

Helsinki, 11 September 2020

Addressees

Registrant(s) as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision

26/05/2019

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

Substance name: Sodium chlorate

EC number: 231-887-4

CAS number: 7775-09-9

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 the deadline of **18 March 2021**.

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

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

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) by oral route, in rats, specified as follows:
 - **Ten weeks pre-mating exposure duration for the parental (P0) generation;**
 - **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
 - **Cohort 1A (Reproductive toxicity);**
 - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**
 - **Cohorts 2A and 2B (Developmental neurotoxicity).**

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

Reasons for the request(s) are explained in the following appendix:

- Appendix entitled "Reasons to request information required under Annex X of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII to X to REACH, for registration at more than

1000 tpa.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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.

Authorised¹ under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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 A: Reasons to request information required under Annex X of REACH

1. Extended one-generation reproductive toxicity study

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

You have provided

- a study with the Substance (2005) which you claim to be "equivalent or similar to EPA OPP 83-4 (Reproduction and Fertility)"
- a grouping and read-across adaptation using a two-generation study with an analogue substance (1998)

We have assessed this information and identified the following issue(s):

Study not fulfilling criteria for an extended one-generation study

To be considered compliant and enable concluding if the Substance is a reproductive toxicant, the study has to meet the requirements of OECD TG 443 (or, if conducted before 13 March 2015, the requirements of a two-generation study, OECD TG 416) as specified in REACH. The following key parameter(s) of these two test guidelines include

- dosing of the Substance from should cover full spermatogenesis and folliculogenesis, mating, gestation, lactation, and exposure of the F1 generation up to the adulthood
- examination of key parameters for postnatal developmental toxicity

In the study you have provided (2005):

- the animals were exposed only during gestation days 6-15;
- no postnatal investigations of the fully exposed F1 generation up to the adulthood.

The provided study does not have a required exposure duration because the exposure does not cover mating, lactation and full exposure of the F1 generation starting *in utero* and continuing up to the adulthood.

The provided study does not include the extensive postnatal investigations of the fully exposed F1 generation up to the adulthood.

Therefore, the study is rejected.

Grouping and read-across

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.

Additional information on what is necessary when justifying a read-across approach can be

found in the ECHA Guidance² and related documents^{3, 4}.

You have included a read-across justification in the provided study record for this information requirement.

You read-across between the structurally similar substances, sodium chlorite, EC No. 231-836-6 (CAS No. 7758-19-2) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: *"Sodium chlorite has similar toxicological properties and has been used as a read-across substance in this case. Chlorite is readily absorbed when administered to rats, then randomly distributed throughout the tissues (Abdel-Rahman et al., 1982). It is transformed mainly into chloride in rats, smaller amounts appearing as unchanged chlorite. Excretion is mainly via the urine, followed by faeces. Similarly, Chlorate is readily absorbed and randomly distributed throughout the tissues of rats (Abdel-Rahman et al., 1982). It is excreted mainly in the form of chloride in the urine, smaller amounts appearing as chlorite and chlorate"*.

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects and that common biotransformation products are formed. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

Observed differences in toxicological properties

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. The observation of differences in the toxicological properties between the source substance(s) and the Substance is a warning sign. An explanation for such a difference resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s).

The results of the information on repeated dose toxicity obtained with the target substance and the source substance vary. Specifically, the investigations of the two-generation reproductive toxicity study you provided with the source substance demonstrated haematological effects but no changes in thyroid hormone levels, whereas the repeated dose toxicity studies performed with the Substance show effects on thyroid (see below).

² Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

³ Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: [Read-Across Assessment Framework \(https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across\)](https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

⁴ Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: <https://doi.org/10.2823/794394>

Furthermore, the source substance is acutely far more toxic (LD₅₀ rat oral: 158 and 177 mg/kg bw/d for males and females, respectively) compared to the target substance (LD₅₀ rat oral: 5000 mg/kg bw/d).

The available set of data on the target and source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the structurally similar target and source substances cause the same type of effect(s). Therefore you have not demonstrated and justified that the properties of the source substance(s) and of the Substance are likely to be similar despite the observation of these differences.

Therefore, your adaptation is rejected.

Based on the above, the information you provided does not fulfil the information requirement.

The specifications for the study design

Premating exposure duration and dose-level setting

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

Ten weeks pre-mating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter pre-mating exposure duration.⁵

Therefore, the requested pre-mating exposure duration is ten weeks.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level must aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a range-finding study (or range finding studies) are reported with the main study.

You must provide a justification with your study report that demonstrate that the dose level selection meets the conditions described above.

Cohorts 1A and 1B

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

Cohorts 2A and 2B

The developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity.

⁵ ECHA Guidance R.7a, Section R.7.6.

Existing information on the Substance itself derived from publicly available repeated dose toxicity studies (subacute and chronic) shows evidence of effects on the thyroid:

- Thyroid colloid depletion in a 90-day study in rats at 128 mg/kg bw/d (moderate to marked severity, observed in all animals)⁶
- Thyroid gland follicular hypertrophy in a 3-week study in rats at 500 mg/kg bw/d and above and in a 2-year study in rats at 35 mg/kg bw/d and above⁷ (NTP 2005)
- Significantly decreased T3 and T4 levels and increased TSH levels in male/female rats after 4 or 21 days of oral exposure in drinking water at 1 g/L or higher⁸

Therefore, the developmental neurotoxicity Cohorts 2A and 2B need to be conducted.

Species and route selection

The study must be performed in rats with oral⁹ administration.

Further expansion of the study design

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B and Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance¹⁰.

Available data

The jointly submitted registration for the Substance contains data which is relevant for this endpoint. In accordance with Title III of the REACH Regulation, you must request it from the other registrant(s) and then make every effort to reach an agreement on the sharing of data and costs.

ECHA considers six months a sufficiently reasonable time for the registrant to seek permission to refer to the other registrant's full study report.

⁶ McCauley et al. (1995) Drug Chem. Toxicol. 18(2-3):185-199.

⁷ NTP (2005) NTP Technical Report TR-517.

⁸ Hooth et al. (2001) Toxicol. Pathol. 29(2):250-259.

⁹ ECHA Guidance R.7a, Section R.7.6.2.3.2.

¹⁰ ECHA Guidance R.7a, Section R.7.6.

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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 summaries¹¹.

B. 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 impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.
2. Information on the Test Material needed in the updated dossier
 - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
 - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess 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 dossiers¹².

¹¹ <https://echa.europa.eu/practical-guides>

¹² <https://echa.europa.eu/manuals>

Appendix C: 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 12 September 2019.

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

ECHA did not receive any comments within the notification 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 D: List of references - ECHA Guidance¹³ and other supporting documents

Evaluation of available information

Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping

Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)¹⁴

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)¹⁴

Physical-chemical properties

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment

Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing

Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents¹⁵

¹³ <https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>

¹⁴ <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>

¹⁵ <http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm>

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix E: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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.