

Helsinki, 04 June 2024

**Addressees**

Registrants of JS\_423-740-1\_█ as listed in Appendix 3 of this decision

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

24 October 2019

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

Substance name: 2-cyclohexylidene-2-phenylacetonitrile

EC/List number: 423-740-1

**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 **9 September 2027**.

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

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

1. Screening study 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.

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

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).

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<sup>1</sup> 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

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

**Appendix 1: Reasons for the request(s)**

<b>Reasons related to the information under Annex VIII of REACH .....</b>	<b>4</b>
1. Screening study for reproductive/developmental toxicity .....	4
<b>Reasons related to the information under Annex IX of REACH .....</b>	<b>6</b>
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**Reasons related to the information under Annex VIII of REACH****1. Screening study for reproductive/developmental toxicity**

1 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1.

*1.1. Information provided*

2 You have provided a combined sub-chronic toxicity study and one-generation reproductive toxicity study (2009) with the Substance (study i).

*1.2. Assessment of the information provided*

*1.2.1. The provided study (i) does not meet the specifications of the test guideline(s)*

3 To fulfil the information requirement, a study must comply with EU B.63/OECD TG 421 or EU B.64/OECD TG 422 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- a) at least three dose levels with concurrent controls are tested, unless the study is conducted at the limit dose;
- b) the highest dose level aims to induce toxicity or aims to reach the limit dose.

4 In study (i):

- a) two dose levels (i.e., less than three dose levels) were tested in the reproductive phase of the study and concurrent controls were included;
- b) the highest dose levels tested was 40 mg/kg bw/d (i.e., below the limit dose of the OECD TG 421/422) and no adverse effect were observed and no sufficient justification for the dose setting was provided as you only state that "[...] *minimal toxic effects expected in terms of bodyweight gain at 40 mg/kg/day.*". You derived a NOAEL (P0 and F1) of 40 mg/kg bw/d;

5 In your comments to the draft decision you disagreed to perform the requested study. You state that in the performed combined sub-chronic toxicity study and one-generation reproductive toxicity study (study i), three doses were tested, however, "*The top dose for females only (Group B for the reproductive part of the study) could not be used due to animal welfare reasons as it turned out to be a level with unexpected excessive toxicity (shown in Group A for the systemic toxicity part of the study).*" You further claim that "*the mid dose [40 mg/kg bw/day] can be considered high enough and relevant for an assessment of potential reproductive effects, as it seems quite close to the highest dose tolerated by the animals, based on the critical effects observed*". Based on the above you conclude that "*A repetition of a reproductive toxicity study is deemed unnecessary by the registrant, as it would only generate additional data for a dose level slightly below 160 mg/kg bw/d that is certain to induce systemic toxicity and as such would not produce useful information for reproductive toxicity potential and classification conclusions on the substance*".

6 In your comments to the draft decision you did not provide any new scientific information but you practically confirmed ECHA's observations that for the reproductive part of the study only two dose levels were tested and that the dose level of 40 mg/kg bw/day (the highest dose tested for the reproduction part of the study) did not show effects that can be considered adverse.

- 7 Such dose level selection is not in conformity with specifications of OECD TG 422, in particular paragraph 29: *"The highest dose level should be chosen with the aim of inducing toxic effects but not death nor obvious suffering. Thereafter, a descending sequence of dose levels should be selected with a view to demonstrating any dosage related response and no adverse effects at the lowest dose level"*.
- 8 Since the current study (i) uses only two dose-levels, no dose-response relationship can be established and the information is not sufficient to conclude on the hazardous properties of the Substance for the tested parameters. i.e. sexual function and fertility and development.
- 9 Therefore, the information provided does not cover the specifications required by the OECD TG 421 or 422.
- 10 Therefore, the information requirement is not fulfilled.

### 1.3. Study design

- 11 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.
- 12 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1., Column 1).
- 13 Therefore, the study must be conducted in rats with oral administration of the Substance.
- 14 Further information on dose-levels selection can be found in ECHA's *"Advice on dose level selection for the conduct of reproductive toxicity studies (OECD TGs 414, 421/422 and 443) under REACH"*<sup>2</sup>.

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<sup>2</sup> The ECHA advice is accessible at [https://echa.europa.eu/documents/10162/17220/211221\\_echa\\_advice\\_dose\\_repro\\_en.pdf/27159fb1-c31c-78a2-bdef-8f423f2b6568?t=1640082455275](https://echa.europa.eu/documents/10162/17220/211221_echa_advice_dose_repro_en.pdf/27159fb1-c31c-78a2-bdef-8f423f2b6568?t=1640082455275)

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

### 2. Pre-natal developmental toxicity study in one species

15 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2.

#### 2.1. Information provided

16 ECHA understands that you have adapted this information requirement by using Annex IX, Section 8.7., Column 2, although you have not explicitly referred to it. You have provided the following information:

(i) *"the study does not need to be conducted because the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure"*

(ii) a combined sub-chronic toxicity study and one-generation reproductive toxicity study (2009) with the Substance.

#### 2.2. Assessment of the information provided

##### 2.2.1. Criteria for the application of the adaptation for Annex IX, Section 8.7., Column 2 not met

17 Under Annex IX, Section 8.7., Column 2, the study does not need to be conducted if the following criteria are met:

- the substance is of low toxicological activity, demonstrated by a comprehensive and informative dataset showing no toxicity in any of the tests available; and
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- that there is no or no significant human exposure.

18 However, the information in your dossier does not support these criteria as:

- The study (ii) shows clear adverse toxic effects such as mortality of female rats and reduction of mean bodyweight gain in male rats at the highest dose level tested (140 mg/kg bw/d).
- No toxicokinetic data was provided to show that there is no systemic absorption, but you conclude that "**██████████** is a small organic molecule with a molecular weight of 197g. It is a liquid and has a water solubility of 7.5 mg/L at 20°C and a log Pow of 4.0. The physico-chemical properties of **██████████** would suggest the substance is likely to be absorbed via dermal, inhalation and gastric routes following exposure. Sub-acute and subchronic toxicity data indicate that **██████████** is absorbed following administration by gavage and metabolised by the liver. No specific studies on the absorption, distribution, metabolism and excretion of **██████████** are available."
- The uses of the Substance include end-use of polishes and wax blends, end-use of washing, cleaning and disinfecting products, air care products, and biocides, and cosmetics.

- 19 The study (ii) shows evidence of systemic toxicity. Therefore, and also based on physico-chemical properties, it is expected that the Substance is systematically absorbed via relevant route of exposure.
- 20 The uses of the Substance, such as widespread uses by professional workers and also consumer uses, indicate that there is significant human exposure which you have not addressed.
- 21 On this basis, you have not demonstrated that the criteria for this adaptation are fulfilled.
- 22 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

### *2.3. Study design*

- 23 A PNDT study according to the test method OECD TG 414 should be performed in rats or rabbits as preferred species.
- 24 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2., Column 1).
- 25 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.
- 26 In your comments to the draft decision you agree to perform the requested study.

## 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 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 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 amended the decision. Information on Sub-chronic (90-day) repeated dose toxicity study is no longer requested.

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]
[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>).