~~Confidential~~

Helsinki, 1 June 2021

Addressees
Registrant(s) of JS_MBTester as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
28/05/2013

Registered substance subject to this decision ("the Substance")
Substance name: Dibutyl methylenedithiodi(acetate)
EC number: 238-289-2
CAS number: 14338-82-0

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 the deadline of ***8 June 2023***.

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

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

1. 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.)

2. 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

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

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

2. 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)

Reasons for the requests are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VIII to IX of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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 Christel Schilliger-Musset, 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 on Reasons common to several requests

1. **Assessment of your substance-tailored exposure-driven testing adaptation under Annex XI, Section 3.2 (a)**

You have sought to adapt the standard information requirements according to Annex XI, Section 3.2 (a) Substance-tailored exposure-driven testing for the following endpoints:

- Short-term repeated dose toxicity (28 day), (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.)

As stated in Annex XI, Section 3, testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR. For this purpose, the manufacturer or importer must provide an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I and communicate the specific conditions of use through the supply chain.

In this context, one of the criteria that must be met is set out under Section 3.2(a) of Annex XI. According to that criterion, the manufacturer or importer shall demonstrate and document three cumulative conditions concerning i) the results of the exposure assessment; ii) the derivation of a suitable, relevant and appropriate DNEL or a PNEC and; iii) the comparison of the derived DNEL or PNEC with the results of the exposure assessment.

You have provided an adaptation in Section 7.5 and 7.8 of your technical dossier, and you conclude that *"no significant exposure occurs in all scenarios of manufacture and identified uses. In a worst case scenario a very conservative oral DNEL based on the TTC concept for chronic toxicity was choosen for MBTester, a Cramer class III substance (high hazard)".*

You provided the following justification for the adaptation:
"No significant exposure in all scenarios of the manufacture and all identified uses were identified. Due to the identified uses exposure to the environment can be excluded. As a basis for exposure-based waiving, the TTC concept as devised by Munro et al. [1996 and 1999] is applied. MBTester is predicted to fall within Cramer Class III (high hazard). Within Cramer class III, the 5th-percentile NOEL has been identified from chronic oral studies or other oral studies e.g., developmental toxicity, if they were more sensitive. The majority of NOELs were defined by studies in the rat. The generic oral NOEL applicable to MBTester (Class III) is 0.15 mg/kg bw/day corresponding to a very low DNEL of 1.5 µg/kg bw/d. The exposure values are well below the derived DNEL or PNEC. "

ECHA notes the following shortcoming(s) with regards to your adaptation according to Annex XI, Section 3.2 (a) Substance-tailored exposure-driven testing:

i. Insufficient demonstration of the absence of or no significant exposure in all scenarios of the manufacture and all identified uses

The first cumulative condition under Annex XI, Section 3.2(a) requires that the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5.

You did not provide adequate and reliable documentation demonstrating the *"absence of or no significant exposure in all scenarios of the manufacture and all identified uses".*

You have developed exposure scenarios in your CSR. Several activities (PROC 1, 3, 8b and 15) indicate potential for exposure in your provided exposure scenarios. For example, for dermal exposure (the only route you have assessed and stated to be relevant), the systemic long-term RCRs values are [redacted] in the described exposure scenarios.

Therefore the first cumulative condition under Annex XI, Section 3.2(a) cannot be fulfilled.

ii. Inappropriate DNEL derivation

The second cumulative condition under Annex XI, Section 3.2(a) requires that a suitable DNEL or a PNEC can be derived from results of available test data for the Substance taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes.

ECHA notes that the DNEL in your dossier is based on a threshold of toxicological concern (TTC) approach (see Appendix R.7-1 of ECHA Guidance R.7c), and not derived from results of available test data for the Substance.

Therefore, the second cumulative condition under Annex XI, Section 3.2(a) cannot be fulfilled.

iii. Insufficient PPE description

The third cumulative condition under Annex XI, Section 3.2(a) requires that the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC.

You have concluded under risk characterisation that dermal exposure can be excluded due to the use of adequate personal protective equipment (PPE) and, therefore, no risk can be identified, when PPE is in place. However, ECHA notes that you have not described the adequate PPE sufficiently and the quantitative and qualitative assessment are not in line in your CSR. According to ECHA Guidance R.14, PPE provided to address residual risk must be suitable (i.e. the right type of equipment taking into account operational conditions and personal factors) and adequate (i.e. capable of providing the right level of protection) and associated with appropriate levels of instruction and training. Annex II, Section 8.2.2 describes the detailed specifications for adequate and suitable protection (which would be for hand protection the type of material and typical or minimum breakthrough time of the glove material).

Therefore, the third cumulative condition under Annex XI, Section 3.2(a) cannot be fulfilled. Based on the above, the information you provided in the dossier does not meet the general rules for adaptation of Annex XI, Section 3.2(a), as none of the cumulative conditions of that adaptation are currently fulfilled.

Therefore your adaptation is rejected.

2. Assessment of the category approach proposed in your comments to the draft decision

In your comments to the draft decision, you indicate your intention to use a category approach for "Mercaptocarboxylic acids, their esters and related compounds" by conducting mechanistic assays *in vitro* to address the repeated dose toxicity and reproductive toxicity and pre-natal developmental toxicity endpoints.

With your comments, you have not provided new supporting (experimental) data to support a read-across adaptation.

ECHA notes that mechanistic data may support your read-across hypothesis if they are relevant to the endpoints of interest, but they do not have the same value as bridging studies for the comparison of effects between substances since *in vitro* mechanistic studies may, for instance, not reflect similarities or differences in absorption or metabolism of the substances.

ECHA cannot conclude on the reliability of the read-across approach proposed in the comments because the acceptability will depend on the outcome of the proposed studies and the relevance of the supporting information. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

Appendix A: Reasons to request information required under Annex VIII of REACH

1. 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)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII (Section 8.6.1) to REACH. 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.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 3.

As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 3. is rejected and ECHA cannot conclude on the reliability of the read-across approach proposed in your comments.

Based on the above, the information you provided does not fulfil the information requirement.

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

The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see Section B.1). According to Column 2 of Annex VIII, Section 8.6.1., and to prevent unnecessary animal testing, a short term toxicity study (28 days) does not therefore need to be conducted.

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.

2. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 3.

As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 3. is rejected and ECHA cannot conclude on the reliability of the read-across approach proposed in your comments.

Based on the above, the information you provided does not fulfil the information requirement.

Information on study design

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 with oral[2] administration of the Substance.

[2] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix B: Reasons to request information required under Annex IX of REACH

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

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX (Section 8.6.2) to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 3. of REACH.

As explained in the Appendix on Reasons common to several requests, your adaptation is rejected and ECHA cannot conclude on the reliability of the read-across approach proposed in your comments.

Based on the above, the information you provided does not fulfil the information requirement.

Information on study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the substance is a liquid.

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 3. of REACH.

As explained in the Appendix on Reasons common to several requests, your adaptation is rejected and ECHA cannot conclude on the reliability of the read-across approach proposed in your comments.

Based on the above, the information you provided does not fulfil the information requirement.

Information on study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[3] administration of the Substance.

[3] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[4].

B. Test material

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 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[5].

[4] https://echa.europa.eu/practical-guides
[5] https://echa.europa.eu/manuals

Appendix D: 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 11 December 2019.

The decision making followed the procedure of Article 51 of the REACH Regulation, as described below:

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 and the deadline.

> The timeline indicated in the draft decision to provide the information requested is 24 months from the date of the decision.
>
> In your comments to the draft decision, you requested an unspecified extension of the timeline for providing a read-across adaptation, stating the following: *"Our intention is to constantly improve and optimize our strategy in the next years. We would like to further develop a strategy for a Category Approach: Mercaptocarboxylic acids, their esters and related compounds. This is a long and tedious process and we are glad to have the support from our former consultants working with us during the last registration periods. However, we see a risk not to comply with the timelines set in the draft decisions.".* You also mention difficulties for small size companies compared to bigger companies large consortia considering their respective resources available.
>
> However, you did not provide any documentation to support your request and did not specify the extra time needed. Furthermore, ECHA observes that the studies you proposed to perform were not requested in the draft decision on the Substance. The present decision does not require you to perform such studies and thereby the imposed deadlines cannot be affected.
>
> On this basis, ECHA has not modified the deadline to provide the information.

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 E: List of references - ECHA Guidance[6] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[7]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Occupational exposure assessment
Guidance on information requirements and chemical safety assessment, Chapter R.14 (Version 3.0, August 2016), referred to as ECHA Guidance R.14 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

OECD Guidance documents[8]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

[8] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix F: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[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.