EUROPEAN CHEMICALS AGENCY

Helsinki, 10 December 2018

Addressee: [redacted]

Decision number: CCH-D-2114453333-55-01/F
Substance name: Ditetradecyl peroxydicarbonate
EC number: 258-436-4
CAS number: 53220-22-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 24/01/2018
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

2. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by ***17 December 2020***. You also have to update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations 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 suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Kevin Pollard, Head of Unit, Evaluation, E1

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

Appendix 1: Reasons

1. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a long-term study[2] on *Daphnia magna* according to OECD test guideline 211 with a test substance different from the registered substance, i.e. with dihexadecyl peroxydicarbonate (EC: 247-611-0, CAS: 26322-14-5)

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests, "*provided that the conditions set out in Annex XI are met*". Annex XI of the REACH Regulation outlines the general rules for adapting the standard information requirements set out in Annexes VII to X of the REACH Regulation.

In particular, Section 1.5. of Annex XI of the REACH Regulation introduces the concept of read-across. This concept is based on the identification of similar substances. Information for one or more source substances may be used to make a prediction for the target substance (i.e. the registered substance). According to Annex XI, Section 1.5. of the REACH Regulation, two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be regarded as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group. Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[3]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

[2] [redacted] (2013). [redacted]

[3] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures.

You have provided, as an attachment to the technical dossier, a justification document for your read-across approach[4]. In this document, you claim that

- the source and target substances are structural analogues,
- both have comparable low water solubility and high log Kow values,
- both have similar ecotoxicological properties and profile.

ECHA notes that both the target and the source substances belong to the group of long-chain aliphatic peroxydicarbonates. The main constituent for the source substance (dihexadecyl peroxodicarbonate (EC: 247-611-0, CAS: 26322-14-5)) shares the same functional groups with the main constituent for the target substance (ditetradecyl peroxydicarbonate (EC: 258-436-4, CAS: 53220-22-7)). The two substances only differ in the lengths of the alkyl chains by two carbon atoms.

ECHA further notes that the two substances are both highly insoluble in water and have high log Kow values. From the studies available, no significant ecotoxicological effects were observed up to the respective water solubility for both substances. However, for the registered substance no long-term ecotoxicity data are available. For the source substance, a long-term study is available only for *Daphnia*.

ECHA notes that short-term tests may not give a true measure of toxicity for poorly soluble substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Poorly soluble substances indeed require longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. Therefore, the absence of toxicity observed in short-term tests does not rule out possible long-term effects which should therefore be investigated. In particular, ECHA notes that Annex VIII 9.1.3. and Annex VII 9.1.1. of the REACH Regulation explicitly recommend that long-term aquatic toxicity tests be considered for substances that are poorly water soluble.

Both the source and the target substances contain impurities. According to the justification document you provided for your read-across approach, the source substance contains [redacted] % (w/w) hexadecyl alcohol (EC: 253-149-0, CAS: 36653-82-4), whereas the target substance contains [redacted] % (w/w) tetradecyl alcohol (EC: 204-000-3, CAS: 112-72-1). Information is available in the literature and in public databases both for tetradecyl alcohol and for hexadecyl alcohol: e.g. REACH registration dossiers[5] exist for both and there is an OECD assessment report available for long-chain alcohols[6].

Main results for the source and target substances as well as for their respective impurities are summarised in the table below:

[4] [redacted] (2018). [redacted]

[5] https://echa.europa.eu/information-on-chemicals/registered-substances

[6] https://hpvchemicals.oecd.org/UI/SIDS_Details.aspx?id=F5F2EDDD-D37A-4658-9D37-743D1D74E7C1

Endpoint	Source substance	Target substance
main constituent	dihexadecyl peroxodicarbonate (EC: 247-611-0, CAS: 26322-14-5)	ditetradecyl peroxydicarbonate (EC: 258-436-4, CAS: 53220-22-7)
impurity	hexadecy alcohol (EC: 253-149-0, CAS: 36653-82-4): [redacted]% (w/w)	tetradecyl alcohol (EC: 204-000-3, CAS: 112-72-1): [redacted]% (w/w)
water solubility	main constituent: <1 µg/L impurity: <1 mg/L	main constituent: <0.001 µg/L (calculated) impurity: 1.3 mg/L
log Kow	main constituent: 15.1 - 15.9 (calculated) impurity: 6.7 (experimental)	main constituent: >> 6.5 (experimental) ; 13 (calculated) impurity: 5.5 (experimental)
biodegradability	main constituent: readily biodegradable impurity: readily biodegradable	main constituent: readily biodegradable impurity: readily biodegradable
short-term toxicity to fish	main constituent: > solubility limit impurity: > solubility limit	main constituent: > solubility limit impurity: > solubility limit
long-term toxicity to fish	main constituent: - impurity: -	main constituent: waiver impurity: waiver
short-term toxicity to *Daphnia*	main constituent: > solubility limit impurity: > solubility limit	main constituent: > solubility limit impurity: > solubility limit (c.a. 10% effects observed at the water solubility limit)
long-term toxicity to *Daphnia*	main constituent: > solubility limit impurity: > solubility limit	main constituent: read across impurity: 21d-NOEC: 1.6 ug/L
toxicity to algae	main constituent: > solubility limit impurity: > solubility limit	main constituent: > solubility limit impurity: > solubility limit

Available long-term data show that tetradecyl alcohol is very toxic to aquatic organisms: a 21d-NOEC of 1.6 µg/L on *Daphnia magna* is reported in the registration dossier for this substance and a 21-day NOEC of 0.0098 mg/L (9.8 µg/L) on *Daphnia magna* is mentioned

in the OECD assessment report on long-chain alcohols for tetradecyl alcohol. Moreover, tetradecyl alcohol is classified as Eye Irrit. 2 H319 and Aquatic Chr. 1 H410.

On the contrary, hexadecyl alcohol is not classified and no short-term and long-term toxicity was observed up to its limit of water solubility. ECHA notes that hexadecyl alcohol is less soluble than tetradecyl alcohol (1.3 mg/L for tetradecyl alcohol vs. < 1 mg/L for hexadecyl alcohol) and has a higher log Kow compared to tetradecyl alcohol (log Kow is 6.7 for hexadecyl alcohol vs. 5.5 for tetradecyl alcohol). As apparent in the OECD assessment report on long-chain alcohols, the low solubility of the longest chain alcohols (i.e. with a number of carbon atoms in the alkyl chains ≥16) tends to limit their dissolved (and hence bioavailable) concentrations to the extent that neither acute nor chronic toxicity are likely to be exhibited.

Therefore, even though tetradecyl alcohol and hexadecyl alcohol only differ in the lengths of the alkyl chain by two carbon atoms, their physicochemical properties and ecotoxicological profiles prove to be quite different.

The available long-term result on the source substance did not show long-term effects on *Daphnia*, which can be explained by the fact that both the main constituent and the impurity of the source substance are highly insoluble and therefore not bioavailable. However, for the target substance, impurity tetradecyl alcohol is known to be highly toxic, at least after long-term exposure. Because of this impurity, long-term toxicity of the registered substance cannot be ruled out. Furthermore, even at the concentration of [redacted]%, this impurity could theoretically trigger the need for classifying the registered substance.

As explained above, your read-across approach does not address the toxicity of impurity tetradecyl alcohol. Therefore, ECHA considers that your read-across is per se not sufficient to enable the prediction of long-term toxicity of the registered substance to *Daphnia*. On that basis, the requirement of Annex XI, Section 1.5. has not been met and your adaptation of the information requirement cannot be accepted. Consequently there is an information gap and it is necessary to provide information for this endpoint.

Daphnia magna reproduction test (test method EU C.20. / OECD TG 211) is a validated standard international test laid down in the Test Methods Regulation (EC) No 440/2008 and therefore it meets the requirements of Article 13(3) of the REACH Regulation. According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) it is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5. of the REACH Regulation.

In your comments following the procedure set out in Article 50(1) of the REACH Regulation you have indicated your agreement to provide this information.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *Daphnia magna* reproduction test (test method: EU C.20./OECD TG 211).

Notes for your consideration

ECHA notes that due to lack of effects in short-term studies it is not possible to determine the sensitivity of species. Therefore, the Integrated testing strategy (ITS) outlined in ECHA

Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), is not applicable in this case and the long-term studies on both invertebrates and fish are requested to be conducted.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 REV1 (6 July 2018) and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

If based on the results of the required study *Daphnia* is observed to be the most sensitive species, then the PNECs will have to be revised accordingly.

The registered substance is currently not classified for environmental endpoints. As explained above, new information on long-term toxicity to *Daphnia* might warrant the need for classifying the substance for aquatic toxicity.

2. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2 of the REACH Regulation.

In your adaptation, you basically consider that long-term toxicity testing on fish is not justified for the following reasons:

- you claim that the registered substance is unstable in the aquatic environment and will degrade to its respective alcohol or acid,
- you claim that the registered substance is highly insoluble in water,
- you claim that releases to the water compartment will be limited throughout the whole life cycle of the substance.

On these bases, you have concluded that the chemical safety assessment (CSA) does not indicate the need to further investigate the effects on aquatic organisms.

ECHA disagrees with your conclusion for the reasons outlined below.

ECHA notes that the registered substance is a monoconstituent substance, but which contains tetradecyl alcohol (EC: 204-000-3, CAS: 112-72-1) as an impurity ([redacted] % (w/w)). Tetradecyl alcohol is also expected to be a degradation product of the main constituent (i.e. ditetradecyl peroxydicarbonate). Information is available in the literature and in public databases for tetradecyl alcohol: e.g. there is a REACH registration dossier[7] and an OECD assessment report[8] available for this substance.

ECHA acknowledges that the main constituent (i.e. ditetradecyl peroxydicarbonate) is highly insoluble in water (<< 1 µg/L) and that this could limit its bioavailability and therefore its short-term toxicity. However, ECHA notes that impurity tetradecyl alcohol has comparatively a much higher water solubility (1.3 mg/L reported in the REACH registration dossier, 0.191 mg/L reported for the OECD evaluation) and is therefore expected to be more bioavailable than the main constituent. Even though tetradecyl alcohol is comparatively much more water soluble than the main constituent, ECHA considers that it is still quite poorly soluble.

Poorly soluble substances require longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. Therefore, short-term tests may not give a true measure of toxicity for poorly soluble substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. ECHA notes that no effects were observed in the short-term tests reported for the registered substance. Still, long-term toxicity cannot be excluded and should be investigated. In particular, Annex VIII 9.1.3. and Annex VII 9.1.1. of the REACH Regulation explicitly recommend that long-term aquatic toxicity tests be considered if the substance is poorly water soluble.

Similarly, no significant effects were observed in the short-term tests available for impurity tetradecyl alcohol. However, it is assessed to be very toxic after long-term exposure: a 21-day-NOEC of 1.6 µg/L on *Daphnia magna* is reported in the REACH registration dossier for tetradecyl alcohol, and in the OECD assessment report, a 21-day NOEC of 0.0098 mg/L (9.8 µg/L) on *Daphnia magna* is mentioned for tetradecyl alcohol. ECHA further notes that tetradecyl alcohol is classified as Eye Irrit. 2 H319 and Aquatic Chr. 1 H410 (self-classification).

Therefore, ECHA considers that long-term effects of the registered substance cannot be ruled out, in particular because of tetradecyl alcohol being an impurity. Furthermore, even at the concentration of [redacted]%, this impurity could theoretically trigger the need for classifying the registered substance.

ECHA acknowledges that, according to the uses reported in the registration dossier, releases of the registered substance to the water compartment will probably be low, but also notes that you have not performed any quantitative exposure assessment for the environment. As explained above, the registered substance might be very toxic and therefore risks cannot be ruled out even for low environmental concentrations. On this basis, ECHA considers that you have not demonstrated the absence of risks.

[7] https://echa.europa.eu/registration-dossier/-/registered-dossier/15422
[8] https://hpvchemicals.oecd.org/UI/SIDS_Details.aspx?id=F5F2EDDD-D37A-4658-9D37-743D1D74E7C1

ECHA further notes that appropriate information on toxicity to fish is necessary for the derivation of predicted no effect concentrations (PNEC) and should be considered for the classification and labelling of the substance. Annex I, Section 3 of the REACH Regulation requires an environmental hazard assessment to be conducted and Step 3 of that section requires PNECs to be established. According to the guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R7b, Section R.7.8.5.3, the chemical safety assessment is to be based on all available toxicity information, and that the information used for the derivation of the PNEC for water should at least cover species of three trophic levels: algae/aquatic plants, invertebrates (*Daphnia* preferred), and fish. However, as explained above, only short-term data are available for fish, whereas they are not suitable for poorly soluble substances. Adequate information on the toxicity to fish is thus missing and no sufficient information is available for deriving the PNEC.

Contrary to your own conclusion, ECHA thus considers that your CSA does not rule out the need to further investigate long-term effects on aquatic organisms and therefore that your adaption does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2 of the REACH Regulation and cannot be accepted. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) can be performed to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), *Chapter R7b, Section R.7.8.4.1*).

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA *Guidance Chapter R7b,* version 4.0, June 2017).

In your comments following the procedure set out in Article 50(1) of the REACH Regulation you have indicated your agreement to provide this information.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration

ECHA notes that due to lack of effects in short-term studies it is not possible to determine the sensitivity of species. Therefore, the Integrated testing strategy (ITS) outlined in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June

2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), is not applicable in this case and the long-term studies on both invertebrates and fish are requested to be conducted.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 REV1 (6 July 2018) and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

If based on the results of the required study fish is observed to be the most sensitive species, then the PNECs will have to be revised accordingly.

The registered substance is currently not classified for environmental endpoints. As explained above, new information on long-term toxicity to fish might warrant the need for classifying the substance for aquatic toxicity.

Deadline to submit the requested information in this decision

In the draft decision notified to you the time indicated to provide the requested information was 12 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 24 months in order to develop and validate an appropriate analytical method and to agree potential data sharing with the registrants of analogue substance, dihexadecyl peroxodicarbonate (EC number: 247-611-0, CAS number: 26322-14-5). Therefore, ECHA has granted the request and set the deadline to 24 months.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 17 January 2018.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took into account your comments and amended the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

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

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.