EUROPEAN CHEMICALS AGENCY

Helsinki, 11 May 2020

Addressees
Registrants of potassium_permanganate_joint listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
30 May 2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Potassium permanganate
EC number: 231-760-3
CAS number: 7722-64-7

Decision number: [Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/D)]

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***18 November 2022***.

A. Requirements applicable to all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method OECD TG 414) in a second species (rabbit), oral route with the Substance.

2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route specified as follows with the Substance:

   - At least two 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) with extension to mate the Cohort 1B animals to produce the F2 generation which shall be followed to weaning;
   - 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.

Conditions to comply with the requests

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier. To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annexes VII to X of REACH, if you have

registered a substance at above 1000 tpa.

Registrants are only required to share the costs of information that they must submit to fulfil the information requirements for their registration.

The Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. In this case, there is a harmonised classification - Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation). The timeline has been set to allow for sequential testing where relevant.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

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 for the requests to comply with Annex X of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier at a tonnage above 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to REACH.

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have provided the following PNDT study with the Substance:

- Pre-natal developmental oral toxicity study according to OECD TG 414 [redacted] 2009) in rats, GLP compliant.

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

In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

You have provided a pre-natal developmental toxicity study in one species (rat) only. You have not provided any information on pre-natal developmental toxicity in another species.

In your comments to the draft decision you stated that you have paid for the data sharing and that you should be in the joint submission, and therefore you do not need to perform the requested studies. You also indicated that you can provide documentary proof of the payment.

ECHA confirms that you are indeed a member in the joint submission "potassium_permanganate_joint". However, the lead registrant has opted out from the jointly submitted information for the endpoints addressed in this decision. As explained in the draft decision, the jointly submitted information does not fulfil the information requirements for these endpoints.

Due to the unclear situation of data sharing in the joint submission, ECHA exceptionally requested you to provide documentary proof that you have a permission to refer to the studies opted out by the lead registrant for the endpoints addressed in this decision. ECHA specifically requested that you provide a list of studies you have paid for, including the study name, endpoint to be covered, author, year, together with a letter of access from the data owner or its representative. ECHA indicated that general documentation not specifying your access to studies to cover the two endpoints addressed in this decision would not be sufficient.

You provided documentary proof of your payments to the lead registrant. However, you provided only general documentation which does not specify your access to the studies requested in the draft decision.

Therefore, and as explained above, the information provided does not fulfil the information requirements addressed in this decision.

Information on study design

The test in the first species was carried out by using a rodent species (rat). A PNDT study according to the test method OECD TG 414 must be performed in rabbit as the preferred non-rodent species.

The study shall be performed with oral[2] administration of the Substance.

Possibility for data sharing for studies involving vertebrate animals

The Lead registrant of the Joint submission has opted out from the jointly submitted information with an adaptation for this endpoint. In accordance with Title III of the REACH Regulation, you may consider sharing this information[3].

[2] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[3] https://echa.europa.eu/regulations/reach/registration/data-sharing

2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

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 One-Generation Reproduction Oral Toxicity Test in rats according to OECD TG 415 ([redacted] 2008) with the Substance.

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

The study you provided does not cover all relevant life stages required in OECD TG 443, as the extensive postnatal investigations of the fully exposed F1 generation up to the adulthood are not included. In addition, the criteria for extension of the Cohort 1B are met for the Substance and there is a particular concern for developmental neurotoxicity according to column 2 of Annex X, Section 8.7.3. and information for those properties are missing. Therefore the study provided is not in line with the requirements in OECD TG 443 as specified under REACH.

You commented the draft decision and submitted the same comment for this endpoint as for request A.1 above.

ECHA's response under Section A.1 above applies to this endpoint as well.

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 premating exposure period must be ten weeks[4] to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

A 2-week premating exposure duration for P0 animals is sufficient for your Substance, because the F1 animals of Cohort 1B are mated to produce the F2 generation and, thus, the premating exposure duration will be 10 weeks for these Cohort 1B animals.

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. Also considering the corrosive properties of the Substance, the tested concentrations should not induce death or severe suffering of the animals (including severe local effect), 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.

[4] ECHA Guidance R.7a, Section R.7.6.2.3.2.

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

Under Section 8.7.3, Column 1 of Annexes IX and X to REACH, Cohorts 1A and 1B belong to the basic study design and must be included.

Extension of Cohort 1B

If the Column 2 conditions of 8.7.3., Annex IX and X are met, Cohort 1B must be extended. The extension is inter alia required, if the use of the Substance is leading to significant exposure of consumers and professionals (column 2, first paragraph, lit. (a) of Section 8.7.3., Annex IX and X) and there are indications of one or more relevant modes of action related to endocrine disruption from available *in vivo* studies or non-animal approaches (column 2, first paragraph, lit. (b), third indent of Section 8.7.3., Annex IX and X).

The use of the Substance is leading to significant exposure of professionals because the Substance is used by professionals (PROCs 3, 5, 8a, 8b, 15) in agriculture, forestry and fishing; manufacture of food products; manufacture of textiles leather, fur; manufacture of wood and wood products; manufacture of plastics products; electricity, steam, gas water supply and sewage treatment.

In addition, there are indications of one or more modes of action related to endocrine disruption because changes in organs/parameters sensitive to endocrine activity are observed. More specifically '*various damage of spermatogenesis*' for which the study report considers it '*could be caused by alteration of testosterone synthesis or with alteration of cell receptors for testosterone*'.

Therefore, Cohort 1B must be extended.

The F2 generation shall be followed to weaning allowing assessment of nursing and lactation of the F1 parents and postnatal development of F2 offspring. Investigations for F2 pups must be similar to those requested for F1 pups in OECD TG 443 and described in OECD GD 151[5]. It is recommended to aim at 20 litters per dose group in order to have similar statistical power for investigations than in P0 generation.

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 the Substance itself derived from the available information (OECD TG 415, [redacted] 2008), showed oedematous appearance of brain and an increase in the weight of the brain in the high dose group. Vacuolisation of cell nuclei in cortex and hippocampus were observed at all dose levels which are triggers for Cohorts 2A and 2B.

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

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5 http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2013)10&doclanguage=en

Species and route selection

The study must be performed in rats with oral[6] administration.

Further expansion of the study design

No triggers for the inclusion of Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including 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 IX and 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 Guidance[7].

Possibility for data sharing for studies involving vertebrate animals

The Lead registrant of the Joint submission has opted out from the jointly submitted information with an adaptation for this endpoint. In accordance with Title III of the REACH Regulation, you may consider sharing this information[3].

[6] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[7] ECHA Guidance R.7a, Section R.7.6.

Appendix B: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The compliance check was initiated on 4 February 2019.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

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 C: Observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. Test guidelines, GLP requirements and reporting

   Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

   Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses shall be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

   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: 'How to report robust study summaries'[8].

4. Test material

   Selection of the test material(s)

   The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account 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.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values [and other parameters relevant for the property to be tested]. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

   Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[9].

[8] https://echa.europa.eu/practical-guides
[9] https://echa.europa.eu/manuals

5. List of references of the ECHA Guidance and other guidance/ reference documents[10]

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 in this decision.

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 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[11]

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.

OECD Guidance documents[12]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD 43.

[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix D: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[redacted]	[redacted]	[redacted]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.