~~Confidential~~

Helsinki, 02 November 2023

Addressee
Registrant of JS_succinofull as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
25 November 2021

Registered substance subject to this decision ("the Substance")
Substance name: succinonitrile
EC/List number: 203-783-9

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 ***11 May 2026***.

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

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

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).

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

2. Pre-natal developmental toxicity study (triggered by Annex IX, Section 8.7.2., Column 2; test method: OECD TG 414) by oral route, in a second species (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.

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 VIII of REACH

1. In vitro gene mutation study in mammalian cells

1 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.

1.1. Triggering of the information requirement

2 Your dossier contains negative results for both an Ames test and an *in vitro* cytogenicity study. Therefore, the information requirement is triggered.

1.2. Information provided

3 You have adapted this information requirement by using Annex VIII, Section 8.4., Column 2. To support the adaptation, you have provided the following information:

(i) Justification that the study does need to be performed "*because an in vivo study mammalian cells OECD 474 is available*";

(ii) *In vivo* mammalian erythrocyte micronucleus test (2016) with the Substance.

1.3. Assessment of the information provided

4 Under Annex VIII, Section 8.4., Column 2, the study may be omitted if adequate data from a reliable *in vivo* mammalian gene mutation test are available. The Guidance on IRs and CSA, Section R.7.7.6.3. clarifies that the *in vivo* study must be a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (TGR), performed according to the OECD TG 488. This test investigates gene mutations using reporter genes.

5 The study (ii) is described as *in vivo* mammalian erythrocyte micronucleus test, performed according to the OECD TG 474. The study is not a TGR assay and does not provide information on gene mutations in mammalian cells. The OECD TG 474 provides information on the detection and quantification of cytotoxicity and the frequency of cells with structural chromosomal aberration(s) in mammals. Therefore, it does not provide relevant information for this information requirement.

6 As the requirements of Annex VIII, Section 8.4., Column 2 are not met, your adaptation is rejected. Therefore, the information requirement is not fulfilled.

1.4. Study design

7 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.

Reasons related to the information under Annex IX of REACH

2. Pre-natal developmental toxicity study in a second species

8 An additional pre-natal developmental toxicity (PNDT) study (OECD TG 414) in a second species may be required by the Agency under Annex IX, Section 8.7.2., Column 2 if there is a concern for developmental toxicity based on the outcome of the first PNDT study and all other relevant data. That could be the case for example if the study on the first species shows developmental toxicity not meeting the criteria for classification in the hazard class reproductive toxicity category 1A or 1B; May damage the unborn child (H360D).

2.1. Triggering of the information requirement

9 You have provided a PNDT study in rat (2016) with the Substance. This study indicates adverse effects on development (reduction in number of live offspring, changes in fetal/pup bodyweight, litter size and weight, skeletal variation). On that basis, you have self-classified the Substance in the hazard class reproductive toxicity category 2; Suspected of causing delayed growth of the unborn child (H361d).

10 The PNDT study in rat (2016) that you submitted shows effects that are not sufficient to meet classification criteria as Category 1B reproductive toxicant. On that basis, there is a concern for developmental toxicity based on the outcome of that study and the information requirement is triggered.

11 You have not submitted any information for this requirement. Therefore, the information requirement is not fulfilled.

12 In your comments to the draft decision you indicate that ECHA's request is based on "*the effects observed in the Two-Generation Reproduction Toxicity Study (OECD 416) conducted in rats are not sufficient to determine a classification for reproductive and developmental toxicity*". You claim that there is "*little sense to carry out an additional OECD 414 developmental toxicity study for succinonitrile*" and you provide the following reasoning to support your claim:

- "*It will not study the most sensitive developmental toxicity endpoint, growth retardation at the start of lactation. Lactation is not included in the OECD 414 prenatal developmental toxicity study;*
- *It will not increase knowledge on the mode of action, the release of toxic HCN".*

13 In addition you state that "[…] *at a dose level of 195 mg/kgbw/day in the OECD 414 prenatal developmental toxicity study in SD rats only growth retardation was observed, and not any signs of malformation were found*".

14 Based on the above you conclude that a PNDT study on a second species "*would not add any new relevant information to the hazard profile of succinonitrile*".

15 As explained above, the information requirement for the PNDT in a second species is triggered by the concern for developmental toxicity, observed in the PNDT study in rats (OECD TG 414, 2016), discerned by adverse effects related to development, such as growth retardation and also statistical significant increase in post implantation loss which consequently leads to a significant reduction in live offspring. According to CLP, Annex I: 3.7.1.4: "[…] *for classification, developmental toxicity essentially means adverse effects induced during pregnancy, or as a result of parental exposure. These effects can be manifested at any point in the life span of the organism. The major manifestations of developmental toxicity include (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency".* The growth retardation and

reduction of live offspring are related to the developmental organism and altered growth. The PNDT study in a second species would allow to investigate further the potential developmental toxicity of the Substance and inform on whether it would merit a stricter classification as Repro 1B for development.

16 In your comments you claim that the growth retardation at the time of lactation is more sensitive than the growth retardation observed prenatally. You have not justified your claim. Furthermore, the growth retardation does not address the concern of increased post-implantation loss that is "*death of developing organism"*.

17 Further, you claim that the highest dose level of the PNDT study, i.e. 195 mg/kg bw/day, is '*in the lethal range of acute LD50 study'*. ECHA notes that the lethal range of the acute LD50 study with the Substance is estimated to be 300-2000 mg/kg bw/day. Therefore, the highest dose level of the PNDT study does not fall within the lethal range.

18 Finally, as indicated above, the PNDT study in a second species is triggered due to a concern for developmental toxicity based on the outcome of the first PNDT study. As explained above, the study would allow to further investigate the potential developmental toxicity of the Substance and to inform weather a stricter classification is merited, rather than to identify the specific mechanisms (e.g. release of toxic HCN), related to the developmental toxicity.

19 Based on the above, ECHA reiterates that there is a concern for developmental toxicity based on the outcome of the available information and the information requirement is triggered.

2.2. Study design

20 A PNDT study in a second species must be performed in rabbits as preferred non-rodent species.

21 As the Substance is a solid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2., Column 1).

22 Based on the above, the study must be conducted in rabbits with oral administration of the Substance.

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

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 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 took into account your comments and did not amend the requests.

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;

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third-party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

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

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

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

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).