EUROPEAN CHEMICALS AGENCY

Helsinki, 11 December 2018

Addressee: [redacted]

Decision number: CCH-D-2114453316-51-01/F
Substance name: Tin sulphide
EC number: 215-248-7
CAS number: 1314-95-0
Registration number: [redacted]
Submission number: [redacted]
Submission date: 07/09/2017
Registered tonnage band: Over 1000

**DECISION ON A COMPLIANCE CHECK**

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered 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 registered substance;**

3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rat or rabbit), oral route with the registered substance;**

4. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance 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) with extension to mate the Cohort 1B animals to produce the F2 generation;**

5. **Classification and labelling (Annex VI, Section 4.): apply classification and labelling on the registered substance for aquatic hazards *or* provide a justification for not classifiying;**

6. **Identification of PNEC (Annex I, Section 3.3.1.) derive relevant PNECs - using the study giving rise to the highest concern according to Annex I, Section 3.1.5 *or* provide a detailed justification for not using the study giving rise to the highest concern;**

**7. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for the environment: should the substance be classified as per point 5, generate an exposure assessment for identified uses and perform a risk characterisation accordingly.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **20 June 2022**. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

**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] by **Claudio Carlon**, Head of Unit, Evaluation **E2**

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

## Appendix 1: Reasons

### 1. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

ECHA notes that the registration dossier contains negative results for both these information requirements. Therefore, adequate information on *in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing two supporting study records for OECD Guideline 476 (In Vitro Mammalian Cell Gene Mutation Test) at the hprt locus, with the analogue substance tin disulphide (EC no 215-252-9).

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus, physicochemical and degradation properties influence the human health and environmental

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[3]- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

You consider to achieve compliance with the REACH information requirements for the registered substance tin sulphide using data of structurally similar substances tin disulphide (EC no 215-252-9) (hereafter the 'source substance').

You have provided a read-across documentation as a separate attachment in the dossier.

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:

**Similar chemical structure.**
All substances of this group are inorganic tin compounds. This category includes tin (II) and tin (IV) substances.

**Similar physico-chemical properties.**
The water solubility for tin sulfide and tin disulfide (0.6 and 0.67 µg/L, respectively) was almost identical. The other physicochemical parameters like melting point support that both substances are very similar and hence read-across can be made. Calculation of water solubility in physiological conditions of the stomach and intestines (pH 2 & 5) indicated that the solubility of both tin sulfide and tin disulfide remains small enough to assume that the dissociation of SnS or SnS2 will be negligible in the gastro-intestinal tract.

**Similar toxicological properties.**
You assume that toxicity is mediated by the tin ion, and so it is possible to read-across to various inorganic tin salts. "*For mammalian toxicity, anchor points for acute oral, inhalation & dermal toxicity, skin & eye irritation, sensitisation, and in vitro bacterial/mammalian mutagenicity and chromosomal aberration demonstrated a fully comparable toxicological profile for tins sulfide and tin disulfide. There was no hazard for these endpoints.*" You also argue that the sulphide ion is not relevant, and that the mode of action is interference with uptake and metabolism of other metals. As an integral part of this prediction, you propose that the source and registered substance have similar properties for the above-mentioned information requirement. ECHA considers that this information is your read-across hypothesis.

[3] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

As an integral part of this prediction, you propose that the source and registered substance have similar properties for the above-mentioned information requirement. ECHA considers that this information is your read-across hypothesis.

*ECHA's evaluation and conclusion*

Your proposed adaptation argument is that the similarity in chemical structure and in some of the physico-chemical,ecotoxicological and toxicological properties between the source and registered substance is a sufficient basis for predicting the properties of the registered substance for other endpoints. Structural similarity is a prerequisite for applying the grouping and read-across approach. However similarity in chemical structure and similarity of some of the physico-chemical, ecotoxicological and toxicological properties does not necessarily lead to predictable or similar human health and environmental properties in other endpoints. Your justification based on structural similarity, similar physico-chemical, ecotoxicological and toxicological properties has not established why the prediction is reliable for the human health and environmental endpoints for which the read across is claimed.

Additionally, there is evidence that tin (II) (corresponding to the registerd substance subject to this decision) and tin (IV) (corresponding to the source substance) behave differently in biological systems. In the context of ecotoxicology data you stated: "*Since tin (IV) has been shown to be slightly less toxic to aquatic organisms when compared to tin (II) (WHO, 2005), read across from tin (II) to tin(IV) substances is conservative. However, the differences were not high, read across from tin (IV) to tin(II) is considered possible as well.*" Moreover, from the Statement on the Toxicokinetics of Tin(1I) Sulfide (attached in the dossier), in relation to biotransformation it is suggested that the tin (II) and tin (IV) may have different toxicokinetic behaviour and toxicities: "*Few data on biotransformation are available. The difference in the relative affinity of the kidneys and liver for tin(II) and tin(IV) indicates a valence stability of the administered tin ([redacted] 1974). The difference observed between tin(II) and tin(IV) chloride in their effects on the immune response in C57BL/6J mice also suggests that these two oxidation states are not readily interconverted in vivo ([redacted] 1981). Together, these data suggest that tin cations are not rapidly oxidized or reduced during absorption and systemic transportation in mammals.*"
This evidence of different properties for tin (II) and tin (IV) contradicts your read-across hypothesis, and would need to be addressed in order to explain how it is possible to predict the properties of the registered substance.

Additionally, ECHA has taken into account all of your arguments together. ECHA firstly notes that you have not provided a reasoning as to why these arguments add to one another to provide sufficient basis for read-across. Secondly, the defects of each individual argument are not mitigated by the other arguments you have provided, and so ECHA considers that the arguments when taken all together do not provide a reliable basis for predicting the properties of the registered substance.

Therefore, ECHA considers that this grouping and read-across approach does not provide a reliable basis whereby the human health effects of the registered substance may be predicted from data for reference substance(s) within the group. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation.

As described above, further elements are needed to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities

and differences between the source and registered substances. This could be achieved (if it is possible) by a well-founded hypothesis of (bio)transformation to a common compound(s), or that the registered and source substance(s) have the same type of effect(s), together with sufficient supporting information to allow a prediction of human health properties.

For the avoidance of doubt, ECHA considers that, when examining systemic toxicity for relevant human health endpoints, read-across between inorganic tin salts of the same valence state is plausible, when allowance is made for the solubility of the ionic species, and where the counter-ion does not impact significantly the toxicity. However, for any specific case, it would be necessary to examine the justification for read-across and any substance-specific considerations to determine if it is acceptable.

Therefore, your adaptation of the information requirement is rejected.

In your comments to the draft decision you have agreed to perform this request.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490).

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a "reproduction/ developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study, such as examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

You also have sought to adapt this information requirement according to Annex IX, Section 8.7.2., column 2, third indent. You provided the following justification for the adaptation:

- *"The studies need not be conducted because the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic 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 and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure."*
- *"Referring to the results of OECD 421 study, there is no evidence that the test item is causing any developmental as well as teratogenetical toxicity. After detailed checking literature situation, even there is no evidence found in epidemiological studies. "*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.7.2., column 2 third indent because there is evidence of systemic exposure and there is significant human exposure through professional and consumer uses. Furthermore, as explained above the provided OECD 421 study does not provide the information required by Annex IX, Section 8.7.2.

Therefore, your adaptation of the information requirement is rejected.

In your comments to the draft decision you have proposed two alternative approaches to fulfil the information requirements for this endpoint:

- *read-across supported by testing* , or
- Alternative approach: testing only

In the first approach ("*read-across supported by testing*") you proposed to read-across data, "*as extensive information is available on other inorganic tin compounds*" and to conduct testing only if additional experimental data are required to further support the read-across approach. Furthermore, you intend to apply an *in vitro* 'bio-elution' or 'dissolution/transformation' testing approach in physiological conditions, for inorganic tin compounds to further support the read-across approach and to convert NOAEL values for the registered substance based on the data available on the selected source substances.

You propose to strengthen the read-across hypothesis by providing a broader discussion on the impact of the oxidation state on the toxicity of tin substances. In your opinion the available data suggests a greater absorption of the tin (II) ion which may explain the observed increased toxicity of the tin (II) ion compared to tin (IV). The study of [redacted] 1974 also concluded that "*it is inappropriate to discuss the absorption, distribution and excretion of any inorganic element without regard to the effects of valence and anion complement.*" As stated in the draft decision, the evidence of different properties for tin (II) and tin (IV) contradicts your read-across hypothesis. While you provide data suggesting higher absorption of tin(II) compounds, you also need to take into account differences in the toxicological properties of tin ions with different valence states and of their counter ions.

You also bring forward a transformation dissolution approach aiming to correct for differences in the bio-availability or bio-accessibility of inorganic tin compounds employing bioelution tests.

ECHA notes that bioelution measures the degree to which a substance/metal ion is released into artificial biological fluids, i.e., substance's bioaccessibility. However, bioaccesibility cannot always be used as a predictor of bioavailability and toxicity in a hazard assessment. Bioaccessibility data should be considered as only one aspect of a read across approach and cannot fill the data gaps. Furthermore, ECHA considers that *in vivo*, other biological processes may come into play (e.g. food composition, passive diffusion, change in pH).

Bioelution results should therefore not be used in isolation to predict toxicity ([redacted] 2018). In addition, ECHA considers that validation of bioelution data by *in vivo* toxicokinetic and/or toxicity data for each substance and route of exposure would be needed in such an approach.

In conclusion, with regard to the first alternative, namely "read-across supported by testing", ECHA considers that providing information on the bioaccessibility may or may not support the read-across approach. Moreover, ECHA notes that the comment provided is speculative and the bioaccessibility information is yet to be provided and hence cannot be taken into account. Furthermore, ECHA emphasises that providing bio-accessiblitity data will not resolve the other deficiencies of the current read-across approach such as the fact that the teratogenicity study with tin difluoride is available only as secondary literature and the quality of the study cannot be assessed. Also the two other teratogenicity study reports mentioned as available data in your comments, are yet to be provided and therefore, cannot be taken into account. Consequently, this alternative cannot be accepted at present.

The second alternative proposes testing but only if "*it should turn out that read across is not appropriate to fulfil the toxicological data gaps*". As described above, the read-across justification is not acceptable at present. You may consider, under your own responsibility, whether it is possible to address the deficiencies identified above and to substantiate a read-across adaptation in accordance with Section 1.5 of Annex XI of the REACH Regulation.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pre-natal developmental toxicity studies (test method OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or

more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier does not contain information on a pre-natal developmental toxicity study with the registered substance.

In the technical dossier you have provided a study record for a a "reproduction/ developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study, such as examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

You also have sought to adapt this information requirement according to Annex IX, Section 8.7.2., column 2, third indent. You provided the following justification for the adaptation:

- *"The studies need not be conducted because the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic 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 and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure."*
- *"Referring to the results of OECD 421 study, there is no evidence that the test item is causing any developmental as well as teratogenetical toxicity. After detailed checking literature situation, even there is no evidence found in epidemiological studies. "*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.7.2., column 2 third indent because there is evidence of systemic exposure and there is significant human exposure including professional and consumer uses. Furthermore, as explained above the provided OECD 421 study does not provide the information required by Annex IX, Section 8.7.2..

Therefore, your adaptation of the information requirement is rejected.

In your comments on the draft decision you have proposed an approach with two alternatives ("Read-across approach, supported by testing" and an "Alternative approach: testing only") to fulfil the information requirements for this endpoint. As already described above under section 2. ECHA cannot support the read-across as it is proposed in your registration dossier.
Regarding the second alternative, you proposed that "*The OECD 414 study in second species would only start if there are no findings in the first species, other classification would be considered.*" However, ECHA's Chapter R.7a: Endpoint specific guidance Version 6.0 –July 2017 states the following: "*At REACH Annex X level, a prenatal developmental toxicity study [...] conducted on a second species is a standard information requirement in addition to a prenatal developmental toxicity study in a first species that is required at REACH Annex IX level.*" and that "*The prenatal developmental toxicity study in a second species can be omitted, if, taking into account the outcome of the first test and all other relevant available data, an adaptation pursuant to REACH Annex X, Section 8.7, Column 2 or pursuant REACH*
*Annex XI can be justified.*" For example, performance of a study in a second species may be justified if effects were observed in the study with the first species that cause further serious concern but are not sufficient to meet classification criteria to Category 1B reproductive toxicant.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the tes t method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a second species (rabbit or rat) by the oral route.

*Notes for your consideration*

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species with other available information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

*a) The information provided*

In the technical dossier you have provided a study record for a "reproduction/developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex X, Section 8.7.3. because it does not cover key elements, such as exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study. More specifically, the main missing key elements are: 10 weeks pre-mating exposure duration, at least 20 pregnant females per group, and an extensive postnatal evaluation of the F1 generation. Therefore, your adaptation of the information requirement is rejected.

Furthermore,you have sought to adapt this information requirement according to Annex IX, Section 8.7.3, column 1. You provided the following justification for the adaptation:

"*In accordance with column 1 of REACH regulation EC (No) 1907/2006 Annex IX, a two-generation reproductive toxicity study (section, 8.7.3) is required if the 28- or 90-day study indicates adverse effects on reproductive organs or tissues. In a screening study with tin sulfide according to OECD 421 no adverse effects on reproductive organs or tissues were observed. In a reproduction/developmental toxicity screening study an effect of tin sulfide on the microscopical structure of the testes was considered to be irrelevant since the spermiogenesis was not effected. Moreover, there were no histopathological findings in testes in a 90-day study according to OECD guideline 408 on tin sulfide. Due to these results a two-generation study is not required.*"

However, ECHA notes that your adaptation refers to the specific rules for adaptation of Annex IX while you have a registration dossier above 1000 tonnes per year for which the provisisons of Annex X applies.

Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

*b) The specifications for the study design*

*Premating exposure duration and dose-level setting*

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required if there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

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 with the other cohorts being tested at the same dose levels.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a conducted range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.
*Extension of Cohort 1B*

If the column 2 conditions of 8.7.3., Annex X are met, Cohort 1B must be extended, which means that the F2 generation is produced by mating the Cohort 1B animals. This extension provides information also on the sexual function and fertility of the F1 animals. The extension is inter alia required, if "*the use of the registered substance is leading to significant exposure of consumers and professionals (column 2, first paragraph, lit. (a) of section 8.7.3., Annex X) and/or if there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure (column 2, first paragraph, lit. (b), second indent of section 8.7.3., Annex X)*".

The use of the registered substance in the joint submission is leading to significant exposure of consumers and professionals because the registered substance is used by professionals as friction agent, lubricant /grease, fuel additive (PROCs 8a, 8b, 11, 13 and 17) and consumers as lubricant.

Furthermore, there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure. Although the absorption of tin sulfide is considered to be low, the literature describes that tin may accumulate in kidney, liver, lung and especially in bone. In rats that received 20 mg Sn/kg/day of stannous fluoride ($^{113}$ Sn[II]F2) or stannic fluoride ($^{113}$ Sn[IV]F4), for a period of 28 days, levels of tin in kidneys and liver were approximately the same as after a single oral dose ([redacted] 1974); however, levels in bone were higher after multiple dosing, suggesting slower elimination kinetics of tin from bone, relative to kidney and liver ([redacted] 2005).

Therefore, ECHA concludes that Cohort 1B must be extended to include mating of the animals and production of the F2 generation because the uses of the registered substance is leading to significant exposure of professionals and consumers and there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure.

In your comments on the draft decision you disagreed with the extension of Cohort 1B. You argued that the bioaccessibility of tin sulphide, as for elemental tin, is expected to be much lower than for stannous fluoride (ECHA notes that in the dossier the only available toxicokinetic information is on stannous fluoride and no data were provided for insoluble tin). You propose, instead of testing the substance in an EOGRTS, to demonstrate the difference in bioaccessibility by means of comparative bio-elution between tin sulfide and other inorganic tin compounds including elemental tin and tin salts. Based on the low water solubility of tin sulfide, you are of the opinion that it is more related to elemental tin and not to soluble tin salts like tin fluoride. You believe that the lower bioaccessibility is expected to be related to a much lower bioavailability and lower toxicity. Therefore, you propose to do a

transformation dissolution approach first, to demonstrate a bioaccessibility trend between inorganic tin compounds and its relation to kinetics and toxicity. You presume that if it can be demonstrated that tin sulphide is more closely related to elemental tin, the systemic exposure and bone deposition of the registered substance is expected to be negligible, therefore the trigger of reaching a steady state in the test animals only after an extended exposure is not considered to be applicable.

ECHA expects that the proposed *in-vitro* comparative bio-elution testing will not be sufficient to inform on whether the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure and neither will it inform on the bioaccumulative potential of the registered substance. In addition, the comment provided is speculative and the bioaccessibility information is yet to be provided and hence cannot be taken into account.

Therefore, ECHA maintains that there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure and that the trigger for the extension of cohort 1B is met.

In your comments on the draft decision you have proposed an approach with two alternatives ("Read-across approach, supported by testing" and an "Alternative approach: testing only") to fulfil the information requirements for this endpoint. As already described above under section 2. ECHA cannot support the read-across as it is proposed in the registration dossier. Furthermore, ECHA emphasises that providing bio-accessiblitity data will not resolve the other deficiencies of the current read-across approach such as the fact that the multigeneration study with stannous chloride is available only as secondary literature and the quality of the study cannot be assessed.
Regarding the second alternative, you proposed that "*The OECD 443 study will only be started if there are no reproductive issues in the OECD 414 study*". ECHA notes that at REACH Annex X level, an OECD 443 study is a standard information requirement and reproductive effects seen in a prenatal developmental toxicity study is not a valid waiver for an extended one-generation study.

*Species and route selection*

According to the test method OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method OECD TG 443), in rats, oral route, according to the following study-design specifications:

- 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) with extension to mate the Cohort 1B animals to produce the F2 generation;

While the specifications for the study design are given above, you shall also submit with the new endpoint study record a scientific justification on each of the following aspects: 1) length of the premating exposure duration and dose level selection, 2) reasons for why or why not Cohort 1B was extended, 3) termination time for F2 generation, and 4) reasons for why or why not Cohorts 2A/2B and/or Cohort 3 were included.

*Notes for your consideration*

No triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the available information, together with the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented.

**5. Classification and labelling (Annex VI, Section 4.): Apply classification and labelling on the registered substance for aquatic toxicity *or* provide a justification for not classifying**

Pursuant to Article 10(a)(iv) of the REACH Regulation your technical dossier shall contain information on classification and labelling of the substance as specified in Annex VI, Section 4 of the REACH Regulation in conjunction with Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP Regulation).

Annex VI, section 4.1. clarifies that the hazard classification of the substance shall result from the application of Title I and II of the CLP Regulation. In addition, for each entry, the scientifically justified reasons why no classification is given for a hazard class or differentiation of a hazard class should be provided. According to Article 5(1) of Title I of the CLP Regulation, a substance shall be classified on the basis of available information.

Furthermore, the technical dossier must include the resulting hazard label for the substance in line with Title III of the CLP Regulation (Annex VI, section 4.2 of the REACH Regulation) and the specific concentration limits and M-factors, where applicable, resulting from the application of Article 10 of the CLP Regulation (Annex VI, Section 4.3 of the REACH Regulation).

Your technical dossier includes an aquatic chronic toxicity study on aquatic invertebrates indicating a NOEC (or equivalent) value equal to or lower than 0.1 mg/l which is considered reliable by you (Klimisch score 1 or 2) and the substance is considered as not rapidly degradable by you. However, you concluded that the observed effects are not relevant as they were observed at concentrations above the water solubility determined by an OECD 105 test.

Based on the results of the submitted chronic toxicity study: OECD 211 (GLP) with the registered substance (Analytical purity: [redacted]% (ICP), content of Sn: [redacted]% ± 1% rel. (ICP), content of S: [redacted]% ± 0.2% abs.; no information on impurities), ECHA disagrees with your statement that the observed effects are not relevant. ECHA considers this study to be acceptable and a clear impact of the test substance on the reproduction of *Daphnia magna* was observed (up to 35.7% reduction).
You have disregarded these results as (i) no clear dose-response was observed and (ii) the effect observed were found at concentrations above the water solubility determined in an OECD 105 test.

First, ECHA notes that the analytical method reported has low sensitivity (LOQ = 5µ/L). Commonly used methods for metallic ion quantification usually reach LOQ in the ng/L range. Additionally, ECHA is of the opinion that, considering the reported analytical monitoring data, a dose-response was observed. Your data suggest that there was no significant difference in the exposure levels arising from application of the 25 and 50% v/v solutions (6 and 7.8 µg/L, respectively), which is supported by a similar reduction in *Daphnia* reproduction (i.e., 12.5 and 10.5% reduction, respectively). At the highest concentration measured (i.e. 11.3 µg/L) a clearly significant decrease in *Daphnia* reproduction was observed (35.7%) indicating that there is a dose response. Furthermore, ECHA disagrees with the argument that the effects were observed at concentrations above the water solubility. The water solubility was determined based on OECD 105 and the solubility of the test substance may differ in pure water and in the Elendt M7 medium. Accordingly, ECHA notes that you have not provided any evidence to suggest that the effects observed were at concentrations above the water solubility in the test media. Finally, you reported measured concentrations following filtration at 0.45 µm and ECHA considers that these measured concentrations reflect the solubilized tin sulfide fraction.

In conclusion, ECHA considers that the study is sufficiently reliable (despite some methodological issues related to test solution preparation and the poor sensitivity of the analytical method).

The technical dossier does not contain scientifically justified reasons relating to why the results of the available study have not been used to classify the substance.

In your comments on the draft decision you agreed that the analytical method had low sensitivity. Youconsider that it led to higher variability in the data as measured concentrations were above the LOQ (i.e. 5 µg/L). However, you agree that this argument does not invalidate the study.

You further specify that you consider the observed dose-response as dubious as it would require a (very) steep dose-response-relationship which is untypical for the tin ion and the counter ion. Finally, you maintain the view that available data indicates that the effects reported were seen at concentrations above the water solubility and that the measured concentrations were higher than the reported water solubility because:

- filters with a larger pore size were used to prepare the test solutions in the invertebrate test (i.e. 0.45 µm) compared to the water solubility study (i.e. 0.1 µm);
- nitrocellulose filters were used in the invertebrate test, while nucleopore filters were used in the water solubility study. You specify that nitrocellulose filter have irregular pore size and that it may not retain all particles with a size greater than 0.45 µm;

As *Daphnia magna* can filter particles in the sub-micrometer range, you consider that daphnids were exposed to undissolved particles which might be responsible for the reduction of reproduction.

You also provided a justification (Annex 3 of the Registrant's comments) on why you consider that the results of the water solubility study provides relevant information to conduct the environmental risk assessment.

Finally, you further supported your hypothesis by referring to a daphnids reproduction study on $SnCl_2*2H_2O$ ([redacted], 1972) in which a 16% decrease in reproduction was observed only at concentrations of about 350 µg $Sn^{2+}$/L. You also refer to acute studies in *Daphnia* ([redacted] 2005) and in *Gammarus pseudolimnaeus* (US-EPA, 1976) in which short-term EC50 were determined at 123 and 21-59 µg $H_2S$/L, respectively. Additionally you specified that, in the US-EPA study, the lowest long-term NOEC was found in fish and was determined to be 1 µg $H_2S$/L. Based on the above argumentation, you claim that the observed effect in the 100 % test solution from the chronic daphnia test was not caused by dissolved tin sulfide. This assessment applies also for other aquatic organisms.

Your hypothesis that the effects seen in the *Daphnia* reproduction study are due to undissolved material is speculative and not substantiated ([redacted], 1972). You have not taken into account the fact that, if undissolved material was present in the test solutions, the density of particles was likely very low (considering the maximum reported concentration of 11.3 µg $SnS_2$/L).
With regard to your comments on the water solubility results ECHA considers that the relevance of water solubility data generated using the OECD TG 105 is low for this type of substance. ECHA reminds you that, as explained in ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a, Section R.7.1.7. (Version 6.0, July 2017), the OECD Test Guidance on transformation/dissolution of metals and sparingly soluble metal compounds (OECD TG 29, 2001) is the preferred method to determine the rate and extent to which metals and sparingly soluble metal compounds can produce soluble bioavailable ionic and other metal-bearing species in aqueous media under a set of standard laboratory conditions representative of those generally occurring in the environment. The outcomes of the transformation/dissolution tests should be used for the identification of any aquatic environmental hazards.

On the results from the US-EPA study, which you use to support that no toxicity of sulfide to aquatic invertebrates is to be expected in the range of concentrations determined in the long-term toxicity test to *Daphnia*, ECHA notes that the effect values reported are for a short-term test (i.e. EC50) which is of little relevance for a poorly soluble substance. ECHA considers that substances that are poorly soluble in water, such as the test substance, require a longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for such substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. ECHA also notes that US-EPA (1976) reports a NOEC (reproduction/mean weight) for *Gammarus pseudolimaeus* of c.a. 2 µg $H_2S$/L which is below the measured concentration of the test substance in the test medium.

Based on the above, your comments on the draft decision do not address the concerns raised by ECHA. Thus, ECHA considers that the study is sufficiently reliable (despite some methodological issues related to test solution preparation and the poor sensitivity of the

analytical method) and the technical dossier does not contain scientifically justified reasons relating to why the results of the available study have not been used to classify the substance.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to classify and label the registered substance taking into account the information above. Altenatively, you are required to provide scientifically justified reasons why no such classification is applied. You are reminded that also for differentiation of a hazard class, scientifically justified reasons need to be provided.

ECHA notes that in reviewing whether you have complied with Sections 4.1. and 4.2. of Annex VI to the REACH Regulation with regard to classification and labelling for aquatic toxicity, ECHA can only base its assessment on data on aquatic toxicity available in the registration dossier. Any other data on aquatic toxicity of the registered substance that you did not submit in your registration dossier but that may need to be considered for classification purposes cannot be taken into consideration by ECHA. If there is any other data available on aquatic toxicity of the substance, you are required to include this information in the registration dossier in line with the second introductory paragraph of Annexes VI to X and step 1 of Annex VI to the REACH Regulation.

**6. Identification of PNEC (Annex I, Sections 3.3.1.)**

Annex I, Section 3.3.1. of the REACH Regulation requires to establish a PNEC for each environmental sphere based on the available information and to use an appropriate assessment factor to the effect values.

In particular, Article 14(3)(c) and Annex I, Section 3. of the REACH Regulation requires to establish a Predicted No-Effect Concentration (PNEC) for each environmental sphere based on the available information and to use an appropriate assessment factor to the effect values. Annex I, Section 3.1.5. of the REACH Regulation requires that the study or studies giving rise to the highest concern shall normally be used to derive the PNECs.

The ECHA *Guidance on information requirements and chemical safety assessment,* Chapter R.10 (May 2008), provides further details and specifically provides default factors which should be applied to derive PNECs.

You have not established any PNECs for any environmental sphere. Instead, you used the following justification: "*The substance is not soluble in water. Aquatic toxicity could not be measured within the performed tests. Therefore a PNEC could not be derived.*"

ECHA considers that based on available information and as explained under request 5, aquatic toxicity was observed. Therefore, you need to identify relevant PNECs.

In your comments on the draft decision you stated that "*Provided that the human health endpoints will not result in classification and labelling, the derivation of PNECs will not be needed. If either classification should be needed for either human health endpoints or environmental endpoints, the registrant will derive the PNECs.*"
As already explained in section 5, ECHA considers the chronic toxicity study on aquatic invertebrates study to be acceptable and that a clear impact of the test substance on the reproduction of *Daphnia magna* was observed (up to 35.7% reduction). In your comments on the draft decision, you provided further arguments why you consider this study should

not be used as a basis for environmental classification of the substance. Nevertheless, ECHA considers that your arguments do not establish that the study is not relevant for environmental hazard characterisation to set an aquatic PNEC, for the following reasons:

- The argumentation made on the relevance of the water solubility data generated using the OECD TG 105 is speculative and not substantiated. ECHA reminds that, as explained in ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a, Section R.7.1.7. (Version 6.0, July 2017), the OECD Test Guidance on transformation/dissolution of metals and sparingly soluble metal compounds (OECD TG 29, 2001) is the preferred method to determine the rate and extent to which metals and sparingly soluble metal compounds can produce soluble bioavailable ionic and other metal-bearing species in aqueous media under a set of standard laboratory conditions representative of those generally occurring in the environment. The outcomes of the transformation/dissolution tests should be used for the identification of any aquatic environmental hazards;
- You refer to the studies by US-EPA (1976) and [redacted] (2005) to support that no toxicity of sulfide to aquatic invertebrates is to be expected in the range of concentrations determined in the long-term toxicity test to *Daphnia*. ECHA notes that the effect values reported refer to a short-term test (i.e. EC50). ECHA also notes that US-EPA (1976) reports a NOEC (reproduction/mean weight) for *Gammarus pseudolimaeus* of c.a. 2 µg $H_2S$/L which would prove the opposite.

Based on the above, your comments on the draft decision do not fully address the concerns raised by ECHA. Consequently ECHA maintains that the study indicates that relevant effects have been observed and consequently, under Annex I, section 3.3 of REACH, an aquatic PNEC must be derived.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to derive relevant PNECs - using the study giving rise to the highest concern according to Annex I, Section 3.1.5 *or* provide a detailed justification for not using the study giving rise to the highest concern;

## 7. Exposure assessment and risk characterisation for the environment (Annex I, Sections 5. and 6.)

In accordance with Articles 10(b) and 14(1) of the REACH Regulation, the registration must contain a chemical safety report (CSR) which documents the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I to the REACH Regulation.

The CSA shall cover 1) human health hazard assessment, 2) human health hazard assessment of physicochemical properties, 3) environmental hazard assessment and 4) PBT and vPvB assessment.

Pursuant to Article 14(4) and Annex I, Section 0.6.3. of the REACH Regulation, if as a result from these steps, the substance meets the criteria for any hazard classes or categories set out in Annex I to the CLP Regulation, or is assessed to be a PBT or vPvB, then the CSA shall also include the additional steps: an exposure assessment, including generation of exposure scenario(s) and exposure estimation, and a risk characterisation. The additional steps of the CSA shall be carried out in accordance with Sections 5 (for the exposure assessment) and 6 (for the risk characterisation) of Annex I of the REACH Regulation.

ECHA notes that your CSR does not contain any exposure assessment nor risk characterisation for any environmental compartment. However, as ECHA outlined in Section 5 of this Appendix, based on current available information in the technical dossier, the registered substance may need to be classified for aquatic hazards, unless you provide scientifically justified reasons based on factual evidence on why no such classification is necessary.

If you cannot provide such justification and you conclude that the substance needs to be subjected to classification, your CSA shall include an exposure assessment and a risk characterisation as required by Article 14(4) and Annex I, Section 0.6.3. of the REACH Regulation.

Furthermore, according to Annex I, Section 5.0., the objective of the exposure assessment is to make quantitative or qualitative estimates of the dose/concentration of the substance to which the environment is or may be exposed. The assessment shall consider all stages of the life-cycle of the substance and shall cover any exposures that may relate to the hazards identified in Sections 1 to 4 of chapter 0.6 of Annex I.

As further outlined in ECHA Guidance on information requirements and chemical assessment, Part B, chapter B.8.1 Scope of Exposure Assessment (version 2.1, December 2011), such identified hazards necessitating exposure assessment include both "*hazards for which there are classification criteria and there is information to establish that the substance meets the criteria*" and "*hazards for which there are classification criteria and there is information on these properties of the substance showing that it does have these properties, but the severity of the effects is lower than the criteria for classification and so the substance is not classified*".

In your comments to the draft decision you have provided a justification for not classifying.

As explained above, ECHA considers the aquatic chronic toxicity study on aquatic invertebrates study to be acceptable for environmental hazard characterisation to set an aquatic PNEC. Therefore an exposure assessment and risk characterisation for the environment is required.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to generate an exposure assessment and a risk characterisation for all identified hazards for all identified uses in the dossier.

**Deadline to submit the requested information in this decision**

In the draft decision communicated to you the time indicated to provide the requested information was 30 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 42 months. You sought to justify this request by the fact that testing will have to be done step-wise in order to use the results from one study to another. Hence, you consider that a 30-month time is not sufficient to work out this justification/studies appropriately. You have submitted documentary evidence from the test laboratory indicating the scheduling timelines for the studies in order to justify why an extension to the stated overall deadline from 30 months to 42 months is required. Therefore, ECHA has granted the request and set the deadline to 42 months.

## Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 17 January 2018.

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.

ECHA took into account your comments. ECHA did not amend the requests but did amend the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

## Appendix 3: Further information, observations and technical guidance

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

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 your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.