~~Confidential~~

Helsinki, 05 May 2023

Addressees
Registrants of JS-Dimethyl Isophthalate as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
06/05/2013

Registered substance subject to this decision ("the Substance")
Substance name: Dimethyl isophthalate
EC/List number: 215-951-9

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 ***10 August 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. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310)

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

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)

3. Screening 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

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

5. 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)

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 request(s)
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 request(s)

Contents

0. Reasons common to several requests

0.1. Read-across approach rejected

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

- 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.)

2 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.

3 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.

4 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).

0.1.1. Predictions for toxicological properties

5 You provide a read-across justification document in IUCLID Sections 7.5.1., 7.8.1. and 7.8.2.

6 You predict the properties of the Substance from information obtained from the following source substance:

DMTP dimethyl terephthalate, EC No. 204-411-8.

7 You provide the following reasoning for the prediction of toxicological properties: "The analogue approach is justified because the two substances have common functional groups. The substances are isomers, which differ only in the location (meta- or para-) of the second carboxylic ester. The common functional groups are two dicarboxylic methyl esters on a benzene ring. It is hypothesized that DMIP exhibits similar toxicokinetic behaviour to DMTP. DMIP breaks down to isophthalic acid, while DMTP is known to break down into terephthalic acid. Isophthalic acid and terephthalic acid differ only with respect to the positioning of the carboxylic acid groups on the ring; they are isomers, as well".

8 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

9 We have identified the following issue with the predictions of toxicological properties:

0.1.1.1. Lack of relevance of the supporting information

10 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 provide supporting information to scientifically justify the read-across explanation for prediction of properties.

11 According to the Guidance on IRs and CSA, Section R.6.2.2.1.f., "it is important to provide supporting information to strengthen the rationale for the read-across approach. Thus, in addition to the property/endpoint being read across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals".

12 In order to support your claim that the Substance and source substance have similar properties for the endpoints under consideration, you only refer to studies relating to the acute toxicity, skin irritation, eye irritation, skin sensitisation properties of the Substance and the source substance.

13 However, these studies do not inform on repeated dose toxicity or on reproductive toxicity potential of the Substance and of the source substance. You have not provided supporting information to scientifically justify the read-across hypothesis for prediction of properties (such as relevant bridging studies to compare the properties of the Substance and the source substance). Accordingly, the information provided is not considered relevant to support your read-across hypothesis.

0.1.2. Conclusion on the read-across approach

14 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 approach under Annex XI, Section 1.5. is rejected

Reasons related to the information under Annex VII of REACH

1. Ready biodegradability

15 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

1.1. Information provided

16 You have provided a ready biodegradability study according to OECD TG 301C (1992) with the Substance.

1.2. Assessment of the information provided

1.2.1. The provided study does not meet the specifications of the test guideline

17 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301C, the following requirements must be met:

18 Reporting of the methodology and results

a) The test design is reported (e.g., number of replicates, sampling schedule for the test suspensions and inoculum blanks (measurements must be done in parallel))

b) The test conditions are reported (e.g., organic carbon content of the dilution water, pre-conditioning treatment of the inoculum (i.e. whether the inoculum was adapted to the test material), inoculum density expressed in cells/mL and mg suspended solids/L, test temperature, pH)

c) The results of measurements at each sampling point in each replicate is reported in a tabular form.

19 In the provided study described as a study on ready biodegradability according to OECD TG 301C:

20 Reporting of the methodology and results

a) you have not provided adequate reporting of the test design. In particular, the following information is missing: number of replicates, sampling schedule for the test suspensions and inoculum blanks

b) you have not provided adequate reporting of the test conditions. In particular, the following information is missing: organic carbon content of the dilution water, pre-conditioning treatment of the inoculum, inoculum density expressed in cells/mL and mg suspended solids/L, test temperature, pH

c) The results of measurements at each sampling point in each replicate are not reported.

21 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically:

- you have not provided adequate information on the test design and test procedure. As a result, ECHA cannot verify that the test was conducted under conditions that are consistent with the requirements of the OECD TG 301C;

- In the absence of reporting of results of measurements at each sampling point in each replicate, ECHA cannot assess whether the validity criteria of the test guideline were met and cannot evaluate the interpretation of the result.

22 Therefore, the requirements of OECD TG 301C are not met and the information requirement is not fulfilled

Reasons related to the information under Annex VIII of REACH

2. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

23 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 of Annex VIII or a general adaptation rule under Annex XI.

24 Annex VIII, Section 8.6.1., Column 2 provides that an experimental study for this information requirement is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

25 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 4). 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 therefore need to be conducted.

26 Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

3. Screening for reproductive/developmental toxicity

27 A screening 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.

3.1. Information provided

28 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substance:

(i) a longer than a one-generation study (1973) with the source substance DMTP, EC No. 204-411-8;

(ii) a prenatal developmental toxicity study (2005) with the source substance DMTP, EC No. 204-411-8.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

29 Already for the general reasons explained in Section 0.1. your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

30 In addition, ECHA identified endpoint-specific issue(s) of your read-across adaptation, as follows.

3.2.2. Source studies not adequate for the information requirement

31 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case EU B.63/OECD TG 421 or EU B.64/OECD TG 422. Therefore, the following specifications must be met:

a) the highest dose level aims to induce toxicity or aims to reach the limit dose;

b) thyroid hormone levels are measured;

c) offspring parameters such as number and sex of pups/stillbirths and live births/gross abnormalities/pup body weight/litter weight/anogenital distance/nipple retention in male pups are reported.

32 In study (i) described as a longer than a one-generation study:

a) the highest dose levels tested was 400 mg/kg bw/d and no adverse effects were observed and no justification for the dose setting was provided. This value is below the limit dose specified in the OECD TG 421/422. You have provided no justification as to why a higher dose could not be tested. You can refer to the Advice on dose-level selection for the conduct of sub-acute and sub-chronic assays under REACH;

b) thyroid hormone levels were not measured;

c) data on number and sex of pups/stillbirths and live births/gross abnormalities/pup body weight/litter weight/anogenital distance/nipple retention in male pups is missing.

33 The study (ii) described as a prenatal developmental toxicity study is not considered reliable. The reasons are given under Request 4. below.

34 Therefore, the information provided does not provide an adequate and reliable coverage of the specifications required by the OECD TG 421/422.

35 Based on the above, the studies do not provide an adequate basis for your read-across predictions and your adaptation is rejected.

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

3.3. Specification of the study design

37 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.

38 The study must be conducted with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

39 Therefore, the study must be conducted in rats with oral administration of the Substance.

Reasons related to the information under Annex IX of REACH

4. Sub-chronic toxicity study (90-day)

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

4.1. Information provided

41 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a combined repeated dose and carcinogenicity study (1979) in rat, with the source substance DMTP, EC No. 204-411-8;

(ii) a combined repeated dose and carcinogenicity study (1979) in mice, with the source substance DMTP, EC No. 204-411-8.

4.2. Assessment of the information provided

4.2.1. Read-across adaptation rejected

42 As explained in Section 0.1. above, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

43 Therefore, the information requirement is not fulfilled.

4.3. Specification of the study design

44 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.

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

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

5. Pre-natal developmental toxicity study in one species

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

5.1. Information provided

48 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substance:

(i) a prenatal developmental toxicity study (2005) with the source substance DMTP, EC No. 204-411-8;

(ii) a longer than a one-generation study (1973) with the source substance DMTP, EC No. 204-411-8.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

49 Already for the general reasons explained in Section 0.1. your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

50 In addition, ECHA identified the following endpoint-specific issue.

5.2.2. Source studies not adequate for the information requirement

51 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 414. Therefore, the following specifications must be met:

a) the exposure duration is at least from implantation until one day prior to scheduled caesarean section;

b) the dams are examined for any structural abnormalities, weight and histopathology of the thyroid gland, thyroid hormone measurements, gravid uterus weight, and uterine content;

c) the foetuses are examined for body weight, number and percent of live and dead foetuses and resorptions, sex ratio, external, skeletal and soft tissue alterations (variations and malformations), measurement of anogenital distance in all live rodent foetuses.

52 In study (i) described as a pre-natal developmental toxicity study:

a) the exposure duration spanned only from gestation days 7 to 16.

b) In study (ii) described as a longer than a one-generation study:

c) data on the examination of the dams, including incidence and severity, are missing; no thyroid gland weights and histopathology are reported and no thyroid hormones were measured.

d) data on the examination of the foetuses, including incidence and severity, are missing; no visceral and skeletal investigations were performed in the pups.

53 The information provided does not provide an adequate and reliable coverage of the specifications required by the OECD TG 414.

54 Based on the above, the studies do not provide an adequate basis for your read-across predictions and your adaptation is rejected.

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

5.3. Specification of the study design

56 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

57 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

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

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

The information requirement for a long-term toxicity study on fish (Annex IX, Section 9.1.6.) is not addressed in this decision. This may be addressed in a separate decision once the information from the screening for reproductive/developmental toxicity study, the sub-chronic toxicity study (90-day) and the pre-natal developmental toxicity study requested in the present decision are provided. This is because this information may indicate that further studies than those listed in Column 1 of Section 9.1.6. of Annex IX may be needed to meet the information requirement.

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 14 March 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.

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the requests or the deadline.

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

As no amendments were proposed, ECHA 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.

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].

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