and necessary to obtain information that, as a first step, will allow to clarify whether there is a potential risk. According to the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance (Version 6.0, July 2017) a Kow calculation based on the measured n-octanol and water solubilities is the first choice for surfactants. No alternative approaches are, therefore, envisaged. Clarification of the Kow and its comparison with the B/vB screening criterion of logKow >4.5 may avoid the need for a fish bioaccumulation test and simulation testing, since such testing is not needed if the logKow is found to be <4.5.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following studies using the registered substance subject to this decision:

- Solubility in pure n-octanol at 20°C: CIPAC MT 181 or, for solubilities below 10 g/L or for higher precision, OECD Test Guideline 105 (Water Solubility).

- Critical micelle concentration in water (CMC) at 20°C: OECD Test Guideline 115 for surface tension measurements.

2. Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/OECD 309, including the identification of relevant degradation products at a temperature of 12 °C.

The concern(s) identified and why new information is needed

Regarding persistence property, the available information is not sufficient to conclude on the P or vP properties, as described in detail below.

Regarding screening tests on biodegradation in water, you provided a ready biodegradability study ([redacted] 2013) conducted according to a standard test protocol (OECD Guideline 301D, Ready biodegradability Closed Bottle test) and in compliance with GLP. The study was performed on the registered substance. After 28 d, no biodegradation was observed (-3%), whereas after a test prolongation up to 60 days a slight biodegradation activity of 10-20% was observed. You concluded that the substance is neither readily biodegradable nor inherently biodegradable.

Moreover, the three estimation models in the EPI suite, Biowin 2 (non-linear model prediction), Biowin 3 (ultimate biodegradation time) and Biowin 6 (MITI non-linear

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model) have been used to screen the substance for criteria of persistence, as suggested by the ECHA Guidance on Information requirements and chemical safety assessment R11, Table R.11-4. The CAS number 63393-96-4 used for BIOWIN, gives a SMILES string [N+](CCCCCCCC)(CCCCCCCC)(C)CCCCCCCC.[Cl-]. The combined results of Biowin 2 (0.94), 3 (3.2) and 6 (0.55) do not fulfil the reported criteria indicating that the substance could be persistent. ECHA highlights that although the molecular weight of the substance is in the range of the training set compounds for the models Biowin 2 and 3, the functional group quaternary ammonium is not represented in the training set of both models.

In addition, the Biowin models 2 and 3 recognise only the linear C4 terminal chain fragments. Therefore, not all the carbon atoms are included in the recognized fragments in the Biowin 2 and 3 predictions. In Biowin 6 all the carbon atoms as well as the quaternary amine are covered by the recognised fragments. Biowin 6 recognises the alkyl chains as 21 -CH2- [linear] fragments. This fragment has a positive coefficient in the model. It should be noted that Biowin models multiply the coefficient for each of the fragments by the number of the fragment and therefore, in the case of a positive fragment coefficient, may overestimate biodegradation because any possible negative effect due to increased number of fragments (such as steric factors) are not considered (further details are available in BIOWIN User's Guide (v 4.10), 9.0. Known Problems with Biowin models (Biowin 1-7)). Thus it is possible that the Biowin 6 result overestimates the biodegradation in this case.

Due to the fact that Biowin 6 prediction (0.55) is close to the cut-off value and the deficiencies in the Biowin predictions, ECHA considers that the fact the Biowin screening criteria are not fulfilled does not support that the substance is not P or vP.

Taking into account this information, you concluded that the substance Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chloride is neither readily biodegradable nor inherently biodegradable. Therefore you concluded that the registered substance is very persistent.

ECHA notes that there was no basis to conclude that the substance is P or vP.

From literature (Quaternary ammonium compounds Analyses in a Nordic cooperation on screening, TemaNord 2014:556), it is known that under aerobic conditions the biodegradability of Quaternary ammonium compounds (QACs) generally decreases with the number of non-methyl alkyl groups; in contrast, under anaerobic conditions, no or very poor primary biodegradation of QACs has been reported and no evidence of ultimate biodegradation.

Summarising, the ready biodegradability study on the registered substance and the results from the QSAR models do not allow to clarify conclusively the persistence property of the registered substance. In order to conclude, the degradation half-life in an environmental compartment is required.

If the Substance degrades under environmental conditions, it may form degradation/transformation products which themselves have potential PBT/vPvB properties. Currently, the identity of any potential degradation/transformation products is unknown. As indicated in REACH Annex XIII and explained in ECHA Guidance R11, section R.11.3.2.1, the identification of PBT/vPvB substances must also take into account

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the PBT/vPvB properties of relevant transformation and/or degradation products. This identification must therefore be included in the requested OECD 309 study.

Considerations on the test method and testing strategy

Regarding request 2 on simulation of biodegradation, the Guidance on IR&CSA, Chapter R.11, specifies the conditions to identify the compartment(s) of concern to decide which simulation test is the most appropriate to clarify conclusively the P property. In general, testing in the aquatic compartment (OECD 309) is the preferred first step, if technically feasible, when there is the need for further information on persistence in the environment. Taking into account the high water solubility of 1023 mg/L at 20 °C and other properties of the substance, like its low volatility, ECHA considers it appropriate to perform the Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25/OECD 309 including the identification of relevant degradation products at a temperature of 12 °C using the registered substance. When performing the OECD TG 309 test, the pelagic test option with natural surface water containing approximately 15 mg_{dw}/L of suspended solids (acceptable concentration between 10 and 20 mg_{dw}/L) must be followed (ECHA Guidance R.11).

Annex XIII indicates that information used for PBT/vPvB assessment must be obtained under relevant conditions. Therefore, the simulation test should be performed at the temperature of 12 °C, the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8). Performing the tests at this temperature is in line with the applicable test conditions of the OECD TG 309.

Quantification of non-extractable residues (NER) needs to be carried out in all simulation studies. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER. Such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance Chapter R.11).

ECHA requires a full study report to be submitted. It is important to have complete information for the assessment of the study. The test substance is a multi-constituent substance and the identification of relevant degradation products and quantification of NER are required. Considering the complexity of interpreting the study, a complete rationale and access to all information available in the full study are needed. This will allow the evaluating MSCA to fully assess the provided information, and to efficiently clarify the concern for persistence.

As you highlighted in your comments, the substance can only be tested at low concentrations and a C14-radio-labelled sample of the substance is necessary to be tested. Therefore ECHA requires you to report the location of radiolabelling in the structure.
ECHA notes that, according to the OECD TG 309, ^{14}C labelling of the most stable part of the molecule ensures the determination of the total mineralisation, while ^{14}C labelling of a less stable part of the molecule, as well as the use of specific analysis, enables the assessment of only primary biodegradation. Furthermore, the OECD TG 309 states: "However, the most stable part does not necessarily include the relevant functional moiety of the molecule (that can be related to a specific property such as toxicity,

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bioaccumulation, etc.). If this is the case, it may be appropriate to use a test substance, which is ^{14}C-labelled, in the functional part in order to follow the elimination of the specific property." ECHA notes that the test should be performed to measure the ultimate degradation, radiolabelling the molecule in the most stable part of the molecule. Primary degradation determination is optional but if that is performed the results may be useful for P/vP assessment (e.g., in the event that the ultimate degradation half-life indicates P or vP, then information on primary degradation and degradation products can be used to assess whether the P or vP criterion is fulfilled).

In a proposal for amendment an MSCA proposed to complement the OECD TG 309 with a second simulation test according to OECD TG 308 due to the substance properties and the potential sediment and soil exposure via sewage treatment plants. However, the technical guidance document for PBT assessment R.11 (ECHA, 2017) states that testing in the aquatic compartment (OECD TG 309) is the preferred first step when there is a need for further information on persistence in the environment. The reported water solubility of the substance is 1023mg/L and it is considered reliable by ECHA, thus, a test according to OECD 309 is the most suitable choice.

In your comments on the PfAs you answered that the substance is exclusively used in industrial applications under closed conditions as a catalyst for chemical reactions or recycling of (precious) metals or as intermediate under strictly controlled conditions. Moreover you cited release fractions of 1*10exp(-6)% (formulation; 1*10exp(-7)% for recycling and catalyst use). In addition, you pointed out, that waste water from (chemical) industrial processes is usually treated in industrial waste water treatment plants and sewage/sludge will be incinerated and not be brought to agricultural soil.

As already stated, ECHA noted that according to information in the registration dossier and in the chemical safety report, exposure to the environment cannot be excluded. Please also refer to our response to similar comments you made regarding exposure in relation to Request 3.

Regarding the MSCA comment on the feasibility of OECD 309, due to low water solubility of the constituents, ECHA agrees with you that these data were results of calculation by EPIWIN which are regarded not reliable by both the evaluating MSCA as well as registrants and were only reported for completeness.

You indicated in your comments on the PfAs that the design of any simulation biodegradation test to be performed either in water or aquatic sediment should be triggered by the relevant Physical-chemical parameters. In your view, the key parameters to be taken into account should be water solubility and the potential for adsorption (KOC). Therefore, to perform an OECD 308 or an OECD 309 test should be based on the result of the derived Kow and the corresponding KOC. You proposed to reach agreement with ECHA on the test design once reliable values for water solubility and adsorption are available and requested to compile a new decision on how to proceed on issue 2 and or issue 3 only after a conclusion on issue 1 is possible e.g. by a subsequent decision on new information request as given by REACH Annex 46(3).

ECHA considers that the test according to OECD 309 is the most suitable simulation study due to the substance properties and exposure information available. ECHA highlights that the stepwise approach does not foresee to be followed necessarily up to the end. Indeed, the scheme of testing is conditional and the conditions when to perform the required tests are specified in the Table 1.

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Deadline for provision of the information

Regarding the timeline, in your comments on the draft decision, you requested 12 months to synthesize a C14-radio-labelled sample of the substance and 24 months to perform the OECD 309 study. According to your statement, the complete synthesis, characterization and GLP-qualification needs in comparable cases 12 months. ECHA accepted an extension of the deadline by 12 months in order to prepare radiolabelled test material.

ECHA did not accept an extension of the deadline for performing the study to 24 months as in our view the standard deadline of 18 months is sufficient time for conduct and reporting of the study. The extension request was not justified with a statement from a contract research organisation that would perform the requested test on the registered substance.

Consideration of alternative approaches

The request for Simulation testing on ultimate degradation in surface water is suitable and necessary to obtain information that will allow to clarify whether there is the persistence property. More explicitly, there is no equally suitable alternative way available of obtaining this information.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using the registered substance subject to this decision:

Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/OECD 309, including the identification of degradation products at a temperature of 12 °C.

3. Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, by applying aqueous exposure, with measurements of the BCF in whole body and inedible portions.

The concern(s) identified and why new information is needed

According to the PBT assessment strategy (ECHA guidance IR/CSA, Chapter R11: PBT Assessment, version 3.0, June 2017), concern on P should generally be addressed before the B and T criteria. In this case the testing strategy of clarifying the B concern by first clarifying the logKow (request 1) to check whether the B screening criterion is met can potentially avoid the need for an expensive simulation test (request 2) or for a vertebrate test (BCF study request 3). If the outcome of the request 2 (Simulation testing on ultimate degradation in surface water) confirms the P/vP property, the request 3 (BCF study) must be performed.

Consideration of estimations of bioaccumulation potential
In the CSR initially assessed by the evaluating MSCA, you provided estimations based on logKow of 6.13 for the C8 substructure of the molecule and 9.08 for the C10

substructure of the molecule, indicating a potential for bioaccumulation. The results were evaluated in a weight-of-evidence approach from QSAR estimations, read across information, and DiamMax-Average arguments. Your conclusion was that the substance is considered to be not bioaccumulative, with a BCF of 7 - 70.8 L/kg.

ECHA considers that the results of the QSAR estimations for BCF are of questionable reliability, mainly due to doubts related to Kow estimations. The assessment by KOWWIN is not reliable as the software database is considered not to be representative for surfactants.

A chemical is considered in domain if its logKow and molecular weight are within the specified ranges, if its structural domain, based on atom-centered fragments (ACFs), are presented in the training chemicals and if its mechanism of bioaccumulation is passive.

Catalogic model predictions are in the parametric domain of the models but none of the compounds in the training set contains a quaternary ammonium substructure. Therefore it is concluded that the substance does not fall in the domain of the model.

Taking into account the unreliability of logKow estimations and of the Water Solubility value used, the model predictions are highly uncertain.

Arnot-Gobas model estimates steady-state bioconcentration factor and bioaccumulation factor values for non-ionic organic chemicals and the model is not recommended at this time for chemicals that appreciably ionize, such as the registered substance. Therefore it is out of domain for this model.

The HPLC Method for Kow measurement is not applicable either, due to the absence of suitable calibration compounds and to the fact that ionic compounds interact with the HPLC column by forces other than partitioning. Also the logKow assessment by KOWWIN is deemed inaccurate, since the software database is very limited for surface active substances.

Consideration of trends related to chain length and substitution
ECHA notes that from literature, the report "Quaternary ammonium compounds Analyses in a Nordic cooperation on screening" describes the findings of a Nordic environmental study (TemaNord 2014:556). It provides property comparisons related to differences in chain length and substitution of a methyl group. For instance it is suggested that the substitution of a methyl group with a benzyl group increases the toxicity but that there is no difference in toxicity between homologues of different chain length (Ying, 2006). This could be attributed to a lower bioavailability of the longest chain homologues due to their decreasing solubility. In general, Quaternary ammonium compounds share the common quaternary ammonium cation. In the cited work, Quat (quaternary ammonium) cations of the types alkyltrimethyl ammonium (ATAC), alkyl dimethyl benzyl (benzalkonium, BAC) and dialkyl dimethyl ammonium (DDAC) were investigated. For the analysed Quats, the compound properties vary with alkyl chain length: water solubility decreases, and adsorptivity to surfaces increases, with increasing chain length.

Consideration of data from related substances in EU risk assessment reports
Several studies on bioaccumulation are available from the EU risk assessment Report (EURAR 2002, addendum 2009) for substance dimethyl dioctadecylammonium chloride (DODMAC, CAS 107-64-2) and Di(hydrogenated tallow alkyl) dimethylammoniumchloride (DHTDMAC, CAS 61789-80-8), listed in the EU risk assessment. DODMAC and DHTDMAC

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belong to the group of the quaternary ammonium compounds (QACs or quats) and are cationic surfactants, like the registered substance. In particular, it is reported that *Lepomis macrochirus* was exposed to 14C-DHTDMAC for 49 days in a continuous flow-through system in river water and laboratory water with mean concentrations in the test period of 18 µg/L and 16 µg/L respectively (no solvent carrier, Lewis & Wee, 1983). In river water BCFs of 13 L/kg in the whole body and 94 in the inedible tissue (viscera) were estimated based on measured concentrations. When laboratory water was used the respective BCFs were 32 and 256 L/kg. In both waters DHTDMAC did not concentrate to a significant degree in edible tissue (BCF of the fillets < 5 L/kg).

In general, bioaccumulation studies in fish and sediment organisms cited in the risk assessment for DOMAC and DHTMAC, show a trend of a reduced bioaccumulation potential.

ECHA notes that the BCFs for DODMAC/DHTMAC show a conflict between whole body and inedible measurements. These studies can be considered just as supporting information indicating that it is possible to perform aqueous BCF tests on substances belonging to the group of the quaternary ammonium compounds.

Moreover the information available on fatty amines tested in a fish aqueous bioaccumulation test (EU RAR, 2008) indicates an adsorption to the surface of fish rather than an uptake.

In conclusion, the above data could be useful as supporting information, rather than for direct read-across, raising the need to clarify whether the registered substance adsorbs to surfaces or is actually taken up.

The evaluating MSCA appreciate the additional information included in the updated registration dossier. However, the available information, in a Weight of Evidence approach, does not clarify conclusively the bioaccumulation property on the registered substance, because ECHA considers that the BCF predictions provided are not reliable.

Considerations on the test method and testing strategy

Taking into account the high water solubility of the substance (1023 mg/L at 20 °C), and the information available on BCF studies for DODMAC/DHTMAC substances and fatty amines (as specified above), indicating the feasibility to perform aqueous BCF tests on cationic surfactants belonging to the group of the quaternary ammonium compounds, ECHA considers it appropriate and feasible to perform an aqueous exposure, rather than a dietary OECD 305 test.

Moreover, as above specified, it is needed to have measurements of the BCF in whole body and inedible portions, in order to distinguish between the fraction possibly only adsorbed to the surface of the fish and the fraction taken up. A substantially higher BCF in whole body compared to inedible portions (viscera) of fish could indicate an adsorption to the surface of fish rather than an actual accumulation and therefore only minor accumulation in edible tissue (fillet) as supported by the evidence from DHTDMAC.

ECHA requires a full study report to be submitted. Considering the complexity of interpreting the study, a complete rationale and access to all information available in the full study report (implemented method, raw data collected, interpretations and calculations, consideration of uncertainties, argumentation, etc.) are needed. This will allow the evaluating MSCA to fully assess the provided information, including the statistical analysis, and to efficiently clarify the concern for bioaccumulation.

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The required BCF study constitutes the third tier in a testing strategy to clarify the concern for Bioaccumulation. As explained above, if the outcome of the request 1 as screening information, allows to clearly exclude B property (i.e. logKow is <4.5), no further testing must be performed for P assessment and, consequently, for B. Otherwise the request 2 (surface water simulation study) must be performed to clarify conclusively the P/vP property. If the request 2 allows to clearly exclude P/vP property, no further testing must be performed for B assessment. Otherwise the request 3 (BCF study) must be performed to conclusively clarify the B/vB property.

In the comments on proposal for amendments, you wondered if the potential release of the substance to the environment by the identified uses and their descriptions justifies to perform a bioaccumulation study with vertebrate animals, even if the bioaccumulation screening criterion logKow >= 4.5 indicates a bioaccumulating property in terms of PBT assessment.

In particular you highlighted that the substance is exclusively used in industrial applications under closed conditions as a catalyst for chemical reactions or recycling of (precious) metals or as intermediate under strictly controlled conditions.

Moreover you cited release fractions of 1*10exp(-6)% (formulation; 1*10exp(-7)% for recycling and catalyst use). In addition, you pointed out, that wastewater from (chemical) industrial processes is usually treated in industrial wastewater treatment plants and sewage/sludge will be incinerated and not be brought to agricultural soil.

However, ECHA notes that in the updated CSR you still applied the processing data for "municipal" STP for the risk assessment calculations in all exposure scenarios. In only one Exposure Scenario the sludge has to be incinerated. ECHA notes that the municipal STP scenario does not warrant incineration as a risk management measure as it cannot be assumed that municipal STP facilities incinerate the sludge produced.

ECHA notes that ERCs reported in the registration dossier and in the chemical safety report foresee releases into environment (ERC 2,4,6B). You use SPERCs without providing information and justification for the refined release factors, as required by the ECHA Guidance R.16.2.3.2.

Therefore, according to information in the registration dossier and in the chemical safety report, significant exposure to the environment cannot be excluded.

Moreover you cited, referring to ECHA Guidance R.11.4.1.2.1 Integrated Assessment and Testing Strategy (ITS),"... and therefore a BCF value may not be available. In that case it should be first considered if the available testing and non-testing data are sufficient to conclude on the B-properties for those substances produced or imported at <100 t/y or if bioaccumulation testing is needed and hence required to draw a reliable conclusion".

As explained above, ECHA highlights that, in this case, the information available are not sufficient to conclude on the B concern, therefore further information is needed.

Moreover, you proposed that a new decision be issued on how to proceed on issue 3 only after a conclusion on issue 1 is possible, e.g. by a subsequent decision on new information request as given by REACH Annex 46(3).

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As already stated, ECHA highlights that the stepwise approach does not foresee to be followed necessarily up to the end. Indeed, the scheme of testing is conditional and the conditions when to perform the required tests are specified in the Table 1.

Furthermore, in response to PfAs from ECHA and another MSCA to include a reference list within the Decision, you commented that '*correct citation of the literature referring to is missing and cannot be followed up by the registrants*'. In response, the evaluating MSCA has included full references to the citations for clarity but notes that the citations could be identified/obtained using the information provided in the previous draft Decision.

Deadline for provision of the information

Regarding the timeline, you request 18 months to perform the OECD 305 study, due to application at very low concentration level of C14-labelled samples.

ECHA has accepted an additional 12 months for preparation of C-14 labelled test material needed to perform the OECD 309 study. Preparation of the test material for the OECD 305 study can also be done at this time. Therefore, ECHA cannot accept an additional 12 months for performance of the OECD 305 test.

ECHA considers that 9 months would be sufficient time for conduct and reporting of the study.

Consideration of alternative approaches

The request for Bioaccumulation in Fish is suitable and necessary to obtain information that will allow to clarify the bioaccumulation property. More explicitly, there is no equally suitable alternative way available of obtaining this information. ECHA notes that there is no experimental study available at this stage that will generate the necessary information and does not need to test on vertebrate animals.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using the registered substance subject to this decision:

Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, aqueous exposure, with measurements of the BCF in whole body and inedible portions.

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Appendix 2: Procedural history

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to suspected PBT/vPvB, wide dispersive use, exposure to environment, high RCR, Quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides (CAS No 63393-96-4, EC No 264-120-7) was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2017.The updated CoRAP was published on the ECHA website on 21 March 2017. The competent authority of Italy (hereafter called the evaluating MSCA) was appointed to carry out the evaluation.

In accordance with Article 45(4) of the REACH Regulation, the evaluating MSCA carried out the evaluation of the above substance based on the information in your registration(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the abovementioned concerns. Therefore, it prepared a draft decision under Article 46(1) of the REACH Regulation to request further information. It subsequently submitted the draft decision to ECHA on 21 March 2018.

The decision making followed the procedure of Articles 50 and 52 of the REACH Regulation as described below.

ECHA notified you of the draft decision and invited you to provide comments.

Registrant(s)' commenting phase

ECHA received comments from you and forwarded them to the evaluating MSCA without delay.

The evaluating MSCA took the comments from you, which were sent within the commenting period, into account and they are reflected in the reasons (Appendix 1). The requests were not amended and the deadline were amended (ECHA agrees the information under request 1 must be generated and provided by 12, instead of 9 months; ECHA accepts an extension of the deadline by 12 months in order to prepare radiolabelled test material for the request 2).

By 3rd August 2018 you submitted update(s) of the registration dossier. The evaluating MSCA took the information in the updated registration dossier into account, and it is reflected in the reasons (Appendix 1). Nevertheless based on the available information, there is still a concern that the substance itself may have PBT/vPvB properties.

Proposals for amendment by other MSCAs and ECHA and referral to the Member State Committee

The evaluating MSCA notified the draft decision to the competent authorities of the other Member States and ECHA for proposal(s) for amendment.

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Subsequently, the evaluating MSCA received proposals for amendment to the draft decision. The evaluating MSCA has reviewed the proposals for amendment received and where appropriate the draft decision has been amended accordingly. In addition, editorial comments improving the decision were taken into account

ECHA referred the draft decision, together with your comments, to the Member State Committee.

ECHA invited you to comment on the proposed amendments.

Your comments on the proposed amendments were taken into account by the Member State Committee. One Registrant demonstrated that the concerns identified in the Decision were not relevant to their specific strictly controlled conditions of use and therefore was removed as an addressee of the Decision.

MSC agreement seeking stage

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-65 written procedure and ECHA took the decision according to Article 52(2) and Article 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided by you in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on your dossier(s) at a later stage, nor does it prevent a subsequent decision under the current substance evaluation or a new substance evaluation process once the present substance evaluation has been completed.

2. Failure to comply with the request(s) in this decision, or to otherwise fulfil the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the required experimental study/ies, the sample of the substance to be used ('test material') has to have a composition that is within the specifications of the substance composition that are given by all registrant(s). It is the responsibility of all the registrant(s) to agree on the tested material to be subjected to the test(s) subject to this decision and to document the necessary information on the composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation.

4. In relation to the experimental stud(y/ies) the legal text foresees the sharing of information and costs between registrant(s) (Article 53 of the REACH Regulation). You are therefore required to make every effort to reach an agreement regarding each experimental study for every endpoint as to who will carry out the study on behalf of the other registrant(s) and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation. This information should be submitted to ECHA using the following form stating the decision number above at:
https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx?CaseNumber=SEV-264-120-7-1

   Further advice can be found at
http://echa.europa.eu/regulations/reach/registration/data-sharing. If ECHA is not informed of such agreement within 90 days, it will designate one of the registrants to perform the stud(y/ies) on behalf of all of them.