~~Confidential~~

Helsinki, 16 January 2024

Addressees
Registrant(s) of JS_MHHPA_generic as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
28/02/2019

Registered substance subject to this decision ("the Substance")
Substance name: Hexahydromethylphthalic anhydride
EC number: 247-094-1

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 the deadline of ***21 October 2026***.

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

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

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

2. 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.

The reasons for the decision(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.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 decision

Contents

Reasons related to the information under Annex IX of REACH

1. Long-term toxicity testing on fish

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

1.1. Information provided

2 In the technical 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 REACH Regulation 1907/2006, Annex IX, Column 2, section 9.1 long-term tests on fish do not need to be conducted as the Chemical Safety Assessment does not indicate the need to further investigate the effects of the substance and/or relevant degradation products on fish. Upon contact with water hydrolysis of MHHPA to the corresponding dicarboxylic acid appears very rapid and therefore, not long-term but acute toxicity effects are relevant. Moreover, the available information about production and processing of MHHPA, and the uses identified, indicates that direct releases of MHHPA to the aquatic compartment can be excluded. Under consideration of these aspects further testing is not in line with animal welfare".

3 In your comments on the draft decision, you propose to adapt this standard information requirement by applying a weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2, using (Q)SAR (ECOSAR v.2.0) to predict chronic fish and daphnia toxicity.

4 You have also provided statements claiming that Daphnia is more sensitive than fish using QSAR predictions and experimental information on Daphnia (OECD TG 202) and fish (OECD TG 203).

1.2. Assessment of the information provided

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

1.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

6 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

7 Your adaptation submitted in your technical dossier is therefore rejected.

1.2.2. Weight of evidence (WoE) adaptation is rejected

8 In the comments to the draft decision, you agree that provided adaptation does not sufficiently meet the information requirement of Annex IX, Section 9.1.6. However, you do not agree that a new study needs to be performed and propose a weight-of-evidence adaptation (Annex XI, Section 1.2.) using:

(i) statements on the lower sensitivity of fish based on existing short-term fish and daphnia studies; and

(ii) QSAR modelling.

9 Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

10 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

11 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

12 On a preliminary note, your statements regarding sensitivity of Daphnia and fish (source of information i) cannot be taken into account in the assessment of your weight of evidence adaptation because they do not provide any relevant information for this information requirement, i.e., relating to survival and development of fish in early life stages in long-term exposure. Aquatic toxicity testing on fish and aquatic toxicity testing on invertebrates are separate information requirements and are not interchangeable. There is no provision in the REACH Regulation allowing for the omission of aquatic toxicity testing on fish based on an available study, or studies, on invertebrates only.

13 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex IX, Section 9.1.6. includes similar information that is produced by the OECD TG 210. This includes parameters related to the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage following exposure to the test substance are measured, including:

1. the stage of embryonic development at the start of the test, and
2. hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3. the appearance and behaviour of larvae and juvenile fish, and
4. the weight and length of fish at the end of the test.

14 The source of information (ii) may provide relevant information on these parameters. However, the reliability of this source of information is significantly affected by the following deficiencies:

1.2.2.1. Applicability domain

15 Under Annex XI, Section 1.3., the substance must fall within the applicability domain of the model whenever a (Q)SAR approach is used.

16 Under Guidance on IRs and CSA R.6.1.5.3., a prediction is within the applicability domain of the model, when, among others, the substance and the structures selected for the prediction fall within descriptor, structural, mechanistic and metabolic domain.

17 In the (Q)SAR Model Reporting Format document (QMRF) which you submitted in the comments on the draft decision, you report the following applicability domain for the model you used: "ECOSAR v2.0: Chemical Class: Neutral Organics: Fish Chronic Value".

18 You further describe in the submitted QMRF that the following chemical compounds are identified by ECOSAR as neutral organics: 1. [redacted].

19 The Substance does not fall in any of the abovementioned chemical classes.

20 Therefore, you have not demonstrated that the Substance (or its hydrolysis products) falls within the applicability domain of the model.

1.2.2.2. Inadequate documentation of the prediction (QPRF)

21 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 identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

22 You submitted QSAR Prediction Reporting Format (QPRF) and (Q)SAR Model Reporting Format document (QMRF) in your comments on the draft decision. However, the information you provided about the prediction lacks documentation of close analogues, including considerations on how predicted and experimental data for analogues support the prediction for the Substance.

23 In absence of such information, ECHA cannot establish that the prediction is reliable.

24 Therefore the provided prediction cannot be considered a reliable source of information that could contribute to the conclusion on this key parameter investigated by the required study.

25 In summary, the source of information (ii) provides relevant information on the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage. However, this source of information has significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for long-term toxicity testing on fish.

26 To conclude, for the reasons stated above it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for long-term toxicity testing on fish. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

1.3. Study design and test specifications

27 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.).

28 The OECD TG 210 specifies that, for difficult to test substances, the OECD GD 23 must be followed. The Substance is difficult to test due to the fast hydrolysis rate (i.e. hydrolysis half life ranging from 1.43 to 1.27 min at 20 °C within a pH range of 4-9). OECD TG 210 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 210. 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.

2. Simulation testing on ultimate degradation in surface water

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

30 You provided a justification to omit the study which you consider to be based on Column 2 of Annex IX, Section 9.2.1.2: "In accordance with REACH Regulation 1907/2006, Annex IX, column 2, simulation testing on biodegradation in water and sediment does not need to be conducted as direct or indirect exposure of the aquatic and terrestrial compartments for this substance are unlikely. The substance is hydrolysed rapidly in a few minutes to the corresponding dicarboxylic acids. In addition based on the intended uses, exposure of water and sediments towards the substance is not likely."

2.1. Assessment of information provided

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

2.1.1. Your justification to omit the study does not refer to any adaptation possibility

32 A registrant may only adapt this information requirement based on either the general rules set out in Annex XI or the specific rules of Column 2, Annex IX, Section 9.2.1.2..

33 Your justification to omit this information refers to unlikely exposure of the aquatic and sediment compartment (Column 2, Annex IX, Section 9.2.1.4) and to rapid hydrolysis, which are not specific rules for adaptation for simulation testing on ultimate degradation on surface water under Column 2, Annex IX, Section 9.2.1.2.. In addition, your justification does not refer to any legal ground for adaptation under Annex XI to REACH.

34 Therefore, you have not demonstrated that this information can be omitted.

35 On this basis, the information requirement is not fulfilled.

2.2. Study design and test specifications

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

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

2) 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.

37 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.).

38 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.

39 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.

40 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)).

41 Relevant transformation/degradation products are at least those detected at ≥ 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.).

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).

All Guidance on REACH is 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 16 June 2021.

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

ECHA took into account your comments and amended the request(s) and the deadline.

You have provided comments during the decision-making phase which were found to address certain incompliance(s) identified in the draft decision and you included this information in an update of your registration dossier (submission date: 12 July 2022 – submission number [redacted]). Therefore, the following original requests were removed:

- In vitro gene mutation study in mammalian cells, Annex VIII, Section 8.4.3.;
- Justification for an adaptation of a Short-term repeated dose toxicity (28 days), Annex VIII, Section 8.6.1.;
- Screening for reproductive/developmental toxicity, Annex VIII, Section 8.7.1.;
- Sub-chronic toxicity study (90-day), Annex IX, Section 8.6.2.;
- Pre-natal developmental toxicity study, Annex IX, Section 8.7.2.;
- Long-term toxicity testing on aquatic invertebrates, Annex IX, Section 9.1.5.).

In your comments on the draft decision, you also requested an extension of the deadline to provide information from 24 to 36 months from the date of adoption of the decision. This request for the extension took into account request(s) for a Sub-chronic toxicity study (OECD TG 408) and Pre-natal developmental toxicity study (OECD TG 414). These request(s) have been removed from the decision. However, you also justify the need for deadline extension to perform the long-term toxicity testing on fish and simulation testing on ultimate degradation in surface water, on the basis of limited laboratory capacity. You indicate that you "*can start the OECD TG 309 and OECD TG 210 study at the earliest towards the end of 2023 and beginning of 2025, respectively*".

On this basis, ECHA has extended the deadline to 30 months.

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.

Appendix 3: Addressees 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 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.

(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 and other parameters relevant for the property to be tested.

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

This information is needed to assess 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[3].

[3] https://echa.europa.eu/manuals