EUROPEAN CHEMICALS AGENCY

Helsinki, 28 July 2020

Addressees
Registrants of JS_Tantalum_231-135-5 listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
13 June 2017

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Tantalum
EC number: 231-135-5
CAS number: 7440-25-7

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

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***2 November 2022***.

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

1. Water solubility (Annex VII, Section 7.7.; test method: OECD series on Testing and Assessment Number 29 - Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous media) with the Substance

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method EU C.3./OECD TG 201) with the Substance

3. The long-term toxicity testing on aquatic invertebrates also requested at C.3. below (triggered by Annex VII, Section 9.1.1., column 2)

B. Requirements applicable to all the Registrants subject to Annex VIII of REACH

1. The long-term toxicity testing on fish also requested at C.4. below (triggered by Annex VIII, Section 9.1.3., column 2)

2. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.; Test method: OECD TG 209) with the Substance

C. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.; test method OECD TG 413) in rats with the Substance

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method EU C.20./OECD TG 211) with the Substance

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210) with the Substance

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 Annex VII of REACH, if you have registered a substance at 1-10 tonnes per annum (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- you have to comply with the requirements of Annexes VII and VIII of REACH, if you have registered a substance at 10-100 tpa;
- you have to comply with the requirements of Annexes VII, VIII and IX of REACH, if you have registered a substance at 100-1000 tpa.

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

When a study is required under several Annexes of REACH, the reasons are provided in the corresponding appendices of this decision. The registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants in accordance with Article 53 of REACH.

The Appendix on general considerations addresses issues relevant for several requests while the Appendices A to C 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. 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 on general considerations

(i) Assessment of the Grouping of substances and read-across approach, in light of the requirements of Annex XI, Section 1.5.

You have provided adaptations in your dossier for the following endpoints:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.);
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.);
- Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.).

Annex XI, Section 1.5. specifies three conditions which must be fulfilled whenever a read-across approach is used:

(i) 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;
(ii) 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;
(iii) adequate and reliable documentation of the applied method must be provided.

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

You read across to your Substance from the structurally similar substance, Tantalum pentachloride, EC No. 231-755-6 (CAS No. 7721-01-9; i.e. the source substance). You have provided a read-across justification document in IUCLID Section 13.

You have provided the following reasoning for the prediction of aquatic toxicity:

- "[The] *source and target substances have similar toxicological properties due to the release of tantalum ions, which are considered to be the relevant moiety with respect to intrinsic hazards of tantalum metal*";
- "*In natural surface waters tantalum is most likely to be present as poorly soluble tantalic acid ($Ta_2O5 \times nH_2O$) or as TaF_5*";
- "*For ecotoxicological and environmental fate endpoints, it is the relative mobility, and the resulting bioavailability in various environmental compartments that determines the potential toxicity to environmental organisms*";
- "*In absence of data for metallic Ta, a conservative approach to hazard evaluation is the assumption that Ta shows the same systemic hazards as other tantalum compounds with similar or higher bioavailability*";
- "*A surrogate for estimating the relative bioavailability is the water solubility of the source substances and the target substance, respectively*";
- "*As the water solubility of Ta is significantly lower compared to $TaCl_5$*, [...] [it] *can be used in a read-across approach to predict the properties of Ta*".

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common compounds under environmentally realistic conditions. The properties of your Substance are predicted based on a worst-case

[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)
[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

approach (i.e. using a source substance having higher bioavailability).

ECHA notes the following issue with regards to prediction of aquatic toxicity:

> Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[5]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).
>
> Your read-across hypothesis states that $TaCl_5$ can be used in a worst-case approach to predict the aquatic toxicity of tantalum as it has a higher bioavailability. You use data on the water solubility of tantalum and $TaCl_5$ in order to demonstrate the higher bioavailability of $TaCl_5$. You provide toxicity studies conducted with $TaCl_5$ to predict the ecotoxicological properties of the Substance for the endpoints listed above.
>
> However, as specified under section A.1. below, the information provided on water solubility for the Substance does not fulfil the information requirement. Furthermore you did not provide a robust study summary for a water solubility study on $TaCl_5$. Hence ECHA cannot verify that the water solubility estimates for both the Substance and the source substance are reliable. Regarding the aquatic toxicity data on the source substance, as explained below in sections A.2., A.3. and B.1., the studies provided on growth inhibition in aquatic plants, short-term toxicity to aquatic invertebrates and short-term toxicity to fish, respectively, do not fulfil the respective information requirements. Therefore the supporting information currently in your dossier does not adequately support that the properties of the Substance can be reliably predicted from the data of the selected source substance.

As explained above and further below in sections A.2., A.3. and B.1., you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. Therefore, your adaptations fail to comply with the general rules of adaptation as set out in Annex XI, Section 1.5 and they are rejected.

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.

Appendix A: Reasons for the requests to comply with Annex VII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 1 to 10 tonnes or more per year must contain, as a minimum, the information specified in Annex VII to REACH.

1. Water solubility (Annex VII, Section 7.7.)

Water solubility is a standard information requirement in Annex VII to REACH.

In your dossier, you have provided a key study ([redacted] 2012) conducted according to EU test method A.6 and OECD TG 105.

We have assessed this information and identified the following issue:

> EU test method A.6 and OECD TG 105 describe two methods (the column elution method and the flask method) for conducting a water solubility study. The test method must be selected based on a water solubility estimate obtained in a preliminary study. For substances with preliminary water solubility below 10 mg/L the column elution method must be used.
>
> You specify that, although the water solubility, determined during the preliminary test, was below 10 mg/L, the flask method was employed since the Substance is inorganic and is not soluble in any volatile solvent to allow coating of the glass support media utilised in the column elution method. You report a water solubility < 21.3 µg/L at 20.0 ± 0.5°C based on the flask method.
>
> Based on the information you provided the column elution method is not applicable. In addition, the reported result falls outside of the applicability domain of the flask method. Therefore, none of the methods described EU test method A.6 and OECD TG 105 are applicable to the Substance.

Therefore, the information requirement is not fulfiled.

In your comments on the draft decision you agreed to conduct the requested study. You also indicate that you intend to "*provide additional information on bioavailability of ditantalum pentoxide in different artificial body fluids*".

The Substance is a sparingly soluble inorganic metal compound, and therefore as specified in ECHA Guidance R.7a, Section R.7.1.7.3., water solubility must be determined according to the OECD GD 29 on Transformation/Dissolution of metals and metal compounds in aqueous media. OECD GD 29 specifies that the test must be conducted using a test material having the smallest representative particle size. It also states that the specific surface area of the test material must be determined. We note that you report under Section 4.5. of your technical dossier a granulometry according to ISO 13320:2009 which shows that the substance you registered may have a D50 as low as 27.93 µm.

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH.

In your dossier, you have provided a key study ([redacted] 2015) conducted according to OECD TG 201 with the analogue substance Tantalum pentachloride (EC No. 231-755-6).

As explained in section i) of the Appendix on general considerations your adaptation is rejected.

In addition, we identified the following issue:

> Tests on substances must be conducted in accordance with the OECD test guidelines or another internationally recognised international test method (Article 13(3) of REACH). For this endpoint the preferred test method is the OECD TG 201 which recommends to use either of the following two mineral medium to perform the test: the AAP medium (US. EPA) and the OECD TG 201 medium. The guidance acknowledges that modification of the growth media may be necessary for certain purposes, e.g. when testing metals. However, it specifies that use of a modified medium must be described in details and justified.
>
> In your dossier you specify that the Holm-Hansen growth medium was used to conduct the test. You report that the test was conducted at a nominal loading ranging from 125 mg/L to 2000 mg/L. You further indicate that due to a strong pH reduction, especially at high loading rate, the pH of the test medium was adjusted using NaOH (leading to a NaCl concentration of 2.92 g/L at the highest nominal test concentration of 2000 mg/L). You did not describe any other modification of the test medium composition.
>
> Accordingly you did not use one of the recommended test media described in OECD TG 201. The Holm-Hansen medium contains a chelating agent (EDTA) in significant excess of iron concentrations (34.2 µmol for EDTA *vs.* 24.5 µmol for Iron citrate). Furthermore, following pH adjustment, the test medium contained high concentrations of sodium, especially at high loading rate. Both the presence of a chelating agent in excess of iron concentrations and the high ionic strength of the test medium following pH adjustment may have reduced the biodisponibility of the Substance. Therefore, this modified medium is not adequate to study the intrinsic properties of the Substance.
>
> In your comments on the draft decision, you state that "*the use of Holm-Hansen medium is incorrectly presented in the study summary. Review of the original study report revealed that Holm-Hansen medium was used in the algal stock cultures, whereas OECD medium was employed in the growth inhibition test*". ECHA understands that the reference to the used of the Holm-Hansen medium to conduct the test is a clerical error. However, we note that you have not provided any justification that the high concentrations of sodium in the test medium did not impact the test results.

Therefore, the information requirement is not fulfiled.

In your comments on the draft decision, you explain that you consider that conducting a "*new study on the registered substance premature*". You first intend to compare the water solubilities of source and target substance when the information requested under A.1 will be available. ECHA agrees that generating reliable information on the water solubility of the source substance and the Substance should provide relevant information to strengthen the read-across justification.

Study design

The OECD TG 201 recommends to use the OECD medium to conduct testing on heavy metals. In this test medium, the molar ratio of EDTA to iron only slightly exceed unity. This prevents iron precipitation and, at the same time, chelation of heavy metal ions is minimised.

Furthermore while selecting the test material you must take into account the impact of parameters relevant for the property to be tested. For the aquatic toxicity studies, you must justify that the selected test material properties (e.g. particle size) constitute a reasonable worst case to cover all the registrants of the Substance. Therefore the selected test material should correspond to the most soluble form of the substance taking into account the range of properties of the substance as registered under REACH.

3. The long-term toxicity testing on aquatic invertebrates also requested at C.3. below (triggered by Annex VII, Section 9.1.1., column 2)

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement in Annex VII to REACH. However, pursuant to Annex VII, section 9.1.1., Column 2, for poorly soluble substances the long-term aquatic toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5.) must be considered.

In your dossier, you have provided a key study ([redacted] 2015) conducted according to OECD TG 202 with the analogue substance Tantalum pentachloride (EC No. 231-755-6).

Based on the information provided in your dossier we have identified the following issues:

A. You have adapted the information requirement according to Annex XI, Section 1.5. However, as explained in section i) of the Appendix on general considerations your adaptation is rejected.

B. For poorly water soluble substances (e.g. water solubility below 1 mg/L or below the detection limit of the analytical method of the test substance) long-term toxicity study on aquatic invertebrates must be considered instead of an acute test as specified in Annex VII, Section 9.1.1., Column2).

   In your dossier, you did not report a water solubility study for the source substance Tantalum pentachloride. However, your report the results of the analytical determination of exposure concentrations in the short-term toxicity study on aquatic invertebrates by [redacted] (2015). At the highest nominal loading (i.e. 3000 mg/L), measured dissolved concentrations after chemical digestion were well below 1 mg/L.

   The information in your dossier supports that upon dissolution Tantalum pentachloride is transformed into a poorly water soluble tantalum species. Poorly water soluble substances require longer time to reach steady-state conditions and the long-term test is required. Therefore the selected study does not provide adequate information on aquatic toxicity for the source substance.

In your comments on the draft decision, you explain that you consider that conducting a "*new study on the registered substance premature*". You first intend to compare the water solubilities of source and target substance when the information requested under A.1 will be available. ECHA agrees that generating reliable information on the water solubility of the source substance and the Substance should provide relevant information to strengthen the read-across justification. However, as already explained above the information available on the source substance for this endpoint is not adequate. Even at extreme loading rates (i.e. up to 3000 mg/L), measured dissolved concentrations after chemical digestion were well below 1 mg/L. Therefore the source substance shall be regarded as poorly water soluble.

In addition, in your comments you acknowledge that "*poorly water-soluble substances require longer time to reach steady-state conditions*" but that you request not "*to confuse equilibration time during solubilisation and exposure periods during toxicity tests*". However,

you do not provide any supporting evidence to substantiate that the duration of short-term toxicity test is sufficient to reach steady-state conditions despite the low solubility of the Substance.

Therefore the information requirement is not fulfilled.

As explained under request A.1., the information you provided on water solubility does not fulfil the information requirement. While there are remaining uncertainties regarding the relative water solubility of the Substance, we consider that the information provided is sufficient to conclude that it is poorly water soluble (i.e. water solubility below 1 mg/L).

Consequently, a long-term aquatic toxicity study on aquatic invertebrates triggered by Annex VII, section 9.1.1., Column 2 must be performed. This test is also required under request C.3. in accordance with Annex IX, Section 9.1.5.

Appendix B: Reasons for the requests to comply with Annex VIII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to REACH.

1. The long-term toxicity testing on fish also requested at C.4. below (triggered by Annex VIII, Section 9.1.3., column 2)

"Short-term toxicity testing on fish" is a standard information requirement in Annex VIII to REACH. However, pursuant to Annex VIII, section 9.1.3., column 2, for poorly soluble substances the long-term aquatic toxicity study on fish (Annex IX, Section 9.1.6.) must be considered.

In your dossier, you have provided a key study ([redacted] 2015) conducted according to OECD TG 202 with the analogue substance Tantalum pentachloride (EC No. 231-755-6).

Based on the information provided in your dossier we have identified the following issues:

A. You have adapted the information requirement according to Annex XI, Section 1.5. However, as explained in section i) of the Appendix on general considerations your adaptation is rejected.

B. For poorly water soluble substances (e.g. water solubility below 1 mg/L or below the detection limit of the analytical method of the test substance) long-term toxicity study on fish must be considered instead of an acute test as specified in Annex VIII, Section 9.1.3., Column2).

   In your dossier, you did not report a water solubility study for the source substance Tantalum pentachloride. However, your report the results of the analytical determination of exposure concentrations in the short-term toxicity study on fish by [redacted] (2015). At the highest nominal loading (i.e. 100 mg/L), the measured dissolved concentrations measured after chemical digestion were well below 1 mg/L.

   The information in your dossier supports that upon dissolution Tantalum pentachloride is transformed into a poorly water soluble tantalum species. Poorly water soluble substances require longer time to reach steady-state conditions and the long-term test is required. Therefore the selected study does not provide adequate information on aquatic toxicity for the source substance.

In your comments on the draft decision, you explain that you consider that conducting a "*new study on the registered substance premature*". You first intend to the water solubilities of source and target substance when the information requested under A.1 will be available. ECHA agrees that generating reliable information on the water solubility of the source substance and the Substance should provide relevant information to strengthen the read-across justification. However, as already explained above the information available on the source substance for this endpoint is not adequate. Even at high loading rates (i.e. up to 100 mg/L), measured dissolved concentrations after chemical digestion were well below 1 mg/L. Therefore the source substance shall be regarded as poorly water soluble.

Futhermore, you acknowledge that "*poorly water-soluble substances require longer time to reach steady-state conditions*" but that you request not "*to confuse equilibration time during solubilisation and exposure periods during toxicity tests*". However, you do not provide any

supporting evidence to substantiate that the duration of short-term toxicity test is sufficient to reach steady-state conditions despite the low solubility of the Substance.

As explained under request A.1., the information you provided on water solubility does not fulfil the information requirement. While there are remaining uncertainties regarding the relative water solubility of the Substance, we consider that the information provided is sufficient to conclude that it is poorly water soluble (i.e. water solubility below 1 mg/L).

Therefore the information requirement is not fulfilled.

Consequently, a long-term aquatic toxicity study on fish triggered by Annex VIII, section 9.1.3., column 2 must be performed. This test is also required under request C.4. in accordance with Annex IX, Section 9.1.6.

2. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.).

Activated sludge respiration inhibition testing is a standard information requirement in Annex VIII to REACH.

You have provided a key study performed according to OECD TG 209 (2015) with the analogue substance Tantalum pentachloride (EC No. 231-755-6).

For the reasons explained in section i) of the Appendix on General considerations regarding read-across, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you consider that conducting a "*new study on the registered substance premature*". You first intend to the water solubilities of source and target substance when the information requested under A.1 will be available. ECHA agrees that generating reliable information on the water solubility of the source substance and the Substance should provide relevant information to strengthen the read-across justification.

Study design

While selecting the test material you must take into account the impact of parameters relevant for the property to be tested. For the aquatic toxicity studies, you must justify that the selected test material properties (e.g. particle size) constitute a reasonable worst case to cover all the registrants of the Substance. Therefore the selected test material should correspond to the most soluble form of the substance taking into account the range of properties of the substance as registered under REACH.

Appendix C: Reasons for the requests to comply with Annex IX of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII to IX to REACH.

1. Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.)

A Sub-chronic toxicity study (90-day) is a standard information requirement in Annex IX to REACH.

You have provided a key study by [redacted] (2016) according to OECD TG 422 (oral route) with the analogue substance Tantalum pentachloride (EC No. 231-755-6).

You have also provided an adaptation according to Column 2 of Annex IX, Section 8.6.2. in your dossier. In support of your adaptation, you consider that the substance is inert and state the following:

- *"the 0 valence state indicates a low potential for biochemical interaction"*;
- *"Tantalum metal forms an oxide layer when exposed to air at room temperature"*.

You consider that that low bioavailability following exposure to relevant routes is expected as:

- *"The substance is considered inert and highly insoluble"* and *"Tantalum is only attacked by concentrated mineral acids such as HF, fused alkalis and fuming sulphuric acid; i.e.* [...] *under extremely oxidising conditions that are not compatible with administration to animals"*;
- *"Due to its insolubility it can be assumed that* [it] *will not be absorbed into the gastrointestinal tract* [...] *at a significant level to cause an adverse effect"* and in a study according to OECD TG 422 on the more soluble tantalum pentachloride *"no toxicity was observed at the highest dose of 1000 mg/kg bw/day"*;
- *"The substance is potentially inhalable as it is a powder. However,* [...] *it was tested in an acute inhalation toxicity study according to OECD 403 up to the limit dose of 5.18 mg/L without showing any adverse effects. Furthermore, supporting toxicokinetic studies in dogs show a good pulmonary clearance without any signs of absorption or toxicity"*.

Finally, you consider that relevant supporting information are available to show that no harmful effect are expected following prolonged exposure to Tantalum. You indicate that:

- "Supporting data to investigate the (sub)-chronic toxicity of tantalum metal is available from two studies implanting tantalum subcutaneously as inert control for uranium", which showed according to you no harmnful effects;
- "no adverse effects have been reported in any other human health related endpoint, even though tantalum is used as contrast agent for laryngotracheograms or bronchographies".

You conclude that *"the standard risk management measures applicable to inhalation of poorly soluble particles (PSP) are considered sufficient for risk assessment. Therefore, conducting a (sub)-chronic toxicity study is not considered to be justified"*.

Based on the information provided in your dossier we have identified the following issues:

A. To be considered compliant and enable concluding whether the Substance has

dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 408.

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) you have submitted does not have an exposure duration of 90 days as required in OECD TG 408, because the exposure duration of the screening test is approximately 54 days (for females) and 28 days (for males). Furthermore the organ weight and histopathological investigations in OECD TG 422 are only conducted using 5 animals per sex per group and not 10 per sex per group as in OECD TG 408. Therefore the study by [redacted] (2016) does not fulfil the information requirement.

B. Annex IX, Section 8.6.2., Column 2 specifies that a sub-chronic toxicty study (90 days) does not need to be conducted if:
   - the substance is unreactive, insoluble and not inhalable, and
   - there is no evidence of absorption, and
   - there is no evidence in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure.

   On this attempt to adapt the information requirement, we note the following issues:

   a) You have not provided an appropriate justification that the substance is unreactive. Tantalum is subject to oxidation when exposed to aerobic conditions. Furthermore Tantalum oxides may be used as solid acid catalysts due to their surface acidic properties. Therefore the physico-chemical properties of the Subtance does not support that it has no inherent chemical reactivity. Consequently, the condition set out in point 1 above is not fulfilled.

      In your comments on the draft decision, you state that "*Tantalum is a non-noble metal and is always coated with a very thin (2-3 nm thick) oxide layer on its surface, which prevents the core metal itself from further oxidation*" and that "*Tantalum pentoxide is commonly described in standard textbook of inorganic chemistry (e.g. Hollemann/Wiberg, Ed 103, 2017, p1839) as being insoluble, stable, and chemically inert at ambient temperatures*". Finally you consider that "*a possible use in chemical catalysis, as mentioned in the draft decision, is probably restricted to mixed metal catalysts or high temperature applications*".

      ECHA agrees that the use of ditantalum pentoxide as a solid acid catalyst is likely limited to conditions that are not physiologically relevant. While the information you have provided in your comments is supportive that the Substance has low reactivity, we note that your dossier currently does not include an appropriate justification that the Substance is unreactive.

   b) As specified in ECHA Guidance R.7c, particles with aerodynamic diameters below 100 µm have the potential to be inhaled. Particles with aerodynamic diameters below 50 µm may reach the thoracic region and those below 15 µm the alveolar region of the respiratory tract. In section 4.5. of your technical dossier you provide a granulometry study conducted according to ISO 13320:2009. You report that the tested sample had a D50 of 27.93 µm and a D90 of 41.11 µm. Therefore you did not demonstrate that the substance is not inhalable. Consequently, the condition set out in point 1 above is not fulfilled.

In your comments on the draft decision, you consider that "*the underlying argument specified in Annex IX, Section 8.6.2, column 2,* [for the selection of the appropriate route] *aims at possible toxicity of inhalable particles that would elicit substance-specific toxic effects in the lung*". You state that "*for insoluble particles like tantalum, the effects in the lung will largely be driven by physical effects rather than substance-specific toxicity*" while you consider that "*substance-specific toxic effects in the lung* [...] *are not expected*".

ECHA disagrees with your comments. As explained in ECHA Guidance R.7a, Section R.7.5.6.3.4, the inhalation route is relevant when a concern for local effects in the respiratory tract might be assumed, for instance for insoluble inhalable dusts that accumulate in the lungs.

c) As specified in ECHA Guidance R.7a, the justification for the absence of absorption must be based on evidence that no absorption occurs. You did not provide experimental evidence showing that the Substance is not absorbed via any relevant route of exposure.

In Section 7.1.1., you report an experimental study (rated with a reliability score of 3) by [redacted] (1972) where "*the absorption and retention to ^{51}Cr, ^{95}Nb, ^{109}Cd and ^{182}Ta after oral administration were investigated in suckling and adult rats*". You state that "*The highest concentration of 182Ta in sucklings was found in the ileum, kidney and bone*". You also refer to [redacted] (1978, reliability score of 4) and state that "*tantalum excretion depends upon dose; small quantities such as radioactive tracer amounts, which are maximally absorbed, are excreted in the urine*". From [redacted] (2001, reliability score of 2) you report that "*Fleshman et al. showed that orally administered 182Ta as tantalate is rapidly excreted by rats through the GI tract. After 7 days, once again more than 97 % is accounted for in the faeces and less than 1 % in the urine*". Finally, referring to a study by [redacted] 1973 on long-term effects of tantalum dust exposure in dogs, you report that "*long-term retention of inhaled powdered tantalum in the alveoli occurred*" and that "*lymphogenic elimination of tantalum particles from the alveoli was clearly marked*".

While, insufficient information is reported to fully assess the reliability of these findings, the data reported in your dossier suggest that at least some absorption following oral administration may occur as tantalum is detected in the urine. Furthermore, it also suggests that following inhalation exposure, systemic exposure may occur through transfer to the lymphatic system. As explained in ECHA Guidance R.7c , Section R.7.12.2.1., while dusts depositing in the tracheo-bronchial region would mainly be cleared from the lungs by the mucocilliary mechanism and swallowed, a small amount may be taken up by phagocytosis and transported to the blood via the lymphatic system. Furthermore, poorly water-soluble dusts depositing in the alveolar region would mainly be engulfed by alveolar macrophages, which may carry particles into the pulmonary interstitium and lymphoid tissues. Based on the above, you did not demonstrate that the Substance is not absorbed via any relevant route of exposure. Consequently, the condition set out in point 2 above is not fulfilled.

In your comments on the draft decision, you state that "*10 entries for basic toxicokinetics, but the majority of the sources were rated Klimisch 3 or 4. Two handbook entries were rated Klimisch 2, but both entries refer to studies with intravenous or intramuscular injection* [which are not] *relevant exposure routes*".

You further specify that "*will provide additional experimental data on the solubility of tantalum in artificial body fluids*".

However, low solubility in artificial fluids does not demonstrate that no absorption occurs. As explained in ECHA Guidance R.7a, Section R.7.5.4.3.4, there has to be evidence of the lack of absorption. Such evidence may include toxicokinetics data to prove that no systemic absorption occurs.

d) With regard to human exposure, you have not provided an exposure assessment in accordance with Section 5 of Annex I in your Chemical Safety Report. Therefore you did not demonstrate that human exposure is limited.

In your comments on the draft decision, you explain that you intend to "*refine the exposure assessment to show there is limited human exposure*". You consider that "*Exposure to hard metal particles in an occupational setting will also be minimised by national and EU-wide regulations and their associated dust limit values*".

Therefore, based on the above and taking into account the information provided as part of your comments on the draft decision, the cumulative conditions described above are not met and your adaptation according to Annex IX, Section 8.6.2., Column 2 is rejected and the information requirement is not fulfilled.

Study design

Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the inhalation route is the most appropriate route of administration to investigate repeated dose toxicity[6]. The sub-chronic toxicity study must be performed according to the OECD TG 413, in rats and with administration of the Substance by inhalation because:

- the Substance is present as fine particles with a significant proportion of particles of inhalable size;
- the use pattern of the Substance includes industrial spraying (PROC 7) and therefore human exposure to the Substance by the inhalation route is likely.

In your comments on the draft decision, you disagree that the "*inhalation route is the most appropriate route of administration to investigate repeated dose toxicity*". You state that "*even though there is a debate about relevant particle size distributions, "fine particles" normally refer to PM10 and PM2.5 and not to particles with a D50 of approx. 30 µm*" and that you "*will rephrase the Chemical Safety Report to indicate that risk management measures are in place to prevent exposure of humans via inhalation*". Based on the above, you conclude that "*the oral route would be the most appropriate route of administration*".

As already explained above the Substance is in the form of a powder of inhalable size. Therefore the inhalation route is considered relevant unless you can demonstrate and document that no significant inhalation exposure occurs throughout the life cycle of the substance.

While selecting the test material you must take into account the impact of parameters relevant for the property to be tested. For the Substance, this includes the particle size. For the requested repeated dose toxicity study (inhalation route), you must justify that the test material has a particle size distribution small enough to cover all the registrants of the Substance.

[6]ECHA Guidance R.7a, Section R.7.5.6.3.4.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

A Pre-natal developmental toxicity study in one species is a standard information requirement in Annex IX to REACH.

In your dossier, you have provided:

1. a key study ([redacted] 2016) conducted according to OECD TG 422 with the analogue substance Tantalum pentachloride (EC No. 231-755-6).
2. a supporting study by Benson (1998) for a pre-natal developmental toxicity study in Sprague-Dawley rats not conducted according to any recommended guideline. "[The] *study was conducted to investigate the transfer of depleted uranium from mother to foetus to gain an understanding of the degree of foetal exposure and developmental effects from maternally implanted uranium. Tantalum was used in the study as a chemically inert control.*"

Furthermore you have provided an adaptation according to Column 2 of Annex IX, Section 8.7. in your dossier. You provide the same lines of evidence as those described under request C.1. to justify that conducting further testing on pre-natal developmental toxicity is not justified.

Based on the information provided in your dossier and in your comments on the draft decision we have identified the following issues:

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

   First, the study by [redacted] (2016) conducted according to OECD TG 422 does not provide equivalent information to a pre-natal developmental toxicity study as some of the key parameters required in OECD TG 414 are not investigated. This includes histopathology of the thyroid gland / thyroid hormone measurements / gravid uterus weight in dams; detailed skeletal and soft tissue alterations (variations and malformations); measurement of anogenital distance in live rodent foetuses. In addition, the number of test animals is lower leading to lower statistical power. Concerning the study by Benson (1998), it is a non guideline study investigating pre-natal developmental toxicity following implantation of dams with tantalum pellets. Furthermore, the exposure route is not relevant to fulfil the information requirement for this endpoint. Therefore, these studies do not fulfil the information requirement.

B. Annex IX, Section 8.7., Column 2 specifies that reproductive toxicity studies listed under this section do not need to be conducted if the following cumulative conditions are met:
   1. the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), and
   2. it can be proven from toxicokinetics data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance in urine, bile or exhaled air), and
   3. there is no or no significant exposure.

   On this attempt to adapt the information requirement, we note the following issues:

a) As specified in ECHA Guidance R.7a, the justification for the absence of absorption must be based on evidence that no absorption occurs. As already explained under request C.1., the information in your dossier does not demonstrate that the Substance is not absorbed via any relevant route of exposure.

In your comments on the draft decision, you explained that, in line with the comments provided on request C.1 above, you intend to provide "*additional information on the solubility of tantalum in water as well as in artificial body fluids*" to support that "*no systemic absorption via relevant routes of exposure*".

However, as already explained, low solubility in artificial fluids does not demonstrate that no absorption occurs. As explained in ECHA Guidance R.7a, Section R.7.5.4.3.4, there has to be evidence of the lack of absorption. Such evidence may include toxicokinetics data to prove that no systemic absorption occurs.

b) With regard to human exposure, you have not provided an exposure assessment in accordance with Section 5 of Annex I in your Chemical Safety Report. Therefore you did not demonstrate that there is no or no significant .

In your comments on the draft decision, you indicated that you will provide further information related to the human exposure.

Therefore, based on the above and taking into account the information provided as part of your comments on the draft decision, the cumulative conditions described above are not met and your adaptation according to Annex IX, Section 8.7., Column 2 is rejected.

Based on the above the information requirement is not fulfilled.

Study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[7] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

and

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Long-term toxicity testing on aquatic invertebrates and on fish are standard information requirements in Annex IX to REACH.

You have adapted these information requirements based on Annex IX, Section 9.1, Column 2 and you have provided the following justification: "*In Annex IX of Regulation (EC) No 1907/2006, it is laid down that chronic toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic species. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a*

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

PBT or vPvB. The hazard assessment reveals neither a need to classify the substance as dangerous to the environment, nor that it is a PBT or vPvB substance, nor that there are any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare, a long-term toxicity study in fish is not provided".

Based on the information provided in your dossier we have identified the following issue:

In order to adapt the information requirement for long-term toxicity testing to aquatic invertebrates and to fish based on Annex IX, Section 9.1, Column 2, the Chemical Safety Assessment needs to demonstrate that risks towards the aquatic compartment arising from the use of the Substance are controlled (as per Annex I, section 0.1). The Chemical Safety Assessment needs to assess and document that risks arising from the Substance are controlled and demonstrate that there is no need to conduct further testing (Annex I, Section 0.1; Annex IX, Section 9.1, Column 2).

In particular, you need to take into account of the following elements in your justification:

- all relevant hazard information from your registration dossier,
- the outcome of the exposure assessment in relation to the uses of the Substance,
- the outcome of the PBT/vPvB assessment including information on relevant constituents present in concentration at or above 0.1% (w/w).

For poorly water soluble substances (e.g. water solubility below 1 mg/L or below the detection limit of the analytical method of the test substance) long-term toxicity study on aquatic invertebrates and on fish) must be considered instead of an acute test (Column 2 of Annex VII, Section 9.1.1. and Annex VIII, Section 9.1.3.).

However, you have not provided any justification that the risks arising from the Substance are controlled, taking account all of the elements above.

As explained under request A.1., while there are remaining uncertainties regarding the relative water solubility of the various forms of the Substance, ECHA considers that information provided is sufficient to conclude that the Substance is poorly water soluble.

Poorly water soluble substances require longer time to reach steady-state conditions. Hence, the short-term tests may not give a true measure of toxicity for this type of substances and the long-term tests are required. Hence, in the absence of long-term testing on aquatic organisms your dossier does not include any relevant hazard information. Furthermore, you did not conduct an exposure assessment in relation to the uses of the Substance.

In your comments on the draft decision, you state that "*the chemical safety assessment has concluded that the risk to aquatic organisms is controlled, based on the finding that no hazard has been identified*". You also refer to "*a T/D test on tantalum will be performed, and furthermore a robust summary of the water solubility of the source substance TaCl5 will be provided in the next dossier update*".

ECHA agrees that generating reliable information on the water solubility of the source substance and the Substance should provide relevant information to strengthen the read-across justification. However, as already explained under request A.2, A.3 and B.1, your adaptation according to Annex XI, Section 1.5. is rejected. Therefore your

dossier does not contains any reliable information to support that risks towards the aquatic compartment arising from the use of the Substance are controlled.

Therefore, your adaptation according to Annex IX, Section 9.1., Column 2 is rejected.

Based on the above, the information requirements on long-term toxicity testing on aquatic invertebrates and on fish set out in Annex IX Section 9.1.5 and 9.1.6.1, respectively, are not fulfilled.

Study design

While selecting the test material you must take into account the impact of parameters relevant for the property to be tested. For the Substance, this includes the particle size. For the aquatic toxicity studies, you must justify that the selected test material properties (e.g. particle size) constitute a reasonable worst case to cover all the registrants of the Substance. Therefore the selected test material should correspond to the most soluble form of the substance taking into account the range of properties of the substance as registered under REACH.

Appendix D: 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 22 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 E: 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 registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. 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, in this case the particle size distribution. 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.

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

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

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 GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

[9] https://echa.europa.eu/manuals
[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 F: 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.