Helsinki, 10 December 2018

Addressee: [redacted]

Decision number: CCH-D-2114453719-37-01/F
Substance name: Pyridinium, 1-(phenylmethyl)-, ethyl methyl derivs., chlorides
EC number: 272-695-0
CAS number: 68909-18-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 05/12/2017
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. **Sub-chronic toxicity study (90-day), oral route (Annex IX, 8.6.2.; test method: OECD 408) in rats;**

2. **Pre-natal developmental toxicity study (Annex IX, 8.7.2.; test method: OECD 414) in rats or rabbits, oral route.**

3. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;**

4. **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;**

5. **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;**

6. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309) at a temperature of 12 °C with the registered substance;**

7. **Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: Aerobic and anaerobic transformation in soil, EU C.23./OECD TG 307) at a temperature of 12 °C with the registered substance;**

8. **Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24./OECD TG 308) at a temperature of 12 °C with the registered substance;**

- **for requests 6-8: The biodegradation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.**

9. **Identification of degradation products (Annex IX, 9.2.3.) using an appropriate test method with the registered substance;**

10. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305, aqueous exposure) with the registered substance;**

    - **The bioaccumulation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.**

You are required to submit the requested information in an updated registration dossier by ***17 March 2023***, except for the information requested under points 1. and 2. above for a Sub-chronic toxicity study (90-day) and Pre-natal developmental toxicity study which shall be submitted in an updated registration dossier by **17 December 2020**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing. 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

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.

Your registration dossier contains for the endpoints sub-chronic toxicity (90-day) study (Annex IX, 8.6.2.) and pre-natal developmental toxicity study (Annex IX, 8.7.2.) adaptation arguments in form of a grouping and read-across approach under Annex XI, Section 1.5. of the REACH Regulation. ECHA has considered first the scientific and regulatory validity of your read-across approach in general (section "0.") before assessing the individual endpoints in sections "1." and "2.").

0. Grouping of substances and read-across approach

You have sought to adapt the information requirements sub-chronic toxicity (90-day) study (Annex IX, 8.6.2.) and pre-natal developmental toxicity study (Annex IX, 8.7.2.) by applying a read-across approach in accordance with Annex XI, Section 1.5. According to Annex XI, Section 1.5., 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 considered 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 (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

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. 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. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

i. Description of the grouping and read-across approach proposed by you

You consider to achieve compliance with the REACH information requirements for the registered substance Pyridinium, 1-(phenylmethyl)-, ethyl methyl derivs., chlorides using data of structurally similar substances, two quaternary ammonium compounds, didecyldimethylammonium chloride (DDAC) and alkyldimethyl benzyl ammonium chloride (ADBAC), (No EC or CAS number is given), hereafter the 'source substances'.

You have not provided a read-across documentation as a separate attachment in the registration.

In the Chemical Safety Report, you use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:
"*Published reviews of the available repeated dose toxicity data for related quaternary ammonium compounds are available in documents published by the US and Canadian authorities. The data do not indicate any notable or clearly treatment-related systemic toxicity and demonstrate that the effect of exposure to this group of compounds is primarily local. The results confirm the findings of older, published studies.*
Read-across between different quaternary ammonium compounds is considered to be appropriate as the available metabolism data do not identify any molecular cleavage, which would liberate different chemical species and potentially result in significantly different toxic effects. "

As an implicit part of your justification, you propose that the source and the registered substance have similar properties for the information requirements for repeated dose toxicity, pre-natal developmental toxicity and toxicity to reproduction. ECHA considers that this (information) is your read-across hypothesis.

You have not provided a comparison of physico-chemical, toxicological or ecotoxicological properties between the target and sources substances of the read-across. No repeated dose toxicity, reproductive toxicity or developmental toxicity studies with the target substance has been provided.

ii. ECHA analysis of the grouping and read-across approach in light of the requirements of Annex XI, 1.5.

With regard to the proposed predictions ECHA has the following observations:

a. Substance characterisation of source and target substances

The substance characterisation of the source substance need to be sufficiently detailed in order to assess whether the attempted prediction is not compromised by the composition and/or impurities. In the ECHA's Practical Guide on "How to use alternatives to animal testing to fulfil your information requirements" (chapter 4.4), it is recommended to follow the ECHA *Guidance for identification and naming of substances under REACH and CLP* (version 2.1, May 2017) also for the source substances. This ensures that the identity of the source substance and its impurity profile allows an assessment of the suitability of the substances for read-across purposes.

Currently the identity of the source substance and its impurity profile cannot be assessed using the information provided in the registration dossier and the suitability of the substances for read-across purposes cannot be verified. No substance identity information has been provided for any of the claimed sources substances. Therefore, ECHA cannot reach a conclusion whether the source substances can be used to predict properties for the registered substance.

b. Explanation on why and how the structural similarities allow predictions

In order to meet the provisions in Annex XI, Section 1.5. to predict human health effects from data for a reference substance within the group by interpolation to other substances in the group, ECHA considers that structural similarity alone is not sufficient. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

ECHA notes the following observations: You have not documented the structural and chemical similarity of the target and sources substances.

ECHA concludes that you have not addressed the obvious structural differences between the source substances and the target substance and did not explain, why those differences would not lead to differences in the toxicity profile of target and source substances.

c. Support of a similar or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.*
One prerequisite for a prediction based on read-across therefore is that the substances involved are structural similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.
ECHA notes:

1. You have not provided any studies on the acute toxicity, skin and eye irritation/corrosion, or skin sensitisation on target or sources substances, which would demonstrate that source and target substances would have similar toxic properties. Furthermore, you have not provided any studies on repeated dose, reproductive or developmental toxicity of the target substance. Therefore, you have not documented that the target and sources substances have a similar or regular pattern of toxicity.

2. You have not provided any data matrix, which would enable comparison of the properties of target and source substances of the read-across.
3. Concerning the claimed structurally similar substances, two quaternary ammonium compounds, didecyldimethylammonium chloride (DDAC) and alkyldimethyl benzyl ammonium chloride (ADBAC), no study records have been provided in your dossier.

ECHA concludes that the presented evidence does not support a similar or regular pattern of toxicity as a result of structural similarity. Therefore it cannot be verified that the proposed group/analogue substance(s) can be used to predict properties of the registered substance.

iii. Conclusion on the read-across approach

The adaptation of the standard information requirements for repeated dose toxicity and pre-natal developmental toxicity in the technical dossier is based on the proposed read-across approach examined above. ECHA does not consider the read-across justification to be a reliable basis to predict the properties of the registered substance for the reasons set out above. Thus, the adaptation does not comply with the general rules of adaptation as set out in Annex XI, 1.5. Therefore, ECHA rejects all adaptations in the technical dossier that are based on Annex XI, 1.5.

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, section 8.6.2. 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 not provided any study record of a sub-chronic toxicity study (90 day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

You have sought to adapt this information requirement of Annex IX, Section 8.6.2. You have justified the proposal for adaptation with the following waiver: *"The substance MK92K is corrosive and (based on physicochemical properties and read-across from similar quaternary ammonium compounds) is considered to be poorly systematically absorbed following oral administration. It is therefore very likely that the effects of the repeated oral administration of MK92K in an animal study will be largely local (due to irritation/corrosion at the site of contact), with little or no systemic effects other that those secondary to the effects of the substances on the gastrointestinal tract."*

Although you have not explicitly claimed a legal basis for your adaptation, ECHA has first evaluated your adaptation according to Annex XI, Section 1.5. of the REACH Regulation. In support of your adaptation you have provided summaries of eight repeated dose toxicity studies (90-day and chronic toxicity studies) on two related quaternary ammonium compounds, dodecyl dimethyl ammonium chloride (DDAC) and alkyl dimethyl benzyl ammonium chloride (ADBAC) in the CSR. No study records were however provided in IUCLID section 7.5. for these studies. As explained above in Appendix 1, section "0." of this decision, your adaptation of the information requirement is rejected.

ECHA has further evaluated your adaptation according to the provisions set out in the fourth indent of Column 2 of Annex IX, 8.6.2. as you state that the substance is *"considered to be poorly systemically absorbed following oral administration"*. According to that provision, a

sub-chronic toxicity study does not need to be conducted if "*the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure.*"

You have however not demonstrated that the conditions of that provision are fulfilled. As regards corrosivity, according to introductory paragraph 4 of Annex IX of the REACH Regulation "*in vivo* testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided". However, ECHA would like to point out that non-corrosive concentration(s) can be tested. As long as this is possible, ECHA considers that *in vivo* testing with corrosive substances at concentration/dose levels causing corrosivity can indeed be avoided and the introductory paragraph 4 cannot be used as a legal basis for adapting standard information requirements.

Recognising that the registered substance is classified as corrosive, you are advised to examine how the concentration of the test substance can be adjusted to avoid corrosion allowing at the same time detection of potential systemic toxicity effects of the substance. The general principle of adjusting the concentration of the test substance to avoid corrosion and irritation is set out in the relevant test guidelines (OECD 413 and OECD 408).

In conclusion, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.6.2., column 2 nor the general rules for adaptation of Annex XI.

Therefore, your adaptation of the information requirement is rejected.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

According to the test method OECD TG 408, the rat is the preferred rodent species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In your comments on the draft decision, you have considered exposure based adaptation and some preliminary tests on dermal penetration, hydrolysis and metabolism. Concerning the adaptation that may be based on strictly controlled conditions, ECHA points out that such adaptation can only be used, when for all relevant exposure scenarios, the conditions specified in Article 18(4) apply. ECHA finds that in the current dossier you have not provided documentation that shows that these conditions apply. Concerning the preliminary studies, ECHA notes that while these studies might be useful in scoping for the more definitive studies, they as such would not provide valid adaptations, neither would they meet any of the information requirements of Annex IX of REACH or fulfil the information requirement for this endpoint.

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: Repeated dose 90-day oral toxicity study (test method: OECD TG 408) in rats.

2. Pre-natal developmental toxicity study (Annex IX, 8.7.2.; test method: OECD 414) in rats or rabbits, oral route.

A "pre-natal developmental toxicity study" (test method OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, section 8.7.2. 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 not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2.

You have sought to adapt this information requirement of Annex IX, Section 8.7.2. You have justified the proposal for adaptation with the following waiver: "*The substance MK92K is corrosive and (based on physicochemical properties and read-across from similar quaternary ammonium compounds) is considered to be poorly systematically absorbed following oral administration. It is therefore very likely that the effects of the repeated oral administration of MK92K in an animal study will be largely local (due to irritation/corrosion at the site of contact), with little or no systemic effects other that those secondary to the effects of the substances on the gastrointestinal tract.*"

Although you have not explicitly claimed a legal basis for your adaptation, ECHA has first evaluated your adaptation according to Annex XI, Section 1.5. of the REACH Regulation. You have only provided summaries of four developmental toxicity studies (with rat and rabbit) on two related quaternary ammonium compounds, dodecyl dimethyl ammonium chloride (DDAC) and alkyl dimethyl benzyl ammonium chloride (ADBAC) in the CSR. However, no study records were provided in IUCLID section 7.5. for these studies. As explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

ECHA has further evaluated your adaptation according to the provisions set out in the fourth indent of Column 2 of Annex IX, 8.7.2. as you state that the substance is "*considered to be poorly systemically absorbed following oral administration*". According to that provision, a reproductive toxicity study does not need to be conducted if "*the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), in can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.*" You have however not demonstrated that the conditions of that provision are fulfilled.

As regards corrosivity, according to introductory paragraph 4 of Annex IX of the REACH Regulation "*in vivo* testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided". However, ECHA would like to point out that non-corrosive concentration(s) can be tested, and the introductory paragraph 4 cannot be used as a legal basis for adapting standard information requirements.

Recognising that the registered substance is classified as corrosive, you are advised to examine how the concentration of the test substance can be adjusted to avoid corrosion allowing at the same time detection of potential systemic toxicity effects of the substance. The general principle of adjusting the concentration of the test substance to avoid corrosion and irritation is set out in the relevant test guidelines (OECD 413 and OECD 408).

Concerning poor systemic absorption ECHA would like to point out that neither column 2 of Annex IX, 8.7.2. nor the general rules for adaptation of Annex XI include such possibility to adapt this standard information requirement.

In conclusion, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.7., column 2 nor the general rules for adaptation of Annex XI.

Therefore, your adaptation of the information requirement is rejected.

According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision, you have considered exposure based adaptation and some preliminary tests on dermal penetration, hydrolysis and metabolism. Concerning the adaptation that may be based on strictly controlled conditions, ECHA points out that such adaptation can only be used, when for all relevant exposure scenarios, the conditions specified in Article 18(4) apply. ECHA finds that in the current dossier you have not provided documentation that shows that these conditions apply. Concerning the preliminary studies, ECHA notes that while these studies might be useful in scoping for the more definitive studies, they as such would not provide valid adaptations, neither would they meet any of the information requirements of Annex IX of REACH or fulfil the information requirement for this endpoint.

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: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. 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.

In the technical dossier you have provided a study records for one key study (study title: "Acute Toxicity of MK92K to the Freshwater Green Algae, Selenastrum capricornutum") and one supporting study (study title: "Ecotox report").

However, those studies do not provide the information required by Annex VII, Section 9.1.2., because the key study was performed without analytical monitoring of the exposure concentrations of the test material and there is no information available about analytical monitoring of the exposure concentrations of the test material in the supporting study.

ECHA notes that constituents of the substance can be present in ionised forms at environmentaly relevant (and at the test medium) pHs and therefore, can be lost due adsorption from the test medium.

Furthermore, vapour pressure of the substance reported in the registration dossier is 200 Pa at 20 °C which indicates that some of the constituents of the substance might be volatile. ECHA observes that in the provided short-term aquatic invertebrates (with *Daphnia magna*) key study up to 20% of the substance (based on total organic carbon measurments) were lost from the test system within 24h periods. Therefore, ECHA concludes that provided studies are not adequate for the purpose of classification and labeling, identification of toxic (T) substances for the identification of persistent, bioaccumulative and toxic (PBT) substances and/or risk assessment.

In your comments to the draft decision, you indicate some preliminary investigations and you state "IF the initial chemical stability work shows the substance to be stable in light and water, then re-doing the test has little value. IF the initial stability checks show rapid degradation, repeating with analysis (eg using parallel abiotic chambers) may be needed; this may demonstrate toxicity of transformation products [It is noted that this test does not involve animals and there is no ethical argument in avoiding new work]".

ECHA notes as outlined in Sections 6- 8 below, these preliminary investigations may be useful in scoping for the more definitive studies. However, it is the registrant's responsibility to adapt the standard information. For any such adaptation to comply with the respective information requirement, it needs to be scientifically justified, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation must be provided in the registration dossier.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. 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) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

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: Algae growth inhibition test, EU C.3./OECD TG 201).

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

"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.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex

IX, Section 9.1.5., column 2. You provided the following justification for the adaptation: "*Two studies are now available that assess the short term (acute) toxicity of MK92K to invertebrates. A study was performed using Acartia Tonsa which is a marine species. There was no media analysis conducted, primarily due to the complex nature of the test compound. The 48h EC50 was 2.85mg/L. A second study has been performed using the fresh water invertebrate, Daphnia Magna. Verification of MK92K in the test media was performed using TOC analysis. This is not a specific analysis method but does nevertheless confirm the presence and concentration in solution.*
The result of this test (48h EC50 was 3.10 mg/L) is consistent with the result of the original test on the marine invertebrate and confirms that invertebrates are not the most sensitive aquatic species. In an algal growth inhibition test, the 72h ErC50 for MK92K was 0.47 mg/L, which is an order of magnitude lower than the acute daphnia endpoint."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 for the following reasons. According to the Annex I, Section 3 of the REACH Regulation the environmental hazard assessment shall consider the potential effects on the environment, including aquatic compartment. The hazard assessment shall comprise classification and labelling and derivation of the PNEC (predicted no-effect concentration). Furthermore, information on long-term aquatic toxicity is necessary for T assessment within PBT assessment. ECHA notes that on the basis of the information reported in the Chemical Safety Report (CSR) risk for marine and fresh waters is not controlled for exposure scenario 3 (Use at industrial sites). Furthermore, ECHA notes that the information on persistence and bioaccumulation of the substance (its relevant constituents) is requested. Thus, there is uncertainty on the PBT/vPvB status of the substance. Therefore, ECHA considers that Chemical Safety Assessment (CSA) indicates the need to investigate further the effects on aquatic organisms.

In your comments to the draft decision, you indicate some preliminary investigations and you state "This non-vertebrate study is considered important to perform and will help improve understanding of environmental impact. It is recommended to perform this, but to first check biotic and abiotic changes that could be found in a prolonged biodegradation assay".

ECHA notes as outlined in Sections 6- 8 below, these preliminary investigations may be useful in scoping for the more definitive studies. However, it is the registrant's responsibility to adapt the standard information. For any such adaptation to comply with the respective information requirement, it needs to be scientifically justified, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation must be provided in the registration dossier.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. 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) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

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).

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

"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.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: "*A study has been conducted to assess the short term toxicity of MK92K to Sheepshead Minnow.*
Although this is a marine species and there was no specific test media analysis, the 96h LC50 was 14.1 mg/L. Since this endpoint is higher than the invertebrate EC50 and the algal EC50, it is not considered necessary to conduct any further tests on fish species. Based on the available aquatic data, the algal NOEC should be used to derive the PNEC for the aquatic risk assessment. In addition, MK92K consists predominantly of quaternary ammonium compounds. For compounds of this nature, sorption to soils, sediment and suspended solids (humic acid) occurs as a result of the positively charged amines. As a result toxicity to aquatic species is likely to be reduced in the presence of humic acid and suspended sediment, thereby reducing long term exposure."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2 for the following reasons. As summarised under section 4 above, ECHA notes that risk for marine and fresh waters is not controlled for exposure scenario 3 (Use at industrial sites). Furthermore, there is uncertainty on the PBT/vPvB status of the substance. Therefore, ECHA considers that the CSA indicates the need to investigate further the effects on aquatic organisms.

In your comments to the draft decision, you indicate some preliminary investigations and you state "It is considered unethical to perform this animal test prior to further work on invertebrates and until degradation routes in the environment are better understood. This study may be subsequently important, but a decision is needed in the light of prior test work".

ECHA notes as outlined in Sections 6- 8 below, these preliminary investigations may be useful in scoping for the more definitive studies. However, it is the registrant's responsibility to adapt the standard information. For any such adaptation to comply with the respective information requirement, it needs to be scientifically justified, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation must be provided in the registration dossier.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. 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).

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

Before conducting any of the tests mentioned above in sections 3-5 you shall consult the ECHA *Guidance on information requirements and chemical safety assessment (*version 4.0, June 2017*)*, Chapter R7b, Section R.7.8.5 and Chapter R.11 (version 3.0, November 2017) to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish.

Due to the low solubility in water, high volatility and/or ionisable nature of some constituents of the substance 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 under section 3-5 aquatic toxicity tests and for calculation and expression of the result of the tests.

ECHA notes that according to Guidance on information requirements and chemical safety assessment, Chapter R.11, (version 3.0, June 2017) on PBT assessment "*Constituents, impurities and additives should normally be considered relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w)*" [...] "*In practice, this means that the registrant should carry out a comparison of the available data with the criteria for all constituents, impurities and additives present in concentration of ≥ 0.1% (w/w).*" Furthermore, ECHA notes that bearing in mind PBT assessment needs and deciding on the aquatic toxicity testing (please note that aquatic toxicity tests are requested under

sections 3-5) and risk assessment strategy for the substance, which is classified as UVCB, you should consider guidance on special considerations for toxicity testing and risk assessment of multi-constituent and UVCB substances which is provided in the Guidance on information requirements and chemical safety assessment, Chapter R7b (version 4.0, June 2017) and Chapter R.7.13 (version 3.0, June 2017), where principles of risk assessment for such substances are discussed (example of use of Hydrocarbon Block method for risk assessment of petroleum substances is provided).

Once results of the tests on aquatic toxicity are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. ECHA notes that for all identified uses safe use of the substance should be justified in the CSR. As noted in Article 14(6) "*Any registrant shall identify and apply the appropriate measures to adequately control the risks identified in the chemical safety assessment, and where suitable, recommend them in the safety data sheets*". If safe use of the substance cannot be proven, the use should not be identified as safe and should be advised against in the registration dossier and safety data sheet.

6. Simulation testing on ultimate degradation in water (Annex IX, Section 9.2.1.2.)

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. 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.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, section 9.2., column 2: "*A ready biodegradability test on MK92K has been conducted using seawater and it is evident from the results that there is little ultimate degradation of these compounds. The aim of a simulation test is to use a low concentration of test compound, quantify any carbon dioxide evolution and employ a specific analysis method to follow primary degradation of the test substance. Formation of carbon dioxide is unlikely under the more realistic nature of simulation tests (compared to a ready biodegradation test) and in the absence of a suitably sensitive analytical method, the primary degradation rate in water, soil and sediments cannot be determined.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2 and 9.2.1.2.
According to Annex IX, Section 9.2.1.2, column 2 of the REACH Regulation, simulation testing on ultimate degradation in surface water does not need to be conducted if the substance is highly insoluble in water or is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable (ca. 13% degradation in OECD TG 306) and has a water solubility of "*ca 3.2 to 109.3 g/L, with one component proving insoluble in water*".

Moreover, ECHA observes with a view to Annex IX, Column 2, Section 9.2. that further investigation of the degradation and the degradation products is indicated, because adequate and sufficient information on persistence (simulation degradation testing as requested in sections 6-8), bioaccumulation (as requested in section 10) and long-term

aquatic toxicity of the substance (as requested in sections 3-5) is missing and therefore requested by this decision. Furthermore, the substance is toxic to algae (based on nominal concentrations of the test material) at the concentration close to fulfil T criterion. Thus, there is uncertainty on the PBT/vPvB status of the substance. Therefore, ECHA considers that the information on degradation in environmental compartments is needed for the PBT/vPvB assessment, i.e. for the Chemical Safety Assessment according to Annex I, and for the identification of the degradation products in relation to the PBT/vPvB assessment.

ECHA considers that it should be possible to develop method for analytical monitoring of some identified relevant (e.g. worst-case in regard of persistence) and representative constituents of the substance while, indeed, monitoring of all constituents might be challenging.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. 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) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of the REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "*attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment*". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 309. Therefore, the test should be performed at the temperature of 12°C.

In the OECD TG 309 Guideline two test options, the "pelagic test" and the "suspended sediment test", are described. ECHA considers that the pelagic test option should be followed as that is the recommended option for P assessment. The amount of suspended solids in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the surface water sample used should therefore be approximately 15 mg dw/L. Testing natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. Furthermore, when reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

ECHA notes that the explanation on the development and justification for the choice of analytical method to quantify the test substance (its constituents) and transformation products (including the choice of the constituents to be measured) should be reported in the dossier.

In your comments following the procedure set out in Article 50(1) of the REACH Regulation you proposed to perform a modified OECD 301 test, with a test duration extended to 60 days, before deciding whether simulation tests need to be conducted.

As explained in ECHA guidance R.11 on PBT/vPvB assessment, version 3.0, June 2017, some modifications of the standard ready biodegradability tests (e.g. from the OECD 301 series or OECD 310) are possible for the purpose of the PBT/vPvB assessment only (but not for the risk assessment or for classification and labelling). Such modified tests are designated as 'enhanced biodegradation screening tests'. The prolongation of the test duration up to 60 days is one of the possible enhancements. A longer test duration may give the microorganisms more time for accessing and degrading substance that are poorly bioaccessible (e.g. adsorptive substances). Substances with limited bioaccessibility would likely not reach a plateau by the end of a standard ready biodegradability test (i.e. after 28 days) but may show some slow but steady biodegradation indicative of a potential for being ultimately biodegraded within 60 days. However, if a sudden acceleration of biodegradation is observed during the late course of the prolonged test, it likely reflects an adaptation of the microorganisms. In that latter case the prolongation of the test duration should not be regarded as adequate for the purpose of the PBT/vPvB assessment. As a general principle, for the purpose of the PBT/vPvB assessment, the test inoculum must not be deliberately adapted.

ECHA further notes that the registered substance is a UVCB made of heterogeneous constituents in particular in terms of their water solubilities or log Kow. As explained in the OECD '*Guidelines for the Testing of Chemicals, Revised Introduction To The OECD Guidelines For Testing Of Chemicals, Section 3 Part I: Principles And Strategies Related To The Testing Of Degradation Of Organic Chemicals*', ready biodegradability tests are intended for pure substances and are generally not applicable for complex compositions containing different types of constituents. For substances consisting of heterogeneous constituents, observed biodegradation measured as DOC removal, CO_2 evolution or O_2 consumption may only reflect the mineralisation of some of the constituents but does not rule out that the rest of them could be persistent. Therefore, mineralisation above 60% would not constitute as such a proof that none of the constituents or their transformation products are persistent or very persistent. Chemical analyses could be performed in order to identify such recalcitrant constituents/transformation products. However, the quantification of potential losses of the substance or of its transformation products (e.g. from adsorption onto the glass vessels or organic matter, other bound residues, volatilisation) would then be necessary for interpreting the results.

It is important to note that contrary to simulation tests, no half-life could be calculated from enhanced biodegradation screening tests as biodegradation during such tests is unlikely to follow first-order kinetics. Moreover, half-lives have to correspond to conditions relevant for the PBT/vPvB assessment (e.g. in terms of biomass and test substance concentrations, temperature, origin of inoculum), which is not the case for enhanced biodegradation screening tests.

With regard to the test method, you proposed to use the OECD 301 test guideline, either the closed bottle test or the CO_2 evolution method. ECHA notes that for volatile substances, both OECD 301D (closed bottle test) and OECD 310 (CO_2 headspace test) are appropriate. However, CO_2 evolution test OECD 301B should not be used for volatile substances.

In your comments, you also proposed to investigate potential abiotic degradation of the substance: hydrolysis studies at pH 1 (synthetic stomach media), 4, 7 and 9 - based on OECD test guideline 111, as well as direct photolysis in water based on OECD test guideline 316.

With regard to direct photolysis in water (OECD test guideline 316), it should not be used for the persistence assessment. As explained in chapter R.11.4.1.1.1 of ECHA guidance R.11 on PBT/vPvB assessment, version 3.0, June 2017, and in chapter R.7.9.4.1 of ECHA guidance on Information Requirements and Chemical Safety Assessment, version 4.0, June 2017, light absorption in natural water is significantly slower than measured in laboratory water, with direct photo degradation occurring around 30 times more slowly for typical fresh water, 400 times more slowly for typical coastal sea water, and 500 times more slowly for ocean water. There are large variation in the light available in the environment, depending on the water body characteristics (depth, turbidity, degree of mixing), but also on seasonal variations and geographical latitudes. In practice, direct photolysis in natural water is deemed to be negligible under environmental conditions which are relevant for the PBT/vPvB assessment and for that purpose it should not be assessed with OECD test guideline 316. Information on phototransformation might help to explain the results of the ecotoxicity tests requested above, but it is not a standard information requirement of REACH and as such need not be conducted.

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: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309). The biodegradation of each relevant constituents present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

7. Soil simulation testing (Annex IX, Section 9.2.1.3.)

"Soil simulation testing" is a standard information requirement as laid down in Annex IX, section 9.2.1.3. of the REACH Regulation for substances with a high potential for adsorption to soil. Some constituents of the registered substance can be present in ionised form at environmentally relevant pHs and adsorption coefficient log Kow values from <1.25 to 5.40 are reported in the registration dossier for constituents of the substance which indicate high potential for adsorption of some constituents. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, section 9.2., column 2: *"A ready biodegradability test on MK92K has been conducted using seawater and it is evident from the results that there is little ultimate degradation of these compounds. The aim of a simulation test is to use a low concentration of test*

compound, quantify any carbon dioxide evolution and employ a specific analysis method to follow primary degradation of the test substance. Formation of carbon dioxide is unlikely under the more realistic nature of simulation tests (compared to a ready biodegradation test) and in the absence of a suitably sensitive analytical method, the primary degradation rate in water, soil and sediments cannot be determined."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2 and 9.2.1.3.
As explained in section 6 above, the registered substance is not readily biodegradable and ECHA considers that the information on degradation in environmental compartments is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.
Furthermore, ECHA considers that it should be possible to develop method for analytical monitoring of some identified relevant (e.g. worst-case in regard of persistence) and representative constituents of the substance while, indeed, monitoring of all constituents might be challenging.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. 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) Aerobic and anaerobic transformation in soil (test method EU C.23. / OECD TG 307) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.3.

As explained in section 6 above, 12°C (285K) is the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 307. Therefore, the test should be performed at the temperature of 12°C.

Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound or incorporated into the biomass. When reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

ECHA notes that the explanation on the development and justification for the choice of analytical method to quantify the test substance (its constituents) and transformation products (including the choice of the constituents to be measured) should be reported in the dossier.

In your comments following the procedure set out in Article 50(1) of the REACH Regulation you proposed to perform a modified OECD 301 test, with a test duration extended to 60 days, before deciding whether simulation tests need to be conducted.

As explained in ECHA guidance R.11 on PBT/vPvB assessment, version 3.0, June 2017, some modifications of the standard ready biodegradability tests (e.g. from the OECD 301 series or OECD 310) are possible for the purpose of the PBT/vPvB assessment only (but not for the risk assessment or for classification and labelling). Such modified tests are designated as 'enhanced biodegradation screening tests'. The prolongation of the test duration up to 60 days is one of the possible enhancements. A longer test duration may give the microorganisms more time for accessing and degrading substance that are poorly bioaccessible (e.g. adsorptive substances). Substances with limited bioaccessibility would likely not reach a plateau by the end of a standard ready biodegradability test (i.e. after 28 days) but may show some slow but steady biodegradation indicative of a potential for being ultimately biodegraded within 60 days. However, if a sudden acceleration of biodegradation is observed during the late course of the prolonged test, it likely reflects an adaptation of the microorganisms. In that latter case the prolongation of the test duration should not be regarded as adequate for the purpose of the PBT/vPvB assessment. As a general principle, for the purpose of the PBT/vPvB assessment, the test inoculum must not be deliberately adapted.

ECHA further notes that the registered substance is a UVCB made of heterogeneous constituents in particular in terms of their water solubilities or log Kow. As explained in the OECD '*Guidelines for the Testing of Chemicals, Revised Introduction To The OECD Guidelines For Testing Of Chemicals, Section 3 Part I: Principles And Strategies Related To The Testing Of Degradation Of Organic Chemicals*', ready biodegradability tests are intended for pure substances and are generally not applicable for complex compositions containing different types of constituents. For substances consisting of heterogeneous constituents, observed biodegradation measured as DOC removal, CO_2 evolution or O_2 consumption may only reflect the mineralisation of some of the constituents but does not rule out that the rest of them could be persistent. Therefore, mineralisation above 60% would not constitute as such a proof that none of the constituents or their transformation products are persistent or very persistent. Chemical analyses could be performed in order to identify such recalcitrant constituents/transformation products. However, the quantification of potential losses of the substance or of its transformation products (e.g. from adsorption onto the glass vessels or organic matter, other bound residues, volatilisation) would then be necessary for interpreting the results.

It is important to note that contrary to simulation tests, no half-life could be calculated from enhanced biodegradation screening tests as biodegradation during such tests is unlikely to follow first-order kinetics. Moreover, half-lives have to correspond to conditions relevant for the PBT/vPvB assessment (e.g. in terms of biomass and test substance concentrations, temperature, origin of inoculum), which is not the case for enhanced biodegradation screening tests.

With regard to the test method, you proposed to use the OECD 301 test guideline, either the closed bottle test or the CO_2 evolution method. ECHA notes that for volatile substances, both OECD 301D (closed bottle test) and OECD 310 (CO_2 headspace test) are appropriate. However, CO_2 evolution test OECD 301B should not be used for volatile substances.

In your comments, you also proposed to investigate potential abiotic degradation of the substance: hydrolysis studies at pH 1 (synthetic stomach media), 4, 7 and 9 - based on OECD test guideline 111, as well as direct photolysis in water based on OECD test guideline 316.

With regard to direct photolysis in water (OECD test guideline 316), it should not be used for the persistence assessment. As explained in chapter R.11.4.1.1.1 of ECHA guidance R.11 on PBT/vPvB assessment, version 3.0, June 2017, and in chapter R.7.9.4.1 of ECHA guidance on Information Requirements and Chemical Safety Assessment, version 4.0, June 2017, light absorption in natural water is significantly slower than measured in laboratory water, with direct photo degradation occurring around 30 times more slowly for typical fresh water, 400 times more slowly for typical coastal sea water, and 500 times more slowly for ocean water. There are large variation in the light available in the environment, depending on the water body characteristics (depth, turbidity, degree of mixing), but also on seasonal variations and geographical latitudes. In practice, direct photolysis in natural water is deemed to be negligible under environmental conditions which are relevant for the PBT/vPvB assessment and for that purpose it should not be assessed with OECD test guideline 316. Information on phototransformation might help to explain the results of the ecotoxicity tests requested above, but it is not a standard information requirement of REACH and as such need not be conducted.

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: Aerobic and anaerobic transformation in soil (test method: EU C.23./OECD TG 307). The biodegradation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

8. Sediment simulation testing (Annex IX, Section 9.2.1.4.)

"Sediment simulation testing" is a standard information requirement as laid down in Annex IX, section 9.2.1.4. of the REACH Regulation for substances with a high potential for adsorption to sediment. Some constituents of the registered substance can be present in ionised form at environmentally relevant pHs and adsorption coefficient log Kow values from <1.25 to 5.40 are reported in the registration dossier for constituents of the substance which indicate high potential for adsorption of some constituents. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, section 9.2., column 2: *"A ready biodegradability test on MK92K has been conducted using seawater and it is evident from the results that there is little ultimate degradation of these compounds. The aim of a simulation test is to use a low concentration of test compound, quantify any carbon dioxide evolution and employ a specific analysis method to follow primary degradation of the test substance. Formation of carbon dioxide is unlikely under the more realistic nature of simulation tests (compared to a ready biodegradation test) and in the absence of a suitably sensitive analytical method, the primary degradation rate in water, soil and sediments cannot be determined."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2 and 9.2.1.4.

As explained in section 6 above, the registered substance is not readily biodegradable and ECHA considers that the information on degradation in environmental compartments is

needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.

Furthermore, ECHA considers that it should be possible to develop method for analytical monitoring of some identified relevant (e.g. worst-case in regard of persistence) and representative constituents of the substance while, indeed, monitoring of all constituents might be challenging.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. 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) Aerobic and anaerobic transformation in aquatic sediment systems (test method EU C.24. / OECD TG 308) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.4.

As explained in section 6 above, 12°C (285K) is the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 308. Therefore, the test should be performed at the temperature of 12°C.
Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound or incorporated into the biomass. When reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

ECHA notes that the explanation on the development and justification for the choice of analytical method to quantify the test substance (its constituents) and transformation products (including the choice of the constituents to be measured) should be reported in the dossier.

In your comments following the procedure set out in Article 50(1) of the REACH Regulation you proposed to perform a modified OECD 301 test, with a test duration extended to 60 days, before deciding whether simulation tests need to be conducted.

As explained in ECHA guidance R.11 on PBT/vPvB assessment, version 3.0, June 2017, some modifications of the standard ready biodegradability tests (e.g. from the OECD 301 series or OECD 310) are possible for the purpose of the PBT/vPvB assessment only (but not for the risk assessment or for classification and labelling). Such modified tests are designated as 'enhanced biodegradation screening tests'. The prolongation of the test duration up to 60 days is one of the possible enhancements. A longer test duration may give the microorganisms more time for accessing and degrading substance that are poorly bioaccessible (e.g. adsorptive substances). Substances with limited bioaccessibility would likely not reach a plateau by the end of a standard ready biodegradability test (i.e. after 28 days) but may show some slow but steady biodegradation indicative of a potential for being

ultimately biodegraded within 60 days. However, if a sudden acceleration of biodegradation is observed during the late course of the prolonged test, it likely reflects an adaptation of the microorganisms. In that latter case the prolongation of the test duration should not be regarded as adequate for the purpose of the PBT/vPvB assessment. As a general principle, for the purpose of the PBT/vPvB assessment, the test inoculum must not be deliberately adapted.

ECHA further notes that the registered substance is a UVCB made of heterogeneous constituents in particular in terms of their water solubilities or log Kow. As explained in the OECD '*Guidelines for the Testing of Chemicals, Revised Introduction To The OECD Guidelines For Testing Of Chemicals, Section 3 Part I: Principles And Strategies Related To The Testing Of Degradation Of Organic Chemicals*', ready biodegradability tests are intended for pure substances and are generally not applicable for complex compositions containing different types of constituents. For substances consisting of heterogeneous constituents, observed biodegradation measured as DOC removal, CO_2 evolution or O_2 consumption may only reflect the mineralisation of some of the constituents but does not rule out that the rest of them could be persistent. Therefore, mineralisation above 60% would not constitute as such a proof that none of the constituents or their transformation products are persistent or very persistent. Chemical analyses could be performed in order to identify such recalcitrant constituents/transformation products. However, the quantification of potential losses of the substance or of its transformation products (e.g. from adsorption onto the glass vessels or organic matter, other bound residues, volatilisation) would then be necessary for interpreting the results.

It is important to note that contrary to simulation tests, no half-life could be calculated from enhanced biodegradation screening tests as biodegradation during such tests is unlikely to follow first-order kinetics. Moreover, half-lives have to correspond to conditions relevant for the PBT/vPvB assessment (e.g. in terms of biomass and test substance concentrations, temperature, origin of inoculum), which is not the case for enhanced biodegradation screening tests.

With regard to the test method, you proposed to use the OECD 301 test guideline, either the closed bottle test or the CO_2 evolution method. ECHA notes that for volatile substances, both OECD 301D (closed bottle test) and OECD 310 (CO_2 headspace test) are appropriate. However, CO_2 evolution test OECD 301B should not be used for volatile substances.

In your comments, you also proposed to investigate potential abiotic degradation of the substance: hydrolysis studies at pH 1 (synthetic stomach media), 4, 7 and 9 - based on OECD test guideline 111, as well as direct photolysis in water based on OECD test guideline 316.

With regard to direct photolysis in water (OECD test guideline 316), it should not be used for the persistence assessment. As explained in chapter R.11.4.1.1.1 of ECHA guidance R.11 on PBT/vPvB assessment, version 3.0, June 2017, and in chapter R.7.9.4.1 of ECHA guidance on Information Requirements and Chemical Safety Assessment, version 4.0, June 2017, light absorption in natural water is significantly slower than measured in laboratory water, with direct photo degradation occurring around 30 times more slowly for typical fresh water, 400 times more slowly for typical coastal sea water, and 500 times more slowly for ocean water. There are large variation in the light available in the environment, depending on the water body characteristics (depth, turbidity, degree of mixing), but also on seasonal

variations and geographical latitudes. In practice, direct photolysis in natural water is deemed to be negligible under environmental conditions which are relevant for the PBT/vPvB assessment and for that purpose it should not be assessed with OECD test guideline 316. Information on phototransformation might help to explain the results of the ecotoxicity tests requested above, but it is not a standard information requirement of REACH and as such need not be conducted.

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: Aerobic and anaerobic transformation in aquatic sediment systems (test method: EU C.24./OECD TG 308). The biodegradation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

Notes for your consideration

Before conducting the tests requested under sections 6-8 you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 4.0, June 2017) and Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017) on PBT assessment to determine the sequence in which the simulation tests are to be conducted and the necessity to conduct all of them. The order in which the simulation biodegradation tests are performed needs to take into account the intrinsic properties of the registered substance and the identified use and release patterns which could significantly influence the environmental fate of the registered substance.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the tests detailed above are available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

9. Identification of degradation products (Annex IX, Section 9.2.3.)

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX 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.

The biodegradation section in the technical dossier does not contain any information in relation to the identification of degradation products, nor an adaptation in accordance with column 2 of Annex IX, Sections 9.2 or 9.2.3. or with the general rules of Annex XI for this standard information requirement.
According to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable.

In your comments to the draft decision, ECHA has addressed them in the above Sections 6 – 8.

Consequently there is an information gap and it is necessary to provide information for this endpoint.

Regarding appropriate and suitable test method, the methods will have to be substance-specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition, degradation half-life, log Kow and potential toxicity of the metabolite may be investigated.

You may obtain this information from the relevant degradation studies also requested in this decision in the sections 6-8 above, or by some other measure. You will need to provide a scientifically valid justification for the chosen method.

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:

Identification of the degradation products (Annex IX, Section 9.2.3.) by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration

Before providing the above information you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

10. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2.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 IX, Section 9.3.2., column 2, i.e. that the bioaccumulation study need not be conducted if the substance has a low potential for bioaccumulation (for instance a log Kow <=3). You provided the following justification for the adaptation: *"The most important and widely accepted indication of bioaccumulation potential is a high value of the partition coefficient, Log Pow, and it is accepted that values of Log Pow in excess of 3 indicate that the substance may bioaccumulate. MK92K displayed a range of Log Pow values from <0.24 to 3.93, with a significant proportion of the components having Log Pow values < 3. As the major proportion of the components have a Log Pow <3, the potential for bioaccumulation of MK92K in aquatic organisms is likely to be minimal."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.3.2., column 2, because the substance qualifies as surfactant (as reported in the registration dossier the surface tension of the substance is 49.65 mN/m) and at environmentally relevant pHs some constituents are present in the ionised form. According to the ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7c. (version 3.0, June 2017) "*for certain types of substances (e.g. surface-active agents and those which ionise in water), the log Kow might not be suitable for calculation of a BCF value. [...] the classification of the bioconcentration potential based on hydrophobicity measures (such as log Kow) should be used with caution. [...] Measured BCF values are preferred.*" and according to *Guidance on information requirements and chemical safety assessment*, Chapter R.11. (version 3.0, June 2017) "*for some groups of substances, such as organometals, ionisable substances and surface active substances, log Kow is not a valid descriptor for assessing the bioaccumulation potential. Information on bioaccumulation of such substances should therefore take account of other descriptors or mechanisms than hydrophobicity.*"

In your comments to the draft decision, you indicate some preliminary investigations and you state "It needs to be noted that the registered substance has a range of partition coefficients of up to Log 3.92 at pH2. No components with a partition coefficient > 4 were identified, but it is proposed that this study is repeated in buffered media. This needs to be linked to water solubility assessments under dilute conditions with 'natural' water (medium hardness). This animal study should only be considered once the environmental fate has been fully evaluated; if metabolites are found that have a Log Kow > 4, then the potential accumulation of these need to be considered."

ECHA notes as outlined in Sections 6- 8 above, these preliminary investigations may be useful in scoping for the more definitive studies.

However, it is the registrant's responsibility to adapt the standard information. For any such adaptation to comply with the respective information requirement, it needs to be scientifically justified, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation must be provided in the registration dossier.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. 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.7c* (version 3.0, June 2017) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2. ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If you decided to conduct the study using the dietary exposure route, you shall

provide scientifically valid justification for your decision. You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG and in OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation, ENV/JM/MONO (2017)16. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.

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: Bioaccumulation in fish: aqueous exposure bioconcentration fish test (test method: OECD TG 305-I). The bioaccumulation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), Chapter R.11.4. and Figure R.11-4 on the PBT assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. In particular, you are advised to first conclude whether the registered substance (any of relevant constituents) may fulfil the REACH Annex XIII criteria of being persistent or very persistent, and then to consult the PBT assessment for Weight-of-Evidence determination and integrated testing strategy for bioaccumulation assessment. You should revise the PBT assessment when information on bioaccumulation is available.

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 1 March 2018.

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

The draft decision was sent to the registrant on 18 June 2018.

The registrant provided comments on the draft decision.

ECHA did not amend the draft decision based on the comments received.

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.