~~Confidential~~

Helsinki, 08 November 2023

Addressee(s)
Registrant(s) of JS IDDPP 249-828-6 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
04 April 2023

Registered substance subject to this decision ("the Substance")
Substance name: Isodecyl diphenyl phosphate
EC/List number: 249-828-6

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 ***13 August 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).

2. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, OECD TG 471).

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

3. If a negative result in Annex VII, Section 8.4.1. *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 request(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the request(s)

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 provided:

(i) a Repeat Insult Patch Test (1968) with the Substance;

(ii) a Two Application Patch Test (1968) with the Substance.

1.2. Assessment of the information provided

3 Although not explicitly stated, we understand that you intended to rely on the general rule for adaptation set out in Annex XI, 1.1.3. regarding historical human data in order to fulfil the standard information requirement. ECHA therefore assessed the information submitted against the requirements set out therein.

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. Annex XI, Section 1.1.3. adaptation rejected

4 Under Annex XI, Section 1.1.3., historical human data must meet the following criteria:

5 The strength of the data for a specific human health effect depends, among other things, on the type of analysis and on the parameters covered and on the magnitude and specificity of the response and consequently the predictability of the effect. Criteria for assessing the adequacy of the data include:

a) adequate characterisation of exposure;

b) valid method for observing an effect

6 In all cases adequate and reliable documentation shall be provided.

7 You have provided a study according to the Human Repeat Insult Patch Test (HRIPT) (study i) and you consider on this basis that the Substance is not a skin sensitiser.

8 The HRIPT method is intended to confirm the absence of irritation and sensitisation potential. However this method does not investigate the intrinsic properties of the Substance as required under the standard information requirement for the purpose of hazard identification. Therefore, the HRIPT is not a valid method for observing an effect and cannot be used to conclude whether the Substance causes skin sensitisation. Moreover, it is not clear which concentration was applied based on what is indicated in the registration dossier "*applied as received*". Therefore, the criterion for adequate characterisation of exposure is not met.

9 You have also provided a study according to the Two Application Patch Test (HMT) (study ii) and you consider that the Substance is not a skin sensitiser.

10 The Two Application Patch Test is not a scientifically accepted human test to assess skin sensitisation potential. The method appears to have only one induction application where generally accepted methods e.g. Human Maximization test (Kligman, 1966) require five induction exposures. One induction exposure, is not enough to induce sensitisation

reactions for the purpose of assessing whether a substance has the potential to produce skin sensitisation. Therefore, the Two Application Patch Test is not a valid method for observing an effect and cannot be used to conclude whether the Substance causes skin sensitisation. Moreover, it is not clear which concentration was applied as the only indication in the technical dossier was "applied as received". Therefore, the criterion for adequate characterisation of exposure is not met.

11 On this basis, you have not demonstrated that studies (i) and (ii) were conducted according to the requirements set out in Annex XI, Section 1.1.3. Therefore, your adaptation is rejected and is not possible to conclude if the Substance causes skin sensitisation.

1.2.1.2. No assessment of potency

12 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).

13 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1. above), this condition cannot be assessed.

14 Therefore, the information requirement is not fulfilled.

1.2.2. Study design

15 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.

16 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated in vitro 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.

2. *In vitro* gene mutation study in bacteria

17 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

2.1. Information provided

18 You have provided:

(i) an *in vitro* gene mutation study in bacteria (1980) with the Substance;

(ii) an *in vitro* gene mutation study in bacteria (1978) with the Substance.

2.2. Assessment of the information provided

2.2.1. The provided studies do not meet the specifications of the test guideline(s)

19 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101);

b) triplicate plating is used at each dose level;

c) concurrent strain-specific positive controls, both with and without metabolic activation, are included in each assay and the number of revertant colonies per plate induced by the positive controls demonstrates the effective performance of the assay;

d) a concurrent negative control is included in each assay and the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;

e) the mean number of revertant colonies per plate is reported for the treated doses and the controls;

f) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

20 In study(i):

a) the test was performed with the strains *S. typhimurium* TA 1535, TA 1537, TA 1538, TA 98, TA 100 (i.e., the strain(s) *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) are missing);

b) triplicate plating was not used at each dose level;

c) the numerical values of concurrent positive controls were not given and therefore it was not possible to assess whether they induced a number of revertant colonies per plate that demonstrated the effective performance of the assay;

d) the numerical values of revertant colonies per plate for the concurrent negative control were not given and therefore it was not possible to assess whether they were inside the historical control range of the laboratory;

e) the mean number of revertant colonies per plate for the treated doses and the controls was not reported;

f) no repeat experiment was performed to confirm the negative results and no justification was provided.

21 In study(ii):

a) the test was performed with the strains *S. typhimurium* TA 1535, TA 1537, TA 1538, TA 98, TA 100 (i.e., the strain(s) *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) are missing);

b) triplicate plating was not used at each dose level;

c) the numerical values of revertant colonies per plate for the concurrent negative control were not given and therefore it was not possible to assess whether they were inside the historical control range of the laboratory;

d) the mean number of revertant colonies per plate for the treated doses and the controls was not reported;

e) no repeat experiment was performed to confirm the negative results and no justification was provided.

22 In addition, the chemical identity of test substance is not reported.

2.2.2. Test material not representative of the Substance

23 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.

24 The study (ii) has been conducted with S-148, Lot QH-28641, BO-78-81, EC 249-828-6, without further information. You state that '*chemical identity of test substance not reported*'.

25 Therefore, you have not demonstrated that the test material is representative for the rest of the Substance.

26 The information provided does not cover the specification(s) required by the OECD TG 471.

27 Therefore, the information requirement is not fulfilled.

2.3. Study design

28 To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

Reasons related to the information under Annex VIII of REACH

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

29 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.

3.1. Triggering of the information requirement

30 Your dossier contains (i) a negative result for *in vitro* cytogenicity study in mammalian cells, and (ii) inadequate data for *in vitro* gene mutation study in bacteria.

31 The in vitro gene mutation studies in bacteria provided in the dossier are rejected for the reasons provided in request 2.

32 The result of the request 2 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3. is triggered.

33 Consequently, you are required to provide information for this information requirement, if the *in vitro* gene mutation study in bacteria provides a negative result.

3.2. Information provided

34 You have provided:

(i) an *in vitro* gene mutation study in mammalian cells (1978) with the Substance.

3.3. Assessment of the information provided

3.3.1. The provided study does not meet the specifications of the test guideline(s)

35 To fulfil the information requirement, a study must comply with the OECD TG 476 or the OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2) (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the maximum concentration tested induces 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration corresponds to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest;

b) the concurrent positive controls induce responses that are compatible with those generated in the historical positive control database and does not induce more than 90% of cytotoxicity compared to the negative control;

c) for the Mouse Lymphoma Assay (MLA), the concurrent positive control meets the acceptability criteria recommended by the MLA Expert Workgroup of the International Workshop for Genotoxicity Testing (IWGT) in terms of mutant frequency and/or small colony induction and described in paragraph 58 of OECD TG 490;

d) for the Mouse Lymphoma Assay (MLA), the concurrent negative control meets the acceptability criteria recommended by the MLA Expert Workgroup of the International Workshop for Genotoxicity Testing (IWGT) in terms of mutant frequency, cloning efficiency and suspension growth and described in paragraph 57 of OECD TG 490;

e) data on the cytotoxicity and the mutation frequency for the treated and control cultures are reported.

36 In study (i):

a) it is unclear whether the maximum tested concentration induced 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance, and it was less than 10 mM, 2 mg/mL or 2 µL/mL. In the dossier only the following information is included: '*Concentrations greater than 0.063 ul/ml were highly cytotoxic and could not be evaluated.*' and '[a] *higher concentration of 0.125 ul/ml was completely toxic in the activation (+S9 mix) test.*'. However there are no numerical data included that indicate 80-90% of cytotoxicity;

b) the numerical values of positive control are not given and therefore it is not possible to assess whether they induce responses that are compatible with those generated in the historical positive control database and/or induce more than 90% of cytotoxicity compared to the negative control;

c) the numerical values of mutant frequency and/or small colonies induced by the concurrent positive control are not given and therefore it is not possible to assess whether they meet the acceptability criteria recommended by the MLA Expert Workgroup of the International Workshop for Genotoxicity Testing (IWGT) and described in paragraph 58 of OECD TG 490;

d) the numerical values of mutant frequency and/or cloning efficiency and/or suspension growth induced by the concurrent negative control are not given and therefore it is not possible to assess whether they meet the acceptability criteria recommended by the MLA Expert Workgroup of the International Workshop for Genotoxicity Testing (IWGT) and described in paragraph 57 of OECD TG 490;

e) data on the cytotoxicity and the mutation frequency for the treated and control cultures were not reported.

37 In addition, the identity of test substance was not reported.

3.3.2. Test material not representative of the Substance

38 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.

39 The study (i) has been conducted with S-148 BO-78-85, EC 249-828-6, without further information. You state that '*chemical identity of test substance not reported*'.

40 Therefore, you have not demonstrated that the test material is representative for the the Substance.

41 The information provided does not cover the specification(s) required by the OECD TG 476/490.

42 Therefore, the information requirement is not fulfilled.

3.4. Study design

43 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 23 January 2023.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the request(s).

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]

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/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

(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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have

harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

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).