~~Confidential~~

Helsinki, 31 August 2023

Addressees
Registrants of JS_236_244_1 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
04 June 2020

Registered substance subject to this decision ("the Substance")
Substance name: 2,6-dimethylheptan-2-ol
EC/List number: 236-244-1

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***8 December 2025***.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.)
    a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and
    b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429).

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

2. *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: EU B.17./OECD TG 476 or EU B.67./OECD TG 490).

The reasons for the requests 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

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

1 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

2 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:

(i) an *in vivo* study in guinea pigs (1988) with the Substance;

(ii) a human repeated insult patch test (1969) with the Substance;

(iii) a maximisation test in humans (1976) with the Substance;

(iv) a human repeated insult patch test (1971) with the Substance.

3 ECHA understands that studies (ii, iii, iv) were provided using Annex XI, Section 1.1.3. (historical human data).

1.2. Assessment of the information provided

1.2.1. Weight of evidence adaptation rejected

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

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

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

1.2.1.1. Lack of documentation justifying the weight of evidence adaptation

7 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

8 You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

9 Beside this critical deficiency, ECHA has also assessed the other aspects of your adaptation.

1.2.1.2. Assessment whether the Substance causes skin sensitisation

10 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 8.3. includes similar information that investigated by the internationally recognised in vitro, in chemico and/or in vivo test methods on skin sensitisation. The key parameters of such test methods address each of the 3 key events of skin sensitisation, either individually or in an integrated approach as follows:

(1) investigation of cell proliferation in the draining lymph nodes (local lymph node assay), or
(2) investigation of local responses in animals or humans (guinea pig assays or human studies), or
(3) investigation of molecular interaction with proteins, inflammatory response in keratinocytes and activation of dendritic cells (*in vitro* and *in chemico* assays).

11 All the sources provide relevant information, as they investigate local responses in animals (study i) or humans (studies ii to iv).

12 However, the reliability of these sources of information is affected by the following deficiencies:

1.2.1.2.1. Test material not representative of the Substance (study i)

13 To comply with this information requirement, the test material in a study must be representative for the Substance; Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.

14 For study (i), under data source, you refer to a publication with the title "[redacted]". Given the information provided in the study record, ECHA was not able to retrieve this publication. However, from the title of this publication, it seems that study (i) has been conducted with [redacted].

15 The substance [redacted] is different than the Substance (2,6-dimethylheptan-2-ol, EC 236-244-1). In the absence of an adequate description of the test material used in study (i), you have not demonstrated that the test material is representative for the Substance.

1.2.1.2.2. The provided studies do not meet the specifications of the test guideline (study i)

16 In principle, to fulfil the information requirement, and to enable concluding whether the Substance causes skin sensitisation, a study should normally comply with the EU Method B.6/OECD TG 406 (Article 13(3) of REACH). Therefore, study (i) should be conducted consistently with the following specifications:

a) a dose level selection rationale is provided;

b) the induction concentration is the highest causing mild-to-moderate irritation to the skin;

c) the challenge dose is the highest non-irritation concentration;

d) the appropriate number of animals is included in the study: minimum 10 in test group and 5 in control, if negative results 20 in test group and 10 in control group highly recommended.

17 In study (i):

a) no dose level selection rationale is provided. Therefore, it is not possible to understand how these dose levels were selected.

b) no information was provided whether the concentration used ([redacted]%) for induction (intradermal and topical) caused mild-to-moderate irritation.

c) no information was provided whether the challenge concentration was the highest non-irritating concentration. Therefore, it is not clear that the animals could not have been exposed to a higher concentration.

d) only 10 animals were used. Therefore, the statistical power of the study is low.

18 Based on the above, study (i) cannot be considered a reliable source of information that could contribute to the conclusion local responses in animals or humans investigated by the required study.

1.2.1.2.3. Annex XI, Section 1.1.3. adaptation rejected (studies ii, iii, iv)

19 Under Annex XI, Section 1.1.3., historical human data must be based on a valid method for observing an effect.

20 As specified by the test method normally required to meet this information requirement, the skin sensitisation potential of the Substance must be investigated with the pure Substance (100%) or with the highest concentration causing irritation to the skin.

21 In studies (ii), (iii), and (iv):

- the test subjects were exposed to 2% of the Substance in dimethyl phthalate, 10% of the Substance, and 5% of the Substance in alcohol [redacted], for studies (ii), (iii) and (iv) respectively;
- no irritation reactions were reported and no dose range finding study was reported;
- no justification was provided why higher concentrations could not be tested.

22 You have provided studies according to the Human Repeat Insult Patch Test (HRIPT) (studies ii and iv) and you consider that the Substance is not a skin sensitiser. The HRIPT method is intended to confirm the absence of irritation and sensitisation potential but does not investigate the intrinsic properties of the Substance as required for the purpose of hazard identification.

23 Similarly, study (iii) is a Human Maximization Test (HMT) aimes at assessing "*a danger of contact-sensitisation in normal, intended use*".

24 The studies (ii), (iii), and (iv) appear to have been designed to establish safe levels for specific intended uses, rather than to investigate the intrinsic properties of the Substance as required for the purpose of hazard identification.

25 Further, the dose levels used in the studies (ii), (iii), and (iv) are far lower than the doses expected to be used for hazard assessment purposes, as doses only up to 10% were used and therefore do not provide information on skin sensitisation potential of the pure Substance (100%) or at the highest concentration causing irritation.

26 On this basis, you have not demonstrated that studies (ii), (iii), and (iv) were conducted according to a valid method for observing effects.

27 Based on the above, the provided studies (ii), (iii), and (iv) cannot be considered reliable sources of information that could contribute to the conclusion local responses in animals or humans investigated by the required study.

28 While you have provided information on the investigation of local responses in animals or humans, the sources of information (i, ii, iii, iv) have deficiencies affecting their reliability

which prevents drawing the conclusion on the investigation of local responses in animals or humans.

29 Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether the Substance causes skin sensitisation.

1.2.1.3. No assessment of potency

30 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

31 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1.2. above), this condition cannot be assessed.

1.2.1.4. Conclusion

32 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for skin sensitisation.

33 Based on the above, your weight of evidence adaptation under Annex XI, Section 1.2. is rejected.

34 Therefore, the information requirement is not fulfilled.

1.3. Study design

35 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

36 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

Reasons related to the information under Annex VIII of REACH

2. *In vitro* gene mutation study in mammalian cells

37 An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

2.1. Triggering of the information requirement

38 Your dossier contains negative results for both an Ames test and an *in vitro* cytogenicity study.

39 Therefore, the information requirement is triggered.

2.2. Information provided

40 You have provided information derived from experimental data from substances using the OECD QSAR Toolbox and flagged the information as (Q)SAR.

41 The OECD QSAR Toolbox was not used to indicate the presence or absence of a certain dangerous property of the Substance as required in Annex XI, Section 1.3.

42 Instead, the OECD QSAR Toolbox was used to identify other substances that were themselves used as source substances to predict the property of the Substance using a read-across approach. Therefore, we understand that you have adapted the standard information requirement for *in vitro* gene mutation study in mammalian cells not under Annex XI, Section 1.3., but under Annex XI, Section 1.5. (grouping of substances and read-across).

43 The document "[redacted]*.pdf*" includes some elements of justification for the use of a read-across approach.

44 In this decision, the following abbreviations are used for the category members:

- Cat. member No.1, CAS 78-69-3;
- Cat. member No.2, CAS 126-86-3;
- Cat. member No.3, CAS 106-21-8;
- Cat. member No.4, CAS 63500-71-0;
- Cat. member No.5, CAS 108-11-2.

45 You justify the grouping of the substances as: "*5 nearest neighbours compared by prediction descriptors*".

46 You have not provided a definition of the structural basis for the grouping.

47 You predict the properties of the Substance from information obtained from several source substances (list of substances provided above).

48 You provide the following reasoning for the prediction of toxicological properties:

49 The substances have a similar profile based on Genotoxicity OASIS and/or ECHA CHEM.

50 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.

2.3. Assessment of the information provided

2.3.1. Read-across adaptation rejected

51 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.

52 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).

2.3.1.1. Incomplete description of the applicability domain of the category

53 A category (grouping) hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint*" (Guidance on IRs and CSA, Section R.6.2.4.1.). Particularly, the applicability domain identifies "*the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made*" (Guidance on IRs and CSA, Section R.6.2.1.2.). Therefore, to reliably predict properties within a category the applicability domain should be described. Such description must cover the borders of the category, define unambiguous inclusion and exclusion criteria, and include a justification for these.

54 You describe the applicability domain of the substances covered by the grouping as: "*Category members are single chemicals or mixtures and are selected based on the profile of the target chemical. Only chemicals having experimental data are listed in the category*". You have not provided a description of the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties for the category.

55 This applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made.

2.3.1.2. Missing supporting information to compare properties of the substances

56 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. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

57 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substances cause the same type of effect. In this context, relevant, reliable and adequate information allowing to compare the properties of the source substances is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substances.

58 For the source substances, you provide the results ("negative") obtained from a database for each endpoint predicted and you include the profiling results from several prediction models. Apart from these records that are specific to the endpoint predicted, your

justification or the registration dossier do not include any robust study summaries or descriptions of data for the Substance that would confirm that both the Substance as well as the source substances cause the same type of effects.

59 In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

2.3.1.3. Missing robust study summaries

60 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 include robust study summary for each source study used in the adaptation.

61 Robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

62 ECHA understands that your read-across adaptation relies on experimental data. You have not provided robust study summaries of the tests with the source substances, whose results are the basis for your prediction.

63 You have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the source studies. Therefore, you have failed to provide a robust study summary for each source study used in the adaptation as required by Annex XI, Section 1.5.

64 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the category members. On this basis, your read-across approach under Annex XI, Section 1.5. is rejected.

65 Therefore, the information requirement is not fulfilled.

2.4. Study design

66 To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

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 (2023).
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

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 24 August 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.

ECHA did not receive any comments within the commenting period.

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

(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.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).