~~Confidential~~

Helsinki, 05 October 2021

Addressees
Registrant(s) of JS_SFS_2010 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
28 October 2019

Registered substance subject to this decision ("the Substance")
Substance name: Sodium hydroxymethanesulphinate
EC number: 205-739-4
CAS number: 149-44-0

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 ***11 July 2024***. The deadline for this compliance check decision takes into account the decision on a testing proposal for second-species pre-natal developmental toxicity study on the same Substance to allow for sequential testing.

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 premating 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); and
   - Cohort 3 (Developmental immunotoxicity).

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 Annexes VII to X of REACH", respectively.

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.

Authorised[1] 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 (OECD TG 443) 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 statement in section 7.8.1 of IUCLID that "*This information will be submitted later based on BoA Case number A-001-2018. In its decision letter, the ECHA Board of Appeal decided that the information on the EOGRTS (Column 1 of Section 8.7.3., test method: EU B.56/OECD TG 443) in rats, oral route, without the extension of cohort 1B to include the F2 generation, must be submitted by 9 April 2021 (Case number A-00 1-2018, 9 April 2019). Following this decision, the study is initiated accordingly by the registrant.*" However, you have clarified to ECHA in an email dated 30 June 2020 that the study has not been initiated due to ECHA's rectification decision of 27 May 2019.

You explain in your comments that the Substance is already classified as Muta 2 and that strict risk management measures are already implemented. Furthermore, you are of the opinion that the requested reproductive toxicity study will not add any valuable information to the hazard and risk assessment data because the users are protected from a potential reproductive hazard.

According to Column 2 of Section 8.7, Annex X of REACH, the EOGRT study does not need to be conducted "*if the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented*". For this adaptation possibility, the ECHA Guidance[2] clarifies that a substance must be classified as germ cell mutagen category 1 (Muta 1A or 1B); in other words, classification as Muta 2 is not sufficient to meet this adaptation. Furthermore, your justification that users are protected against reproductive hazard based on risk management measures implemented based on Muta 2 classification cannot be accepted because this is not a column 2 adaptation possibility under REACH. In this respect, ECHA emphasises that the hazard for reproductive toxicity for the Substance must be clarified for the purpose of classification and labelling, risk assessment and identification of substances of very high concern. Therefore, your adaptation justification cannot be accepted and the study needs to be performed.

The information requirement is not fulfilled and therefore there is a data gap for an EOGRT study.

<u>Species and route selection</u>

The study must be performed in rats with oral[3] administration.

In your comments you agree that the oral route is the most appropriate route.

<u>The specifications for the study design</u>

Premating exposure duration and dose-level setting

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

[2] ECHA Guidance R.7a, Section R.7.6.2.3.2, Stage 1 and 1.2
[3] ECHA Guidance R.7a, Section R.7.6.2.3.2.

In the draft decision sent to you for commenting, a 2-week premating exposure duration for P0 animals was considered sufficient for your Substance, because the production of the F2 generation was requested and, thus, the premating exposure duration would have been 10 weeks for these Cohort 1B animals. The request for the extension of Cohort 1B was removed from this decision based on your comments and therefore, the requested premating exposure duration is ten weeks to allow meaningful assessment for fertility as explained above.

You explain in your comments that the premating exposure duration of 10 weeks is not needed and that a 2-week premating exposure duration is sufficient because an OECD TG 422 and 408 study with the Substance do not indicate a potential adverse effect on fertility.

ECHA disagrees with your explanation. As outlined above and in ECHA Guidance, a 10-week premating exposure duration is the default requirement to appropriately cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility. This is important because "*the premating exposure duration … should be appropriate to meet risk assessment and classification and labelling purposes as required by Regulation (EC) No 1907/2006 and Regulation (EC) No 1272/2008 of the European Parliament and of the Council.*"[4] ECHA Guidance[5] clarifies that only "*based on substance specific justifications the premating exposure duration may be shorter than ten weeks but should not be shorter than two weeks (see Appendix R.7.6–3 of this Guidance).*"

You refer to the results of an OECD TG 422 and 408 study with the Substance and that these studies do not indicate a potential adverse effect on fertility. However, the OECD TG 422 study was only conducted with a 2-week premating exposure duration and therefore its results do not exclude observing potential effects on sexual function and fertility after a premating exposure duration of 10 weeks. The OECD TG 408 does not address functional fertility aspects such as mating, gestation, parturition and lactation and can therefore also not inform on potential effects on sexual function and fertility after a 10-week premating exposure duration.

Therefore, your justification cannot be accepted and a 10-week premating exposure duration is required.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level shall 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. 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 relevant data to be used for dose level setting, it is recommended that range-finding results are reported with the main study.

You agree in your comments that the results of the dose range finding study are reported with the results of the main study.

You have to provide a justification with your study results that demonstrates that the dose level selection meets the conditions described above.

Cohorts 1A and 1B

[4] Recital (7) of Commission Regulation (EU) 2015/282 of 20 February 2015 amending Annexes VIII, IX and X to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards the Extended one-generation reproductive toxicity study

[5] ECHA Guidance R.7a, Section R.7.6.2.2.3

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

You explain in your comments that the uses in the joint submission are not leading to significant exposure of consumer and professionals. ECHA agrees with you because in the latest dossier updates, there are no such uses reported. Therefore, Cohort 1B does not need to be extended.

Inclusion of Cohorts 2A/ 2B and 3

Inclusion of Cohorts 2A, 2B and 3 is justified due to the concern that stems from formaldehyde which is formed from the Substance (see sections *Cohorts 2A and 2B* and *Cohort 3* below).

You explain in your comments that "*the potential degradation to formaldehyde is not relevant under physiological conditions*"; i.e. that release of formaldehyde is observed at temperatures significantly above body temperature, and that the solid Substance and a 40% aqueous solution thereof are stable. You also exemplify that the use of the Substance in emulsion polymerisation and discharge printing would result in negligible exposure. You consider hydrolysis at lower pH (acid environment) likely but based on the uses, the possibility for oral exposure could be excluded and only inhalation and dermal exposure needs to be assessed.

ECHA disagrees with your explanation. By requesting the EOGRT study, the intrinsic properties of the Substance are addressed for hazard identification and to adequately inform on classification and labelling and risk assessment. According to ECHA Guidance[6], "*the selection of the 'most appropriate route of administration' focuses on identification of hazards … and depends on the most appropriate route for identification of the intrinsic properties of the substance for reproductive hazard. According to the test methods for reproductive toxicity which focus on the detection of reproductive hazards, the oral route (gavage, in diet, or in drinking water) is the "default" route, except for gases.*" Uses and occupational exposure scenarios are not an intrinsic property of the Substance and are not considered when addressing hazard identification. In your comments you have also agreed that the oral route is the most appropriate route.

In the registration dossier for the Substance, you state that "*the pre-test indicates that [the] substance is not resistant against hydrolysis*" and that "*the substance is readily biodegradable*". This conclusion is based on testing of aqueous solutions of the Substance at pH 4 and 7 at 20 °C with recovery rates of 68% and 77% after 5 days, respectively. This shows that the Substance degrades at temperatures even below body temperature in neutral (pH 7) and slightly acidic (pH 4) conditions. ECHA also agrees with your expectation that the Substance undergoes hydrolysis under acidic conditions after oral administration. During stomach passage, relevant amounts of formaldehyde can be released by hydrolysis and the formed formaldehyde is then available for absorption into the body. Degradation takes also place at neutral and physiologic pH. Therefore, there is a remaining concern resulting from the formation of formaldeyde, which is formed before absorption. Furthermore, formaldehyde can also be released continously from the absorbed Substance while in systemic circulation thereby directly exposing target tissues to formaldehyde (comparable to a "*pro-drug*" mechanism that can enhance toxicological effects).

ECHA concludes that the concern resulting from the formation of formaldhyde remains.

Structural similarity

You explain in your comments that "*while the registered substance may have the potency to break down to formaldehyde, the toxicological profile of the registered substance does not*

[6] ECHA Guidance R.7a, Section R.7.6.2.3.2, Stage 4.1 (iv)

indicate that formaldehyde is formed in concentrations relevant to the hazard evaluation of the registered substance." Your conclusions are based on acute toxicity, skin and eye irritation and skin sensitisation studies. Furthermore, you explain that formaldehyde disproportionates by the Cannizzaro reaction. You conclude that formaldehyde "*plays a negligible role for possible toxic effect in this case*".

However, the Substance is unstable in aqueous solution towards decomposition to formaldehyde. The formaldehydewhich is released by hydrolysis from the Substance, is structurally identical to formaldehyde. As decomposition to formaldehyde is an inherent property of the Substance, information on formaldehyde is considered relevant for deciding on the study design of the EOGRT study. Therefore, information from formaldhyde is *per se* relevant for toxicological evaluation of the Substance.

With respect to different toxicological properties for acute toxicity, eye/ skin irritation and skin sensitisation, ECHA emphasises that these properties do not allow a prediction for the effects of formaldehyde on sexual function, fertility and development.

From your explanation on the Cannizzarro reaction, it is unclear how this reaction contributes to reducing the formaldehyde concentration under the conditions after oral administration, *e.g.* when formaldehyde is formed and diluted in acidic stomach fluid or in different compartments of the body after absorption, where formaldehyde molecules are not in direct contact with each other. It is also unclear how the necessary alkaline conditions for the Cannizzarro reaction, which is usually carried out in test tubes under laboratory conditions, can occur under physiological conditions.

Formaldehyde is formed from the Substance and after oral exposure the organism is exposed to the parent Substance and its hydrolysis product formaldehyde. The exposure to formaldehyde raises concern for (developmental) neurotoxicity and (developmental) immunotoxicity as outlined below.

Cohorts 2A and 2B

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

Existing information on formaldehyde derived from available *in vivo* studies, non-animal approaches and epidemiological investigations show that formaldehyde is a neurotoxin that affects memory, learning, and behaviour. Formaldehyde can cause nervous system damage by its known ability to react with and form cross linking with proteins, DNA and unsaturated fatty acids and long-term exposure to formaldehyde may cause irreversible neurotoxicity and is related to brain cancer (astrocytoma). Furthermore, inhaled formaldehyde has been shown to cause behavioural and memory disorders in rats and has been described as 'probable neurotoxic'.[7]

Formaldehyde is considered to be a substance structurally analogous to the Substance because the Substance, sodium hydroxymethanesulfinate, is unstable in aqueous solution towards decomposition to formaldehyde.[8] As decomposition to formaldehyde is an inherent property of the Substance, information on formaldehyde is considered relevant for deciding on the study design of the EOGRT study.

[7] International Journal of Anatomy and Physiology ISSN: 2326-7275 Vol. 3 (3), pp. 50-59, January, 2014.
[8] Polenov YV, Egorova EV and Pushkina VA. Mechanism of Decomposition of Sodium Hydroxymethanesulfinate in Aqueous Solution. Russian Journal of General Chemistry, Vol. 71, No. 5, 2001, pp. 675-678.

You explain in your comments that you are "*aware that formaldehyde has been linked to effects to the nervous system via in vivo studies, non-animal approaches and epidemiological investigations when exposed to elevated doses or by prolonged exposure. However, as discussed in detail above, the registrant concludes that formaldehyde formation is of no toxicological relevance for the registered substance. Moreover, actual test data on the substance of interest is available.*" You refer to acute toxicity tests, and studies according to OECD TG 414, 422 and 408 with the Substance and conclude that based on this information the Substance including its (bio)transformation products do not induce neurotoxicity.

According to ECHA Guidance[9], "*triggers are findings which challenge the existing toxicity database. This means that due to existing triggers it is not possible to conclude on the potential for adverse health effects for a substance, and to address the concern, further information may be needed or is needed, depending on the condition.*" It clarifies that "*a trigger is any factor present in the existing toxicological database, whether based on theoretical substance specific scientific considerations or from experimental or observational data that raises concerns that a substance may cause toxicity but information is not comprehensive enough to allow a conclusion to be drawn.*" As explained above, the Substance hydrolyses to formaldehyde, which is considered a neurotoxin. This existing knowledge raises a concern for the Substance to cause adverse effects on the developing brain/ nervous system. From the existing acute toxicity, OECD TG 414, 422 and 408 studies, it cannot be excluded that the Substance is not a developmental neurotoxicant because these studies do not include thorough investigations on developmental neurotoxicity comparable to those of the Cohorts 2A and 2B of the EOGRT study. For example, the acute toxicity and OECD TG 408 studies do not investigate developmental toxicity at all as it is a study on adult animals only; the OECD TG 414 does not investigate developmental parameters postpartum because caesarean section is performed before parturition; and the OECD TG 422 is limited in statistical power, lacks investigations for developmental neurotoxicity in F1 pups and the study was terminated on lactational day 5. In particular, none of these studies includes a 10-week premating exposure duration and investigates the F1 pups thoroughly for effects on the developing brain/ nervous system at weaning and adulthood. In your comments you also refer to exposure considerations based on the use of the Substance. As explained above, these cannot be considered for hazard identification, which aims at clarifying the intrinsic properties of the Substance.

To conclude, the existing concern cannot be clarified from the existing toxicological database and information on the hydrolysis product formaldehyde raises the concern that the Substance may cause developmental neurotoxicity. To address this concern, further information on developmental neurotoxicity is needed.

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

Cohort 3

The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity.

Existing information on the Substance and formaldehyde derived from available *in vivo* studies, non-animal approaches and epidemiological investigations show evidence of immunotoxicity as described here below.

For formaldehyde, a decrease in the proportion of T-cells was observed, indicating altered immunity. Long-term exposure to formaldehyde was associated with auto antibodies and immune activation. Formaldehyde may induce hypersensitivity which may account for a

[9] ECHA Guidance R.7a, Appendix R.7.6–5

mechanism for asthma and other health complaints.[7]

Formaldehyde is considered to be a substance structurally analogous to the Substance as explained under the section on Cohorts 2A and 2B above.

As supportive evidence, in the provided OECD TG 422 study using the Substance, higher white blood cell count in males and females at 1000 mg/kg bw/day was observed.

The higher white blood cell counts in both genders at 1000 mg/kg bw/day is of concern as it indicates a response of immune system. The animals should be pathogen free for toxicity testing and, thus, it is likely that the effects are caused by the administration of the Substance and not an infection.

You refer in your comments to the column 2 requirements for triggering the developmental immunotoxicity cohort: Cohort 3 can be requested "*if there is evidence of adverse effects on the immune system or specific mechanisms/modes of action of the substance with an association to (developmental) immunotoxicity (e.g. cholinesterase inhibition or relevant changes in thyroidal hormone levels associated to adverse effects), or existing information on effects caused by substances structurally analogous to the substance being studied, suggesting such effects or mechanisms/modes of action.*" You explain that the increased white blood cell count observed at 1000 mg/kg bw/day in the OECD TG 422 study with the Substance did not reach statistical significance in males and cannot be considered adverse. This finding was not observed in the OECD TG 408 study with the Substance up to a top dose of 600 mg/kg bw/day. Furthermore, you state that exposure to formaldehyde does not lead in increased white blood cells counts in repeat-dose toxicity studies. You also state that you are "*aware that formaldehyde has been linked to effects to the immune system via in vivo studies, non-animal approaches and epidemiological investigations when exposed to elevated doses or by prolonged exposure*" but a lack of reference would hamper an in-depth analysis.

You generally explain that immunotoxicity includes both immunosuppression as well as immunopotentiation and that neither the REACH registration dossier nor other assessment reports on formaldehyde address immunosuppression of formaldehyde. You also refer to a publication by Vargova et al. (1993), a published immunotoxicity study in rats that found that oral administration of formaldehyde for 28 days did not induce significant immunotoxic effects. You state that "*no data on developmental immunotoxicity are available for formaldehyde.*" Furthermore, you refer to the harmonised classification of formaldehyde as skin sensitiser category 1 and you compare this with a negative finding in an OECD TG 406 study with the Substance. You make reference to a report by the German Competent Authority questioning the relationship of IgE antibodies against formaldehyde and asthma or allergic respiratory diseases. You also refer to a study on human volunteers showing no inhalative sensitisation response to the Substance. You conclude that the toxicological profile of formaldehyde and the Substance are very different and you conclude "*that while the registered substance may have the potency to break down to formaldehyde, the toxicological profile of the registered substance does not indicate that formaldehyde is formed in concentrations relevant for the hazard evaluation"* and that *"the available studies and assessment reports do not provide any robust evidence substantiating a concern for potential immunotoxicity of the registered substance.*" You therefore disagree with the inclusion of the Cohort 3.

According to column 2 of Section 8.7.3, Annex X, the developmental immunotoxicity Cohort 3 can be triggered based on a particular concern justified "*by existing information on effects caused by substances structurally analogous to the substance being studied, suggesting such effects or mechanisms/modes of action.*" According to ECHA Guidance[10], "*triggers are findings*

[10] ECHA Guidance R.7a, Appendix R.7.6–5

which challenge the existing toxicity database. This means that due to existing triggers it is not possible to conclude on the potential for adverse health effects for a substance, and to address the concern, further information may be needed or is needed, depending on the condition." It clarifies that "*a trigger is any factor present in the existing toxicological database, whether based on theoretical substance specific scientific considerations or from experimental or observational data that raises concerns that a substance may cause toxicity but information is not comprehensive enough to allow a conclusion to be drawn."* As explained above, it is an inherent property of the Substance to hydrolyse to formaldehyde and exposure to formaldehyde is associated with immunotoxicological effects that are inherent to its high electrophilic reactivity. The existing knowledge raises a concern for the Substance to cause adverse effects on the developing immune system. The increased white blood cell count, which was observed in both genders at 1000 mg/kg bw/day in the OECD TG 422 study, supports the concern for the Substance. In this respect, the difference between the OECD TG 422 and 408 studies with respect to white blood cell count might be explained by the lower dosing in the OECD TG 408 study. Although white blood cell counts were not statistically significantly increased in males, the statistical significant increase in females and the trend to higher values constitute a concern, irrespectively of their adversity. The harmonised classification for skin sensitisation category 1 for formaldhyde is also used to support triggering as it shows that formaldehyde exerts adverse effects on the immunesystem based on its high electrophilic reactivity. The report by the German Competent Authority cannot clarify the concern as it does not address the potential of formaldehyde to cause developmental immunotoxicity. You also refer to Vargova et al. (1993). ECHA has no access to this article but from the abstract it seems that there is a concern for immunosuppression because "*oral administration of formaldehyde to rats resulted in dose-dependent reduction of antibody responses (IgG + IgM) at doses of 20, 40, and 80 mg/kg."* Furthermore, the lack of information on the immunosuppressive potential of formaldhyde and the Substance is not considered a valid argument to not request Cohort 3. To the contrary: The concern that the Substance may cause developmental immunotoxicity together with the lack of information preventing a conclusion to be drawn for developmental immunotoxicity meets the criteria of the trigger deifintion according to ECHA Guidance[10].

To conclude, the existing concern stemming from formaldehyde cannot be clarified from the existing toxicological database and information on the hydrolysis product formaldehyde raises the concern that the Substance may cause developmental immunotoxicity. To address this concern, further information on developmental immunotoxicity is needed.

Based on the substance specific considerations on formaldehyde and the Substance, ECHA concludes that the developmental immunotoxicity Cohort 3 needs to be conducted.

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 summaries[11].

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 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 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 dossiers[12].

[11] https://echa.europa.eu/practical-guides
[12] https://echa.europa.eu/manuals

Appendix C: Procedure

The Substance is listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2022.

The compliance check was initiated on 29 July 2019, as ECHA rectified and withdrew the EOGRTS section of the previous compliance check decision of 10 November 2017 on your registration dossier for the same substance on 27 May 2019, following the ECHA Board of Appeal decision in case A-001-2018.

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 29 July 2019.

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

ECHA took into account your comments and amended the request but did not amend the deadline.

Deadline

In your comments on the draft decision, you requested with reference to this compliance check decision and the testing proposal decision on the same Substance an extension of the deadline to provide the requested information from 30 to 41 months from the date of adoption of the decision.

You explain the timelines as follows:
- PNDT study: 12 months,
- EOGRT study: 18 months,
- Preparing the reports for each study: up to 4 months, and
- Preparing the dossier update: 3 months.

In your comments, you have not provided evidence for your claims that extension of the timeline is needed, *e.g.* in form of a written, case-specific statement by a test laboratory explaining why an extension of deadline is needed.

Therefore, ECHA invited you by letter of 31 May 2021 to substantiate your request by submission of documentary evidence from the selected test laboratory indicating the scheduling timelines for the studies in question of the laboratory facility in order to justify why an extension to the stated deadlines from 30 months to 41 months is required.

You provided a letter from a test laboratory relating to a proposal for the PNDT study in rabbits. From this letter, the timelines for conducting the preliminary and main studies is 10 months form start of experimental phase to draft report, although the experimental phase is calculated to be around 11 months. The timeline for conducting the EOGRT study is 14/15 months from start of experimental phase to draft report, although the experimental phase is calculated to be around 19 months. You add "*another 3 months for study commissioning and procurement of the animals per study, in total another 6 months, as the studies are to be conducted consecutively. The dossier update will take another 3 months.*" Furthermore, you have provided a letter

issued by a consultant relating to a quote to update the IUCLID dossier and Chemical Safety Report within 3 months.

You state that the studies "*are to be conducted consecutively*" but you state no reason for this. ECHA emphasises that in this case it is not necessary to finalise one study before initiating the other study. In particular, the PNDT study in rabbits and EOGRT study in rats could be run in parallel because these studies are conducted with different species and therefore have only very limited use to inform on each other. Furthermore, the registration dossier of the Substance already contains OECD TG 408, 422 and 414 studies in rats, which should be sufficient to inform on designing and conducting the EOGRT study in rats.

The set deadline, relevant for both this compliance check decision and the testing proposal decision on the same Substance, already includes time for administrative tasks and is considered sufficient for all the necessary tasks including preparatory work, reporting and dossier submission.

On this basis, ECHA has not modified the deadline to provide the information.

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 Guidance[13] 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 documents[15]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[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 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 their corresponding information requirements

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.