

Helsinki, 01 September 2023

Addressee(s)

Registrant(s) of JS_7526-26-3_DPP as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision

16/06/2022

Registered substance subject to this decision ("the Substance")

Substance name: diphenyl methylphosphonate

EC number/List number: 231-388-1

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by **7 December 2026**.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

1. Skin sensitisation (Annex VII, Section 8.3.)
 - a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and
 - b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);
2. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, OECD TG 471 (2020)).

Information required from all the Registrants subject to Annex VIII of REACH

3. *In vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei;
4. Justification for an adaptation of the short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1., Column 2) based on the request 6 below,
5. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats.

Information required from all the Registrants subject to Annex IX of REACH

6. Sub-chronic toxicity study (90 days), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats;

7. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit);
8. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211);
9. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210);
10. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25/OECD TG 309) at a temperature of 12°C;
11. Identification of degradation products (Annex IX, Section 9.2.3.; test method: EU C.25/OECD TG 309).

The reasons for the request(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report**, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to <http://echa.europa.eu/regulations/appeals> for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised¹ under the authority of Mike Rasenberg, Director of Hazard Assessment

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 for the request(s)

Appendix 2: Procedure

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Appendix 1: Reasons for the request(s)

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Reasons common to several requests

0.1. (Q)SAR adaptation rejected

1 You seek to adapt the following standard information requirements by applying (Q)SAR approaches in accordance with Annex XI, Section 1.3.:

- Skin sensitisation (Annex VII, Section 8.3.)
- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)

2 ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation(s) in general before assessing the specific standard information requirements in the following appendices.

3 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

- (1) the prediction needs to be derived from a scientifically valid model,
- (2) the substance must fall within the applicability domain of the model,
- (3) results need to be adequate for the purpose of risk assessment or classification and labelling, and
- (4) adequate and reliable documentation of the method must be provided.

4 Regarding these conditions, we have identified the following issue(s):

0.1.1. Inadequate documentation of the prediction (QPRF)

5 Guidance on IRs and CSA R.6.1.6.3. states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the relationship between the modelled substance and the defined applicability domain, and
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

6 The applicability domain assessment provided in the report of the software does not include an explanation on how the specific target substance fits in the applicability domain. There is no information on the identity of close analogues or on how data for analogues support the prediction.

7 In absence of such information, ECHA cannot establish that the predictions can be used to meet these information requirements.

0.1.2. Conclusion on the (Q)SAR adaptation

8 Based on the above, your (Q)SAR adaptations under Annex XI, Section 1.3. are rejected.

0.2. Read-across adaptation rejected

9 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Sub-chronic toxicity (90 day), (Annex IX, Section 8.6.2.)

10 You have provided information derived from experimental data from a group of substances using the OECD QSAR Toolbox and flagged the information as QSAR.

11 As the group of substances are used as source substances to predict the property of the Substance, we understand that you have adapted the standard information requirements under Annex XI, Section 1.5 of REACH (grouping and read-across).

12 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

13 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used.

14 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.

15 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

16 We have assessed this information accordingly and identified the following issues:

0.2.1. Absence of read-across documentation

17 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from information on the source substance(s).

18 You have provided information derived from experimental data from a group of substances using the OECD QSAR Toolbox in order to comply with the REACH information requirements.

19 However, you have not provided documentation to explain why this information is relevant for the Substance and why the properties of the Substance may be predicted from information on the source substance(s).

20 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substances.

0.2.2. Missing robust study summaries

21 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include robust study summary for each source study used in the adaptation.

22 Robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

23 You have not provided any robust study summaries for the substances used in the prediction.

24 You have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the studies.

25 Therefore, you have failed to provide a robust study summary for each source study used in the adaptations as required by Annex XI, Section 1.5.

0.2.3. Conclusion on the read-across approach

26 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approaches under Annex XI, Section 1.5. are rejected.

0.3. Substance-tailored exposure-driven testing adaptation rejected

27 ECHA understands that you have adapted the following standard information requirement(s) under Annex XI, Section 3.2 (a) or (c) substance-tailored exposure-driven testing:

- (i) Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- (ii) Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- (iii) Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- (iv) Long-term toxicity to aquatic invertebrates (Annex IX, Section 9.1.5.)
- (v) Long-term toxicity to fish (Annex IX, Section 9.1.6.)
- (vi) Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

28 To support the adaptation with regard to human health, points (i) to (iii), you have provided the following justification:

29 *"In accordance with Annex XI section 3 of REACH Regulation (EC) No. 1907/2006, a repeated dose toxicity study does not need to be conducted since relevant human exposure to monomer DPP can be excluded.*

[REDACTED] DPP itself is [REDACTED] used in [REDACTED] process which will take place in fully automated closed systems under nearly strictly controlled conditions. Therefore, any relevant exposure to human can be ruled out as indicated by the exposure assessment. The RCRs for the dermal exposure [REDACTED] for all contributing activities. Regarding the inhalation exposure the RCRs are [REDACTED] for all contributing activities. Oral exposure is not relevant since on the one hand this is not a relevant exposure route for workers. On the other hand, no consumer uses are indicated for DPP. For further information please refer to section 9 of the CSR."

30 To support the adaptation with regard to the environment, points (iv) to (vi), you have provided the following justification:

31 *"According to REACH Annex XI, Section 3 certain information requirements in Annex IX and X based on an exposure scenario(s) developed as a part of a Chemical Safety Report (CSR) in accordance with section 5 of Annex I can be omitted. The CSR adequately addresses the relevant exposure scenarios showing the absence or no significant emission of the test item into the environment throughout the whole life cycle. Since there are no wide-spread uses relevant during the substance's life cycle, direct emissions to the environment are in general highly unlikely. At all industrial sites the substance is handled with caution by trained professionals. Moreover, the substance is handled under nearly strictly controlled conditions during the manufacture of polymers as indicated by the assigned use descriptors. Additionally, no water discharge is expected during normal operations. In general, the substance is not in contact to water. Nevertheless, a release of [REDACTED] to wastewater is assumed which represents a worst-case approach. In addition, indirect exposure via air is also marginal since [REDACTED] and the substance is not expected to pass through these absorber. It can be concluded that direct emissions to the water are not expected during standard operations. Indirect emission are negligible as well. Having a PEC/PNEC ratio of well below 1 for all exposure scenarios for the freshwater and marine water compartment as well as the associated sediment compartments, indicate that there is no risk identified towards aquatic organisms. A long-term toxicity study on aquatic invertebrates can be exempted due to the minimal*

exposure demonstrated in the chemical safety assessment of the test substance. Consequently, this endpoint can be waived in accordance to REACH, Annex XI, Section 3."

32 A substance-tailored exposure-driven testing adaptation must fulfil the cumulative conditions set out under Annex XI, Sections 3(1) as well as 3(2)(a), (b) or (c).

33 Based on the above ECHA understands that you base your adaptations on Annex XI, Sections 3(1) as well as 3(2)(a) or (c).

0.3.1. Assessment of the information provided against the conditions of Annex XI, Sections 3(2)(a).

0.3.1.1. Absence of or no significant exposure not demonstrated

34 Under Annex XI, Section 3(2)(a)(i), the results of the exposure assessment covering all relevant exposure throughout the life cycle of the substance must demonstrate absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

35 As explained in section 0.3.2.1 below, you have not provided exposure scenarios for the full life-cycle of the Substance.

36 Therefore, you have not demonstrated absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

37 In your comments on the draft decision, you provide additional information regarding the life-cycle of the Substance which addresses this issue. You are requested to update the dossier with this information.

0.3.1.2. Exposure always well below PNEC not demonstrated

38 The results of the exposure assessment must show that exposures are always well below the PNEC, i.e. RCRs must always be well below 1. This means that a high level of confidence is needed to demonstrate that every RCR is low enough to ensure that the risks are always controlled, under every plausible condition of the manufacture and all identified uses of the Substance. For this purpose, the possible sources of variability and uncertainty must be considered in the assessment of exposure (Guidance on IRs and CSA Chapter R.16, page 68).

39 Uncertainty must be taken into account, either by carrying out the environmental exposure assessment using conservative assumptions and default values, which are provided in Guidance on IRs and CSA Chapters R.16. (Guidance on IRs and CSA Chapter R.19).

40 Alternatively, when the environmental exposure assessment is not based on these generic assumptions, a stepwise, tiered approach including an uncertainty analysis must be conducted. This analysis can be qualitative, deterministic, or probabilistic, to demonstrate that the risk is adequately controlled (Guidance on IRs and CSA Chapter R.19 provides a framework for carrying out a stepwise, tiered approach to uncertainty analysis). The results must be provided in the dossier to demonstrate that the application of such tiered uncertainty analysis gives a clear indication that the risk is adequately controlled (e.g. an increased belief that the (distribution of the) RCR is less than 1).

41 In your dossier you claim that *"no water discharge is expected during normal operations. In general, and the the substance is not expected to be in contact with water. Nevertheless, a release of ██████████ to wastewater is assumed which represents a worst-case approach"*. Accordingly you conclude that *"direct emissions to the water are not expected during standard operations"*.

42 Further, you also claim the following *"Having a PEC/PNEC ratio of well below 1 for all exposure scenarios for the freshwater and marine water compartment as well as the*

associated sediment compartments, indicate that there is no risk identified towards aquatic organisms"

- 43 You have used release factors that differ considerably from those recommended in ECHA Guidance R.16. The default release factor of 5% recommended in ECHA guidance is [REDACTED] times higher than the release factor of [REDACTED] applied by you.
- 44 Consequently, you have not demonstrated that worst case conditions are covered by these release factors.
- 45 Therefore, you have not demonstrated that your exposure assessment is always conservative enough and the RCRs always low enough to cover the possible sources of variability and uncertainty.
- 46 In your comments to the draft decision, you state that *"...the Chemical Safety Report adequately addresses the relevant exposure scenarios showing no significant emission of the substance into the environment throughout the whole life cycle. This is also indicated by the PEC/PNEC ratios which all are well below 1."* To support your conclusion, you further explain that the release factors are set based on the provided site-specific information and that the Substance is never in contact to water. In addition, you explain that active carbon beds are used to remove the Substance from air. Based on these arguments, you believe that assuming release of [REDACTED] and [REDACTED] to air represent the worst-case-approach. You also state that *"the substance is handled under nearly strictly controlled conditions"*.
- 47 However, you have not provided any specific evidence to demonstrate that every RCR is low enough to ensure that the risks are always controlled, under every plausible condition of the manufacture and all identified uses of the Substance (e.g. distribution of monitoring data). More specifically, based on the available data it is not clear if the whole life-cycle is considered, e.g. cleaning and maintenance. In addition, you do not provide information confirming that strictly controlled conditions are achieved and that as a result, release to environment would not happen.
- 48 Therefore, based on the information in your registration dossier and your comments, you did not provide evidence that exposures can be regarded as being always well below the PNEC.

0.3.1.3. Lack of appropriate DNEL

- 49 Under Annex XI, Section 3.2(a)(ii), a relevant and appropriate derived no effect level (DNEL) must be derived.
- 50 For repeated dose toxicity, a DNEL derived from a 28-day repeated dose toxicity study is not considered appropriate to omit a 90-day repeated dose toxicity study.
- 51 For the reasons explained in Section 0.2. your read-across adaptation is rejected. As a result, you cannot derive a no effect level based on the available information.
- 52 For pre-natal developmental toxicity, a DNEL derived from a screening test for reproductive/developmental toxicity is not considered appropriate to omit a pre-natal developmental toxicity study.
- 53 You have not provided any information which can be used to derive a no effect level.
- 54 Therefore, you have not provided a relevant and appropriate DNEL.
- 55 In your comments to the draft decision, you propose to perform the short-term repeated dose toxicity (28 days) study. You propose to use the NOAEL obtained from this study as a starting point for the DNEL derivation and use that to waive the 90-day repeated dose toxicity study, the screening test for reproductive/developmental toxicity and the pre-natal developmental toxicity studies based on the substance-tailored exposure-driven testing adaptation given by REACH Annex XI.

56 However, according to Annex XI, Section 3.2. (a) (ii) "a DNEL derived from a 28-day repeated dose toxicity study shall not be considered appropriate to omit a 90-day repeated dose toxicity study, and a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit a prenatal developmental toxicity study".

57 ECHA therefore points out that your proposal to conduct a 28-day study will not provide the appropriate DNELs required for an adaptation of the 90-day repeated dose toxicity study, the screening test for reproductive/developmental toxicity or the pre-natal developmental toxicity studies according to Annex XI, Section 3.

0.3.2. Assessment of the information provided against the conditions of Annex XI, Sections 3(1) and 3(2)(c)

58 We have assessed this information accordingly and identified the following issues:

0.3.2.1. Lack of or incomplete exposure assessment

59 Under Annex XI, Sections 3(1) and (2), testing may be omitted based on the exposure scenario(s) developed in the chemical safety report (CSR) by providing an adequate and scientifically supported justification based on a thorough and rigorous exposure assessment.

60 This also applies to monomers in polymer for which the justification must cover in particular absence of unreacted monomers and demonstration that the polymer does not degrade to monomers under use or waste stage (see Guidance for monomers and polymers, April 2012, Version 2.0), in particular Sections 2.2, 3.2.1 and 4.2, and the decision of Board of Appeal for A-001-2020 (in particular paragraphs 109 and 110 thereof).

61 The CSR does not contain a chemical risk assessment covering all relevant exposures of the entire life cycle of the (monomer) the Substance.

62 In your dossier you claim that "relevant human exposure to monomer DPP can be excluded" and "exposure scenarios showing the absence or no significant emission of the test item into the environment throughout the whole life cycle".

63 You have provided only one exposure scenario (ES 1: Manufacture of polymers (plastics) at industrial sites) which covers only the manufacture of the polymer from the Substance.

64 No other exposure scenario is provided.

65 You have not considered the presence of, and exposure to, unreacted (unbound) monomer which may remain or could be re-formed in the polymer, i.e. the quantities of the monomer substance which did not react during the polymerisation reaction and remained in the composition of the polymer or can be formed as a result of degradation of the polymer.

66 Therefore, you have not provided an adequate and scientifically supported justification based on a thorough and rigorous exposure assessment.

0.3.3. Conclusion on the substance-tailored exposure driven testing adaptation

67 Based on the above, your substance-tailored exposure driven testing adaptations under Annex XI, Section 3. are rejected.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

68 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitizer and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

69 You have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships, (Q)SARs). To support the adaptation, you have provided a prediction from SciQSAR model (Danish QSAR database) made on 23 May 2022.

1.2. Assessment of the information provided

1.2.1. (Q)SAR adaptation rejected

70 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

71 On this basis, it cannot be concluded whether the Substance causes skin sensitisation.

1.2.2. No assessment of potency

72 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

73 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation, this condition cannot be assessed.

74 Therefore, the information requirement is not fulfilled.

1.3. Specification of the study design

75 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitizer (Cat 1A or 1B) is warranted.

76 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated in vitro/in chemico data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

77 In your comments to the draft decision, you agreed to conduct the study as requested.

2. In vitro gene mutation study in bacteria

78 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

2.1. Information provided

79 You have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships, (Q)SARs). To support the adaptation, you have provided a prediction from Battery model (v1.0) in Danish QSAR database made on 23 May 2022.

2.2. Assessment of the information provided

2.2.1. (Q)SAR adaptation rejected

80 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

81 In addition, the following issue was identified for this information requirement:

2.2.1.1. The QSAR result is not equivalent to results obtained from the required experimental test

82 Results from (Q)SAR models are adequate for risk assessment or classification and labelling when they are equivalent to results obtained from the required experimental test. The corresponding study that must normally be performed for this particular information requirement is OECD TG 471, which measures: gene mutations in 5 strains of bacteria : four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 *uvrA* or *E. coli* WP2 *uvrA* (pKM101).

83 You have provided the prediction from a (Q)SAR model SciQSAR version 3.1.00 (OECD QSAR Toolbox v4.5, Danish QSAR database), which predicts gene mutation in bacteria.

84 However, the data in the training set does not consistently consider all 5 strains required by the OECD TG 471, but any results based on one or more strains has been considered.

85 Therefore, the prediction is not adequate to meet the information requirement for in vitro gene mutation study in bacteria. for the purpose of classification and labelling and/or risk assessment.

86 Based on the above, your QSAR adaptation under Annex XI, Section 1.3. is rejected and the information requirement is not fulfilled.

2.3. Specification of the study design

87 To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

88 In your comments to the draft decision, you agreed to conduct the study as requested.

Reasons related to the information under Annex VIII of REACH

3. *In vitro* micronucleus study

89 An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

3.1. *Information provided*

90 You have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships, (Q)SARs). To support the adaptation, you have provided a prediction from SciQSAR version 3.1.00 in Danish QSAR database made on 23 May 2022.

3.2. *Assessment of the information provided*

91 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

92 Therefore, the information requirement is not fulfilled.

3.3. *Specification of the study design*

93 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the *in vitro* mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the **in vitro** mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations *in vitro*.

94 However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2). Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential *in vitro*.

95 Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

96 In your comments to the draft decision, you agreed to conduct the study as requested.

3.3.1. *Assessment of aneugenicity potential*

97 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

98 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

4. Short-term repeated dose toxicity (28 days)

99 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 or a general adaptation rule under Annex XI.

4.1. Information provided

100 You have provided information derived from experimental data from a group of substances using the OECD QSAR Toolbox and flagged the information as QSAR.

101 As the group of substances are used as source substances to predict the property of the Substance, we understand that you have adapted the standard information requirements under Annex XI, Section 1.5 of REACH (grouping and read-across).

102 You have further adapted this information requirement by using Annex XI, Section 3 (substance-tailored exposure-driven testing), see section 0.3.

4.2. Assessment of the information provided

103 We have assessed this information and identified the following issue:

4.2.1. Read-across adaptation rejected

104 As explained in Section 0.2., your adaptation based on Grouping of substances and read-across under Annex XI, Section 1.5. is rejected.

4.2.2. Substance-tailored exposure-driven testing adaptation rejected

105 As explained in Section 0.3., your adaptation based on exposure-based waiving under Annex XI, Section 3 is rejected.

106 Based on the above, the information requirement is not fulfilled.

4.3. Justification for an adaptation of the short-term repeated dose toxicity study (Annex VIII, Section 8.6.1., Column 2)

107 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 6).

108 According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not need to be conducted. Therefore, to comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to provide a justification for adaptation, as provided in Annex VIII, Section 8.6.1., Column 2.

5. Screening study for reproductive/developmental toxicity

109 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

- 110 You have not submitted any information for this requirement.
- 111 Therefore, the information requirement is not fulfilled.
- 112 In your comments to the draft decision, you express your intention of adapting this information requirement based on Annex XI, Section 3.
- 113 However, we refer to the limitations of the evidence provided and the REACH requirements for the DNEL derivation in this context, as explained in the 'Reasons common to several requests', section 0.3. above, which apply *mutatis mutandis* to adaptation of this information requirement.

5.1. Specification of the study design

- 114 A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats.
- 115 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1, Column 1).
- 116 Therefore, the study must be conducted in rats with oral administration of the Substance.

Reasons related to the information under Annex IX of REACH

6. Sub-chronic toxicity study (90 days)

117 A sub-chronic toxicity study (90 days) is an information requirement under Annex IX, Section 8.6.2.

6.1. Information provided

118 You have provided information derived from experimental data from a group of substances using the OECD QSAR Toolbox and flagged the information as QSAR.

119 As the group of substances are used as source substances to predict the property of the Substance, we understand that you have adapted the standard information requirements under Annex XI, Section 1.5 of REACH (grouping and read-across; see section 0.2 in the above).

120 We understand that you have further adapted this information requirement by using Annex XI, Section 3 (substance-tailored exposure-driven testing; see section 0.3 in the above).

6.2. Assessment of the information provided

121 We have assessed this information accordingly and identified the following issue:

6.2.1. Read-across adaptation rejected

122 As explained in Section 0.2., your adaptation based on Grouping of substances and read-across under Annex XI, Section 1.5. is rejected.

6.2.2. Substance-tailored exposure-driven testing adaptation rejected

123 As explained in Section 0.3., your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected.

124 Based on the above, the information requirement is not fulfilled.

125 In your comments to the draft decision, you reiterated your intention of adapting this information requirement based on Annex XI, Section 3. However, we refer to the limitations of the evidence provided, and in particular the REACH requirements for the DNEL derivation in this context, as explained in section 0.3. above.

6.3. Specification of the study design

126 Following the criteria provided in Annex IX, Section 8.6.2., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.2., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance.

127 According to the OECD TG 408, the rat is the preferred species.

128 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

7. Pre-natal developmental toxicity study in one species

129 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2.

7.1. Information provided

130 You have adapted this information requirement by using Annex XI, Section 3 (substance-tailored exposure-driven testing), see section 0.3.

7.2. Assessment of the information provided

131 As explained in Section 0.3., your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected.

132 Therefore, the information requirement is not fulfilled.

133 In your comments to the draft decision, you reiterated your intention of adapting this information requirement based on Annex XI, Section 3. However, we refer to the limitations of the evidence provided, and in particular the REACH requirements for the DNEL derivation in this context, as explained in section 0.3. above.

7.3. Specification of the study design

134 A PNDT study according to the test method OECD TG 414 should be performed in rats or rabbits as preferred species.

135 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2., Column 1).

136 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

8. Long-term toxicity testing on aquatic invertebrates

137 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

8.1. Information provided

138 You have adapted this information requirement by using Annex XI, Section 3 (substance-tailored exposure-driven testing; see section 0.3. above), and you provided additional justification for such an adaptation in your comments on the draft decision.

8.2. Assessment of the information provided

139 As explained in Section 0.3., reflecting on both the information in your registration dossier and your comments, your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected.

140 Therefore, the information requirement is not fulfilled.

9. Long-term toxicity testing on fish

141 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

9.1. Information provided

142 You have adapted this information requirement by using Annex XI, Section 3 (substance-tailored exposure-driven testing; see section 0.3. above), and you provided additional justification for such an adaptation in your comments on the draft decision.

9.2. Assessment of the information provided

143 As explained in Section 0.3., reflecting on both the information in your registration dossier and your comments, your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected.

144 Therefore, the information requirement is not fulfilled.

9.3. Study design and test specifications

145 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.).

10. Simulation testing on ultimate degradation in surface water

146 Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

10.1. Information provided

147 You have adapted this information requirement by using Annex XI, Section 3 (substance-tailored exposure-driven testing; see section 0.3. above), and you provided additional justification for such an adaptation in your comments on the draft decision.

10.2. Assessment of the information provided

148 As explained in Section 0.3., reflecting on both the information in your registration dossier and your comments, your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected.

149 Therefore, the information requirement is not fulfilled.

10.3. Study design and test specifications

150 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1):

- (2) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
- (3) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

- 151 You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).
- 152 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.
- 153 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Paragraph 52 of the OECD TG 309 provides that the "total recovery (mass balance) at the end of the experiment should be between 90% and 110% for radiolabelled substances, whereas the initial recovery at the beginning of the experiment should be between 70% and 110% for non-labelled substances". NERs contribute towards the total recovery. Therefore, the quantity of the (total) NERs must be accounted for the total recovery (mass balance), when relevant, to achieve the objectives of the OECD TG 309 to derive degradation rate and half-life. The reporting of results must include a scientific justification of the used extraction procedures and solvents.
- 154 For the persistence assessment by default, total NERs is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NERs may be differentiated and quantified as irreversibly bound or as degraded to biogenic NERs, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website ([NER - summary 2019 \(europa.eu\)](http://europa.eu)).
- 155 Relevant transformation/degradation products are at least those detected at $\geq 10\%$ of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; Guidance on IRs and CSA, Section R.11.4.1.).

11. Identification of degradation products

- 156 Identification of abiotic and biotic degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).
- 157 You have not submitted any information for this requirement.
- 158 As far as you provide justification for using Annex IX, Section 3 to adapt this information requirement, we refer to section 0.3. above and in particular Section 0.3.1.2, where the reasons are set out why it is not demonstrated that exposures are always well below the PNEC.
- 159 Therefore, the information requirement is not fulfilled.

11.1. Study design and test specifications

- 160 Regarding the selection of appropriate and suitable test method(s), the method(s) will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible.

- 161 In addition, degradation half-life, log K_{ow} and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation study requested in Request 10 or by some other measure. If any other method is used for the identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.
- 162 To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Request 10) must be conducted at 12°C and at a test concentration < 100 µg/L.
- 163 However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, e.g. 20°C) and at higher application rate (i.e. > 100 µg/L).

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

- Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

Guidance for monomers and polymers; ECHA (2012).

Guidance on intermediates; ECHA (2010).

All guidance documents are available online: <https://echa.europa.eu/guidance-documents/guidance-on-reach>

Read-across assessment framework (RAAF)

- RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:

<https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>

OECD Guidance documents (OECD GDs)

- OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 02 May 2022.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA took into account your comments and did not amend the requests.

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH. The editorial change was made to the request 4 to remove an obsolete alternative.

Appendix 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

- (1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.
- (2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.
- (3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries².
- (4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values.

² <https://echa.europa.eu/practical-guides>

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (<https://echa.europa.eu/manuals>).