

Helsinki, 17 January 2023

**Addressees**

Registrant(s) of dibutyl maleate JS [203-328-4] as listed in Appendix 3 of this decision

**Date of submission of the dossier subject to this decision**

04/12/2017

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

Substance name: Dibutyl maleate

EC number: 203-328-4

**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 **22 October 2025**.

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

**Information required from all the Registrants subject to Annex X of REACH**

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (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<sup>1</sup> 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

---

<sup>1</sup> 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**

<b>Reasons related to the information under Annex X of REACH.....</b>	<b>4</b>
1. Pre-natal developmental toxicity study in a second species.....	4
<b>References .....</b>	<b>6</b>

## Reasons related to the information under Annex X of REACH

### 1. Pre-natal developmental toxicity study in a second species

1 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X to REACH (Section 8.7.2.).

2 Information provided

3 You have adapted this information requirement by using weight of evidence and read-across based on the following information:

- i. Justification argument: *"A weight of evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed. [...] This data shows that DBM and its metabolites show a clear pattern of nephrotoxicity: [...] In a pre-natal developmental toxicity study (OECD 414) with dibutyl maleate in rabbits it is expected that significant nephrotoxicity will confound the results of any reproductive/developmental study. Due to the effects described in the read across rationale, maternal toxicity in pre-natal testing will mask any reproductive effects which might occur"*

4 and the following studies on furan-2,5-dione, EC No. 203-571-6 (source substance 1) and butan-1-ol EC No. 200-751-6 (source substance 2):

- ii. Pre-natal developmental toxicity study in rat (1986) with source substance 1, via oral route
- iii. Pre-natal developmental toxicity study in rat (2005) with source substance 2, via oral route
- iv. Pre-natal developmental toxicity study in rat (2005) with source substance 2, via inhalation route
- v. Combined screening for reproductive/developmental toxicity and repeated dose toxicity study in rats (1989) with source substance 2, via oral route
- vi. Non-guideline teratology study of two cohorts in rat (1989) with source substance 2, via inhalation route.

#### 1.1. Assessment of the information provided

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

##### 1.1.1. Weight of evidence adaptation

6 Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

7 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 that the Substance has or has not the (dangerous) property investigated by the required study.

- 8 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.
- 9 Your adaptation is rejected because there is no supporting information in a second species available to support the arguments claiming testing in a second species is not needed. More specifically, there is no evidence that maternal kidney effects masking any reproductive effects would occur in rabbits, when testing with the Substance. General comparison of kidney toxicity sensitivities between the rat and the rabbit without information on the Substance is not informing whether the Substance is a developmental toxicant in rabbits.
- 10 In addition, your adaptation is rejected because lack of supporting information for justification and the information requirement is not fulfilled.
- 11 Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.
- 12 Relevant information that can be used to support a weight of evidence adaptation for the information requirement of Section 8.7.2 at Annex X includes similar information that is produced by the OECD TG 414 on a second species (two species taking the first species into account to address the potential species differences). The following aspects are covered: 1) developmental toxicity in two species, 2) maternal toxicity in two species, and 3) maintenance of pregnancy in two species.
- 13 None of the sources of information provide the relevant information on a second species.
- 14 Your weight of evidence adaptation does not include any relevant sources of information to conclude on the property of prenatal developmental toxicity on a second species.
- 15 It is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 414 study.
- 16 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

#### *1.2. Specification of the study design*

- 17 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species. The study in the first species was carried out by using a rodent species (rat). Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.
- 18 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).
- 19 Based on the above, the study must be conducted in rabbits with oral exposure 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).

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 4 May 2021.

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 request(s).

In your comments on the draft decision, you requested an extension of the deadline to provide information from 18 to 30 months from the date of adoption of the decision. You justified your request with a statement from a testing laboratory. The deadline of the draft decision was set based on standard practice for carrying out OECD TG tests. It has been extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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]
[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<sup>2</sup>.

#### 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<sup>3</sup>.

---

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

<sup>3</sup> <https://echa.europa.eu/manuals>