~~Confidential~~

Helsinki, 23 February 2024

**Addressee(s)**
Registrant(s) of TMPDM_25265-77-4_SIEF as listed in Appendix 3 of this decision

**Date of submission of the dossier subject to this decision**
10 June 2022

**Registered substance subject to this decision ("the Substance")**
Substance name: Isobutyric acid, monoester with 2,2,4-trimethylpentane-1,3-diol
EC/List number: 246-771-9

**Decision number:** Please refer to the REACH-IT message which delivered this communication (in format TPE-D-XXXXXXXXXX-XX-XX/F)

## DECISION ON TESTING PROPOSAL(S)

Under Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***31 May 2027***.

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

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

1. Extended one-generation reproductive toxicity study also requested below (triggered by Annex IX, Section 8.7.3., column 1)

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

2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) by oral route, in rats, specified as follows:

- At least two weeks premating exposure duration for the parental (P0) generation;
- The highest dose level in P0 animals must be determined based on clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals as specified further in Appendix 1 (section 2.2.3), or follow the limit dose concept. The reporting of the study must provide the justification for the setting of the dose levels;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation which shall be followed to weaning;
- Cohorts 2A and 2B (Developmental neurotoxicity).

You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

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 addressee(s) of the decision and their corresponding information requirements based on registered tonnage band are listed

in Appendix 3.

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

You are only required to share the costs of information that you must submit to fulfil your information requirements.

**How to comply with your information requirements**

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report**, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

**Appeal**

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

**Failure to comply**

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

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

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 for the decision(s) related to the information under Annex IX of REACH**

**1. Extended one-generation reproductive toxicity study**

1 An extended one-generation reproductive toxicity study (EOGRTS; OECD TG 443) is an information requirement under Annex IX, Section 8.7.3. if the available repeated dose toxicity studies indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity.

2 Your dossier contains an OECD TG 408 study (2022) which indicates a concern in relation with reproductive toxicity. More specifically, the study reports thyroid toxicity:

- Significantly increased thyroid gland weights in treated males, and a similar trend in females;
- Effects in histopathology of the thyroid: follicular cell hypertrophy was reported in all treated groups of males and females (not observed in control animals). You report that the follicular cell hypertrophy was '*often associated with lower follicular colloid content.'*;
- Changes in T4 and TSH levels in males and females.

3 You consider that the changes in hormone values were '*driven by a small number of individual animals with large outlying values and most values in the 1000 mg/kg/day group were within the range of values of the respective control group*.' Initially, you had not provided individual data to support your claim. In your comments on the draft decision, you consider that requesting the study as an information requirement under Annex IX is not warranted. You provide individual tabular data, historical control data and detailed arguments on the findings on thyroid gland weights, histopathology and thyroid hormones.

4 You consider that thyroid weight relative to body weight is the appropriate predictor of target organ toxicity. While you agree that '*the 1000 mg/kg/day males have several animals with higher weights as compared to the highest concurrent control value*', you note that *'lack of a dose-response effect in females, the lack of statistical significance, and accordance with historical data shows these effects are considered to be non-adverse.'*

5 ECHA notes that for example in males at 1000 mg/kg bw/day, the absolute thyroid gland weight is statistically significantly increased by 21% compared to concurrent controls. The respective value relative to body weight is +19% compared to concurrent controls (not statistically significant). ECHA considers that ca. 20% increase in the thyroid gland weight (both absolute and relative) is a clear treatment-related effect, and the absolute value is also statistically significantly different from concurrent control animals. ECHA agrees that the thyroid gland weight changes in males are within the historical control ranges but notes that the primary reference point should be the concurrent control data (OECD GD 43, paragraph 67).

6 ECHA acknowledges that for females, there is no dose-response and no statistically significant differences in thyroid gland weights compared to concurrent controls. However, there is a trend towards increased thyroid gland weights in all female treatment groups: compared to concurrent controls, the absolute thyroid glands weights were increased by 14-25% and relative weights were increased by 9-21%.

7 For thyroid histopathology, you acknowledge that minimal follicular cell hypertrophy was observed with a consistent dose-related pattern across treatment groups. You however consider that since there was no increase in severity with increasing doses, nor any thyroids having hyperplasia, this supports '*minimal nature of this effect on the thyroid'*. ECHA notes that histopathologic changes in the thyroid gland, such as follicular cell height increase

(hypertrophy) and colloid area decrease, are indicative of thyroid-related activity (OECD GD 150, see e.g. pages 64-65 for thyroid-related activity / histopathologic changes within repeated-dose studies). ECHA also emphasises that follicular cell hypertrophy was reported in all treated groups of males and females (not observed in control animals). Therefore, ECHA considers that the histopathological changes are relevant and test substance related.

8 Finally, you consider that there were no test substance-related adverse effects on thyroid hormones. You note the significantly higher mean T4 levels in mid-dose males as well as in high-dose females and explain that those are due to few individual animals and fall within historical control data. You also note the higher mean TSH levels in high-dose males and females when compared to concurrent controls but consider that '*most of the TSH values for treated males were below the highest concurrent control animal*' and '*TSH data for females shows that all individual values for treated animals are within the range of the concurrent female controls except for one female'*.

9 ECHA acknowledges that for T4, only two mid-dose males and one high-dose male were above the highest concurrent control value. However, for females, 6/9 high-dose animals were above the concurrent controls. ECHA does therefore not agree that the increased mean value of T4 for high-dose females is due to few individual animals. ECHA further notes that the primary reference point should be the concurrent control data (OECD GD 43, paragraph 67). Compared to the concurrent control, there is a significant increase in mean T4 levels in high-dose females.

10 ECHA maintains that there is a trend of increased mean TSH values in high-dose male and female groups when compared to concurrent controls. For example, while 8/10 female control values are <1000 pg/ml (mean: 1017 pg/ml), in the high-dose female group 7/9 values are >1000 pg/ml (mean: 1932 pg/ml).

11 Furthermore, you initially considered that '*the downstream effects of hepatocellular enzyme induction often leads to similar changes in serum thyroid hormones*'. In your comments on the draft decision, you further discuss the role of the liver on the possible effect on the thyroid, stating that '*There are no data from the 90-day study, beyond higher liver weight and hepatocellular hypertrophy, which provide support for the role of the liver on the possible effect on the thyroid however, the data […] speaks for itself even in the absence of comprehensive liver findings*.'

12 ECHA notes that you have not provided substance-specific proof[2] to support your assumption that the changes in thyroid physiology would be secondary to hepatocellular enzyme induction. In summary, the OECD TG 408 study reports thyroid toxicity as evidenced by changes in multiple parameters (organ weight, histopathology and hormone levels). Thyroid toxicity indicates a concern for reproductive toxicity.

13 Therefore, the concern for reproductive toxicity must be further investigated.

14 ECHA agrees that an EOGRTS is necessary to address the identified concerns in relation with reproductive toxicity.

15 For the assessment of your testing proposal, see the reasons in section 2 below.

[2] Appendix A of the ECHA/EFSA Guidance for the identification of endocrine disruptors: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311
ECHA emphasises that even though the ECHA/EFSA Guidance was developed for hazard identification for endocrine-disrupting properties for other regulatory purposes, the same scientific principles apply also under the REACH Regulation.

**Reasons for the decision(s) related to the information under Annex X of REACH**

## 2. Extended one-generation reproductive toxicity study

16 The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement under Annex X. Furthermore, Annex X, Section 8.7.3., Column 2 defines when the study design needs to be expanded.

### *2.1. Information provided to fulfil the information requirement*

17 You have submitted a testing proposal for an EOGRTS according to OECD TG 443 with the Substance.

18 ECHA requested your considerations for alternative methods to fulfil the information requirement for Toxicity to reproduction. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

19 ECHA agrees that an EOGRTS is necessary.

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

#### *2.2.1. Species and route selection*

20 You proposed testing by oral route in rats. ECHA agrees with your proposal.

#### *2.2.2. Pre-mating exposure duration*

21 The length of the pre-mating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

22 You did not specify the pre-mating exposure duration.

23 A minimum of 2-week pre-mating exposure duration for P0 animals is required because the full spectrum of parameters on sexual function and fertility will be covered in the F1 animals (Guidance on IRs & CSA, Appendix R.7.6-3).

#### *2.2.3. Dose-level setting*

24 The aim of the requested test must be to demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance (OECD TG 443, para. 22; OECD GD 151, para. 28; introductory part of Annexes IX/X to REACH; Annex I Section 1.0.1. of REACH and Recital 7, Regulation 2015/282), and whether the Substance meets the criteria for a Substance of very high concern regarding endocrine disruption according to Art.57(f) of REACH as well as supporting the identification of appropriate risk management measures in the chemical safety assessment.

25 To investigate the properties of the Substance for these purposes, the highest dose level must be set on the basis of clear evidence of an adverse effect on sexual function and fertility, but no deaths (i.e., no more than 10% mortality; Annex I, Section 3.7.2.4.4. to the CLP Regulation) or severe suffering such as persistent pain and distress (OECD GD 19, para. 18) in the P0 animals.

26 In case there are no clear evidence of an adverse effect on sexual function and fertility, the limit dose of at least 1000 mg/kg bw/day or the highest possible dose level not causing severe suffering or deaths in P0 must be used as the highest dose level. A descending sequence of dose levels should be selected to demonstrate any dose-related effect and aiming to establish the lowest dose level as a NOAEL.

27 In summary: Unless limited by the physical/chemical nature of the Substance, the highest dose level in P0 animals must be as follows:

(1) in case of clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals, the highest dose level in P0 animals must be determined based on such clear evidence, or
(2) in the absence of such clear evidence, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(3) if there is such clear evidence but the highest dose level set on that basis would cause severe suffering or death, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(4) the highest dose level in P0 animals must follow the limit dose concept.

28 You have to provide a justification with your study results demonstrating that the dose level selection meets the conditions described above.

29 Numerical results (i.e. incidences and magnitudes) and description of the severity of effects at all dose levels from the dose range-finding study/ies must be reported to facilitate the assessment of the dose level section and interpretation of the results of the main study.

#### *2.2.4. Cohorts 1A and 1B*

30 Cohorts 1A and 1B belong to the basic study design and must be included.

##### *2.2.4.1. Splenic lymphocyte subpopulation analysis*

31 Splenic lymphocyte subpopulation analysis must be conducted in Cohort 1A (OECD TG 443, para. 66; OECD GD 151, Annex Table 1.3).

##### *2.2.4.2. Investigations of sexual maturation*

32 To improve the ability to detect rare or low-incidence effects, all F1 animals must be maintained until sexual maturation to ensure that sufficient animals (3/sex/litter/dose) are available for evaluation of balano-preputial separation or vaginal patency (OECD GD 151, para. 12 in conjunction with OECD TG 443, para. 47). For statistical analyses, data on sexual maturation from all evaluated animals/sex/dose must be combined to maximise the statistical power of the study.

#### *2.2.5. Extension of Cohort 1B*

33 If the conditions of Annex X, Section 8.7.3., Column 2 are met, Cohort 1B must be extended by mating the Cohort 1B animals to produce the F2 generation.

34 The extension is required, among others, if the use of the Substance is leading to significant exposure of consumers or professionals (column 2, first para., point (a) of Section 8.7.3.) and there are indications of one or more relevant modes of action related to endocrine disruption from available *in vivo* studies or non-animal approaches (column 2, first para., point (b), third indent of Section 8.7.3.).

35 The use of the Substance reported in the joint submission is leading to significant exposure of consumers and professionals because the Substance is used by consumers and professionals e.g. in cleaning and agrochemicals (PROCs 10, 11, 13). Furthermore, the

Substance is used in writing, drawing and creative design described as '*pens With intended release of substances*'.

36 Furthermore, there are indications of one or more modes of action related to endocrine disruption because changes in organs/parameters sensitive to endocrine activity are observed. More specifically, the available OECD TG 408 study (2022) reports thyroid toxicity:

- Significantly increased thyroid gland weights in treated males, and a similar trend in females;
- Effects in histopathology of the thyroid: follicular cell hypertrophy was reported in all treated groups of males and females (not observed in control animals). You report that the follicular cell hypertrophy was '*often associated with lower follicular colloid content.*'
- Changes in T4 and TSH levels in males and females.

37 You consider that the changes in hormone values were '*driven by a small number of individual animals with large outlying values and most values in the 1000 mg/kg/day group were within the range of values of the respective control group*.' Initially, you had not provided individual data to support your claim.

38 Within your comments on the draft decision, you provide individual tabular data, historical control data and detailed arguments on the findings on thyroid gland weights, histopathology and thyroid hormones. Your comments have been addressed in the reasons in section 1 above.

39 Furthermore, you consider that '*the downstream effects of hepatocellular enzyme induction often leads to similar changes in serum thyroid hormones*'. You have not provided substance-specific proof[3] to support your assumption that the changes in thyroid physiology would be secondary to hepatocellular enzyme induction.

40 You have not proposed to include an extension of Cohort 1B.

41 For the reasons stated above, ECHA considers that Cohort 1B must be extended.

42 Organs and tissues of Cohort 1B animals processed to block stage, including those of identified target organs, must be subjected to histopathological investigations (according to OECD TG 443, para. 67 and 72) because there is a concern for reproductive toxicity/endocrine activity indicated by the toxicity-triggers to extend the Cohort 1B.

43 The F2 generation must be followed to weaning allowing assessment of nursing and lactation of the F1 parents and postnatal development of F2 offspring. Investigations for F2 pups must be similar to those requested for F1 pups in OECD TG 443 and described in OECD GD 151.

#### *2.2.6. Cohorts 2A and 2B*

44 Annex IX/X, Section 8.7.3., Column 2 provides that the developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity.

45 Existing information on the Substance shows evidence of thyroid toxicity, as described above in section 2.2.5. The available OECD TG 408 study shows biologically relevant

[3] Appendix A of the ECHA/EFSA Guidance for the identification of endocrine disruptors: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311
ECHA emphasises that even though the ECHA/EFSA Guidance was developed for hazard identification for endocrine-disrupting properties for other regulatory purposes, the same scientific principles apply also under the REACH Regulation.

changes in thyroid hormone (T4 and TSH) levels. This is considered a specific mechanism/mode of action with an association to developmental neurotoxicity (OECD GD 150, p. 545).

46 In your comments on the draft decision, you consider that '90-day repeat dose thyroid findings were of little biological relevance and would not be of a magnitude that would result in adverse effects to workers or the general population and therefore insufficient to trigger the additional investigation'.

47 However, as also explained in the ECHA/EFSA Guidance[4] for the identification of endocrine disruptors, 'Substances inducing histopathological changes (i.e. follicular cell hypertrophy and/or hyperplasia and/or neoplasia) in the thyroid, with or without changes in the circulating levels of THs, would pose a hazard for human thyroid hormone insufficiency in adults as well as pre- and post-natal neurological development of offspring.' Therefore, ECHA considers that the reported histopathological effects as well as changes in thyroid hormone levels have biological relevance.

48 You did not propose to include Cohort 2A and 2B.

49 For the reasons stated above, the developmental neurotoxicity Cohorts 2A and 2B must be conducted.

### *2.3. Outcome*

50 Under Article 40(3)(b) your testing proposal is accepted under modified conditions, and you are requested to conduct the test with the Substance, as specified above.

#### *2.3.1. Further expansion of the study design*

51 No triggers for the inclusion of Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including Cohort 3 if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex IX/X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in Guidance on IRs & CSA, Section R.7.6.

[4] https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311
ECHA emphasises that even though the ECHA/EFSA Guidance was developed for hazard identification for endocrine-disrupting properties for other regulatory purposes, the same scientific principles apply also under the REACH Regulation.

**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**

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 1 July 2022.

ECHA held a third-party consultation for the testing proposal(s) from 22 September 2022 until 7 November 2022. ECHA did not receive information from third parties.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA took into account your comments and did not amend the deadline.

In your comments, you request a longer deadline, referring to 8-12 months wait times at test laboratories. As explained above, the deadline has already been extended by 12 months for this same reason. Therefore, the deadline has not been modified further.

Following the Board of Appeal's decision in cases A-002-2022 and A-003-2022 ECHA removed the request to perform additional investigations in learning and memory function as part of the information requirement of the second column of Annex IX/X, section 8.7.3

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: Addressee(s) of this decision and their corresponding information requirements**

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in 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] |
| [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[5].

(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.

[5] 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[6].

## 2. General recommendations for conducting and reporting new tests

References to Guidance on REACH and other supporting documents can be found in Appendix 1.

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