~~Confidential~~

Helsinki, 10 October 2023

Addressee(s)
Registrant(s) of CAS-1395383-69-3 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
21/02/2018

Registered substance subject to this decision ("the Substance")
Substance name: 1,3-Isobenzofurandione, hexahydro-, reaction products with epichlorohydrin
EC number/List number: 696-026-0

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 ***16 July 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. *In vivo* mammalian alkaline comet assay or transgenic rodent somatic and germ cell gene mutation assays, also requested below (triggered by Annex VII, Section 8.4., Column 2);

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202).

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

3. In vivo mammalian alkaline comet assay; or Transgenic rodent somatic and germ cell gene mutation assays also requested below (triggered by Annex VIII, Section 8.4., column 2);

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203);

5. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111).

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

6. In vivo mammalian alkaline comet assay in rats, or if justified, in other rodent species, oral route, on the following tissues: liver, glandular stomach and duodenum; or Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach; germ cells and duodenum must be harvested and stored for up to 5 years. Duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive;

7. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211);

8. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210).

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.

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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.

Authorised[1] 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)

Contents

Reasons related to the information under Annex VII of REACH

1. Transgenic rodent somatic and germ cell gene mutation assays or *in vivo* mammalian alkaline comet assay

1 Under Annex VII, Section 8.4., Column 2, further mutagenicity studies must be considered in case of a positive result in an *in vitro* gene mutation study in bacteria.

1.1. Triggering of the information requirement

2 Your dossier contains positive results for the *in vitro* gene mutation study in bacteria with the Substance (1984) which raise a concern for gene mutation.

3 Therefore, the information requirement is triggered.

1.2. Information requirement not fulfilled

4 The information provided in your dossier and in your comments on the draft decision, its assessment and the specifications of the study design for the requested study are addressed under request 6.

2. Short-term toxicity testing on aquatic invertebrates

5 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

2.1. Information provided

6 You have provided a short-term toxicity study on daphnia magna (1992) with the Substance.

2.2. Assessment of the information provided

7 To fulfil the information requirement, a study must comply with the OECD TG 202 and the specifications of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Characterisation of exposure

a) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

8 In the study provided:

Characterisation of exposure

a) no analytical monitoring of exposure was conducted

9 Based on the above, the Substance is difficult to test since it is a viscous UVCB substance with unknown hydrolysis potential and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not performed

analytical verification of the exposure concentration. The available data in the dossier (i.e., growth inhibition study on algae reported in IUCLID 6.1.5) indicates difficulties on solubilising the substance in test media. Therefore, you have not demonstrated that the reported effect values are representative of the test doses applied.

10 On this basis, the specifications of OECD TG 202 are not met and the information requirement is not fulfilled.

2.3. Study design and test specifications

11 The Substance is difficult to test due to the UVCB and viscous (1153.1mm²/s) nature of the Substance which may impact it's solubility in media. As indicatedin the growth inhibition study on algae report (reported in IUCLID 6.1.5: Toxicity to aquatic algae and cyanobacteria endpoint), "*The test substance was not completely soluble in test medium at the loading rates initially prepared*".

12 Furthermore, the Substance is potentially hydrolysable based on structure (i.e., presence of epoxide functionalities). The outcome of the study requested under request 5 must be used to assess whether the Substance is difficult to test also due to rapid hydrolysis (i.e. resulting in a loss of 20% of the initial concentration of a test chemical), prior conducting this study.

13 OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

14 In case the hydrolysis half-life is less than 3 days, it is important to take into account the relative toxicities of the parent test chemical and degradation products in order to determine the appropriate test design and test media preparation methods for the Substance.

15 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

16 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);

- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

17 In the comment to the draft decision, you agree to perform the requested study.

Reasons related to the information under Annex VIII of REACH

3. In vivo mammalian alkaline comet assay or Transgenic rodent somatic and germ cell gene mutation assays

18 Appropriate *in vivo* mutagenicity studies must be considered under Annex VIII, Section 8.4., Column 2 in case of a positive result in any of the *in vitro* genotoxicity studies under Annex VII or VIII.

3.1. Triggering of the information requirement

19 Your dossier contains positive results for the *in vitro* gene mutation study in bacteria with the Substance (1984) and *in vitro* gene mutation study in mammalian cells with the Substance (1985) which raise the concerns for gene mutations.

Therefore, the information requirement is triggered.

3.2. Information requirement not fulfilled

20 The information provided in your dossier and in your comments on the draft decision, its assessment and the specifications of the study design of the requested study are addressed under request 6.

4. Short-term toxicity testing on fish

21 Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

4.1. Information provided

22 You have provided:

(i) a short-term toxicity study on fish (1991) with the Substance;

(ii) a short-term toxicity study on fish (1996) with the Substance.

4.2. Assessment of the information provided

23 To fulfil the information requirement, a study must comply with the OECD TG 203 and the specifications of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Validity criteria

a) the analytical measurement of test concentrations is conducted;

Characterisation of exposure

b) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

24 In studies (i) and (ii):

Validity criteria

a) no analytical measurement of test concentrations was conducted;

Characterisation of exposure

b) no analytical monitoring of exposure was conducted.

25 Based on the above, for both studies (i) and (ii)

- the validity criteria of the OECD TG 203 are not met as analytical monitoring of the test concentration was not performed. This criterion is of critical importance for the Substance since
- the Substance is difficult to test due to it's viscous UVCB nature and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not performed analytical verification of the exposure concentration. The available data in the dossier (i.e., growth inhibition study on algae reported in IUCLID 6.1.5) indicates difficulties on solubilising the substance in test media. Therefore, you have not demonstrated that the reported effect values are representative of the test doses applied.

26 On this basis, the specifications of the OECD TG 203 are not met and the information requirement is not fulfilled.

27 In the comments to the draft decision, you do not agree to perform the requested study. Instead, you indicate that you intend to adapt this information requirement.

28 You propose the following adaptation possibilities:

A. grouping and read-across according to Annex XI, Section 1.5, of the REACH Regulation;

B. using a long-term toxicity to aquatic invertebrates study (OECD TG 210) according to Annex VII section 9.1.1 column 2 of the REACH Regulation.

29 You propose to (A) adapt this information requirement according to Annex XI, Section 1.5, of the REACH Regulation.

30 You intend to predict the short-term toxicity on fish properties of the Substance from a studies on source substance EC 244-435-6. The study summary is not reported in your dossier nor provided in the comments to the draft decision.

31 You consider the Substance and the source substance to be structuraly similar. Therefore, you present a strategy relying on the similar solubility and degradation properties, but provide limited supporting information.

32 Furthermore, you shared your intention to perform the short-term toxicity study on aquatic invertebrates (Request 2) to "*act as a bridging study*" in support of the read-across approach used on the analogue's registration dossier.

33 ECHA notes that Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. 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 (addressed under 'Assessment of prediction(s)').

34 You intent to read-across from a mono-constituent (analogue substance) to a UVCB (the Substance) therefore, the impact of all constituents of the substances on the prediction must be considered.

35 As this strategy relies on a read-across approach that has not yet been fully described and justified, as well as on data which is yet to be generated for the proposed source substance (including bridging studies and supporting information), no conclusion on the compliance of the proposed adaptation can be made. to You remain responsible for complying with this decision by the set deadline.

36 You also propose (B) to adapt this information requirement based on Annex VII section 9.1.1 column 2 of REACH Regulation.

37 ECHA notes that the long-term toxicity testing on fish (OECD TG 210) is requested in of this decision (Request 7).

38 REACH Annex VII section 9.1.1 column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on invertebrates is available. At present no long-term toxicity study on aquatic invertebrates is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

4.3. Study design and test specifications

39 The OECD TG 203 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design and test specifications" under request 2.

5. Hydrolysis as a function of pH

40 Hydrolysis as a function of pH is an information requirement under Annex VIII to REACH (Section 9.2.2.1.).

5.1. Information provided

41 You have adapted this information requirement by using Annex XI, Section 2. (testing is technically not possible). To support the adaptation, you have provided the following information: *"In accordance with section 2 of REACH Annex XI, the hydrolysis as a function of pH study (section 9.2.2.1) does not need to be performed as the substance is an UVCB, the components may hydrolyze at different rates compounding the determination of this endpoint."*.

5.2. Assessment of the information provided

42 Under Annex XI, Section 2., a study may be omitted if it is technically not feasible to conduct because of the properties of the substance.

43 You claim that it is not possible to conduct the study, because the Substance is a UVCB however, you do not provide any evidence to demonstrate that conducting the study is technically not feasible. In particular, OECD TG 111 does not indicate that UVCB substances are outside the applicability domain of the test. As indicated in Guidance on IRs and CSA, Section R.7.9.4.1, this method is generally applicable to chemical substances (14C-labelled or non-labelled) for which an analytical method with sufficient accuracy and sensitivity is available. Furthermore, in case the constituents of the UVCB would hydrolyse at different ratios, an assessment strategy as defined in Guidance on IRs and CSA, Section

R.11.4.2.2.2 can be considered and the hydrolysis half-life of the Substance can be provided as a range of values. In summary, you have not demonstrated that it is technically not feasible to conduct the test, because of the properties of the Substance.

44 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

45 In the comments to the draft decision, you agree to perform the requested study.

Reasons related to the information under Annex IX of REACH

6. In vivo mammalian alkaline comet assay; or Transgenic rodent somatic and germ cell gene mutation assays

46 Under Annex IX, Section 8.4., Column 2, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study.

6.1. Triggering of the information requirement

6.1.1. Positive in vitro study

47 In relation to the first condition, your dossier contains positive results for the *in vitro* gene mutation study in bacteria and *in vitro* gene mutation study in mammalian cells which raise a concern for gene mutation.

6.1.2. No appropriate in vivo study

48 In relation to the second condition, your dossier contains the following *in vivo* studies:

(i) Mammalian Erythrocyte Micronucleus Test (TG 474) with the Substance (2012);
(ii) Sister Chromatid exchange with the Substance (1984);
(iii) Similar to micronucleus test with the Substance (1985).

49 We have assessed this information and identified that the provided studies do not address the concern raised by the positive *in vitro* results

50 The Guidance on IRs and CSA, Section R.7.7.6.3. clarifies that in order to justify that an in vivo somatic cell genotoxicity study does not need to be performed in accordance with Annex IX, Section 8.4., Column 2, the results of the available *in vivo* studies must address the specific concern raised by the *in vitro* positive result.

51 However, the *in vivo* studies provided are not addressing the gene mutation concern raised by the *in vitro* data.

52 There are no appropriate results already available from an *in vivo* somatic cell genotoxicity study in your dossier.

53 Based on the above, the conditions set out in Annex IX, Section 8.4., Column 2 are met and the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered.

54 In your comments on the draft decision you agree with ECHA that the positive results obtained in the *in vitro* gene mutation studies warrant the conduct of an *in vivo* follow-up study.

6.2. Specification of the study design

6.2.1. Comet assay

55 In case you decide to perform the comet assay, according to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified (OECD TG 489, paragraph 23).

56 Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

57 In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

6.2.1.1. Germ cells

58 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overalll assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

6.2.1.2. Cross-linking properties

59 You are reminded that you may decide to take into account the potential cross-linking properties of the Substance in the experimental setup of the comet assay and perform a modified comet assay in order to detect cross links. Therefore, you may consider preparing and analysing two sets of slides: one set of slides submitted to the standard experimental conditions (as described in the OECD TG 489); the other set of slides submitted to modified experimental conditions that enable the detection of DNA crosslinks. The modified experimental conditions may utilise one of the following options: (1) increase of electrophoresis time, e.g. as described in reference 23 [1] in the OECD TG 489; (2) treatment of isolated cells (either in suspension or embedded in the slides) with a chemical (e.g. MMS); or (3) treatment of isolated cells (either in suspension or embedded in the slides) with ionising radiation (options 2 and 3 are described e.g. in references 36-39 [2-5] in the OECD TG 489 or Pant et al. 2015 [6]). In order to ensure the robustness of the test result a specific positive control group of animals would be needed.

[1] Nesslany *et al.* (2007) *In vivo* comet assay on isolated kidney cells to distinguish genotoxic carcinogens from epigenetic carcinogens or cytotoxic compounds. *Muta Res*;630(1-2):28-41.
[2] Merk and Speit (1999) Detection of crosslinks with the comet assay in relationship to genotoxicity and cytotoxicity. *Environ Mol Mutagen*;33(2):167-72.
[3] Pfuhler and Wolf (1996) Detection of DNA-crosslinking agents with the alkaline comet assay. *Environ Mol Mutagen*;27(3):196-201.
[4] Wu and Jones (2012) Assessment of DNA interstrand crosslinks using the modified alkaline comet assay. *Methods Mol Biol*;817:165-81.
[5] Spanswick *et al.* (2010) Measurement of DNA interstrand crosslinking in individual cells using the Single Cell Gel Electrophoresis (Comet) assay. *Methods Mol Biol*;613:267-282.
[6] Pant K *et al.* (2015) Modified *in vivo* comet assay detects the genotoxic potential of 14-hydroxycodeinone, an α,β; -unsaturated ketone in oxycodone. *Environ Mol Mutagen*;56(9):777-87.

6.2.2. TGR assay

60 In case you decide to perform the TGR assay, according to the test method OECD TG 488, the test must be performed in transgenic mice or rats.

61 Also, according to the test method OECD TG 488, the test substance is usually administered orally.

62 Based on the OECD TG 488, you are requested to follow the 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals.

63 According to the test method OECD TG 488, the test must be performed by analysing tissues from liver, as slowly proliferating tissue and primary site of xenobiotic metabolism and from glandular stomach and duodenum, as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70 ºC) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed, only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

6.2.2.1. Germ cells

64 You must collect the male germ cells (from the seminiferous tubules) at the same time as the other tissues, to limit additional animal testing. According to the OECD 488, the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

6.2.3. Mammalian erythrocyte Pig-a gene mutation assay

65 In your comments on the draft decision you request the inclusion of the option to consider the mammalian erythrocyte Pig-a gene mutation assay (OECD TG 470), integrated into a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test as an alternative option to the Comet assay and the TGR assay.

66 You consider that the OECD TG 470 is a relevant test to assess *in vivo* mutagenicity and that it could be considered to follow-up on the positive *in vitro* results observed with the Substance. You highlight that "*the Pig-a assay can be integrated into 28-day repeated dose toxicity studies*" and "*such a study has recently been requested in an ECHA draft decision for the substance EC 244-435-6 which is a structural analogue to the substance*". You express your intention to use this information on the analogue substance in a read-across adaptation to address the information requirement of Annex IX, Section 8.4., Column 2 for the Substance.

67 ECHA notes that, as you point out in your comments, the Substance is very reactive and has the potential to cause site-of-contact toxicity. Therefore, the potential of the Substance to cause site-of-contact gene mutation *in vivo* needs to be investigated. This is reflected in the selection of organs/tissues specified for examination in the Comet assay or in the TGR assay with the inclusion of the glandular stomach and of the duodenum as site-of-contact tissues. While the mammalian erythrocyte Pig-a gene mutation assay is potentially suitable to follow-up on *in vitro* gene mutation positive results, this test cannot be used to measure mutations in site-of-contact tissues. Therefore, considering the reactivity of the Substance

and the associated concern for gene mutation at the site-of-contact, the mammalian erythrocyte Pig-a gene mutation assay does not constitute an appropriate test method to follow-up on the positive *in vitro* results of the Substance.

68 Therefore, ECHA has not included the mammalian erythrocyte Pig-a gene mutation assay (OECD TG 470) as an alternative to the Comet assay or to the TGR assay in this decision.

7. Long-term toxicity testing on aquatic invertebrates

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

7.1. Information provided

70 In the registration dossier you have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following justification: *"In accordance with column 2 of REACH (Regulation (EC) No 1907/2006) Annex IX, the long-term toxicity testing on invertebrates (required in section 9.1.5) does not need to be conducted based on the findings of the Chemical Safety Assessment; the substance does not fulfill classification criteria according to the applicable regulations and does not fulfill the criteria for vPvB or PBT."*

71 In your comments to the draft decision, you reiterate your intention to adapt this information requirement by using Column 2 of Annx IX, Section 9.1. You claim that:

- if the fish species is demonstrated to be the most sensitive species, based on data yet to be generated, the requested study would not align with the 3R principles, and
- PNEC derivation would still be based on the lowest key endpoint value.

7.2. Assessment of the information provided

72 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to aquatic invertebrates referred to under Column 1, Section 9.1.5.

73 Your adaptation is therefore rejected and the information requirement is not fulfilled.

7.3. Study design and test specifications

74 The OECD TG 211 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design and test specifications" under request 2.

8. Long-term toxicity testing on fish

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

8.1. Information provided

76 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following justification: "*In accordance with column 2 of REACh (Regulation (EC) No 1907/2006) Annex IX, the long-term toxicity testing on fish (required in section 9.1.6) does not need to be conducted based on the findings of the Chemical Safety Assessment; the substance does not fulfil classification criteria according to the applicable regulations and does not fulfil the criteria for vPvB or PBT.*"

8.2. Assessment of the information provided

77 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to fish referred to under Column 1, Section 9.1.6.

78 Your adaptation is therefore rejected and the information requirement is not fulfilled.

8.3. Study design and test specifications

79 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.).

80 The OECD TG 210 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design and test specifications" under request 2.

81 In the comment to the draft decision, you agree to perform the requested study.

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 01 February 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.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments agreeing with the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee unanimously agreed on the draft decision in its MSC-83 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

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;

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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 summaries[2].

(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.

(2) 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.

(3) 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.

[2] https://echa.europa.eu/practical-guides

- The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods,

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).