ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114428714-48-01/F
Substance name: N-[3-(trimethoxysilyl)propyl]butylamine
EC number: 250-437-8
CAS number: 31024-56-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 28.05.2014
Registered tonnage band: 100-1000T

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined your testing proposal(s) and decided as follows.

While your originally proposed tests for

> Sub-chronic toxicity study (90-day), oral route in rats (OECD TG 408) using the analogue substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6), and
>
> Pre-natal developmental toxicity study (EU B.31./OECD TG 414) oral route in rats using the analogue substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6)

are rejected, you are requested to perform:

1. **Sub-chronic toxicity study (90-day), oral route in rats (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) using the registered substance, and**

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rats or rabbits), oral route using the registered substance.**

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 of the REACH Regulation. In order 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 an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **27 July 2020**. You shall also 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. 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, shall 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 Ofelia Bercaru, Head of Unit, Evaluation E3

[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

The decision of ECHA is based on the examination of the testing proposals submitted by you for the registered substance N-[3-(trimethoxysilyl)propyl]butylamine (CAS No 31024-56-3, EC No 250-437-8 (hereafter referred to as target substance).

In relation to the testing proposals subject to the present decision, you propose a testing strategy intending to fulfil the standard information requirements for a

- Sub-chronic toxicity (90-day) (Annex IX, Section 8.6.2.).
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.).

In your testing strategy you propose to test the analogue substance N-(3-(trimethoxysilyl)-propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6), hereafter referred to as source substance. The results from the structural analogue(s) will then be used to adapt the standard information requirements by using read-across and grouping approach following Annex XI, Section 1.5. of the REACH Regulation. To the extent that all human health related proposed testing relies upon an identical read-across justification, ECHA has considered first the scientific validity of the proposed read-across and grouping approach (preliminary considerations; Section 0, below), before assessing the testing proposed (Sections 1 and 2 below).

0. Grouping of substances and read-across approach

a. Legal Background on ECHA's assessment of the grouping of substances and read-across hypothesis

The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. To this end, it is necessary to consider whether programmes of testing proposed by you are appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting wherever possible the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping of substances and read-across), "*provided that the conditions set out in Annex XI are met*".

The first Recital and the first Article of the REACH Regulation establish the "*promotion of alternative methods for assessment of hazards of substances*" as an objective pursued by the Regulation. In accordance with that objective, ECHA considers whether a prediction of the relevant properties of the substance subject to the present decision by using the results of the proposed tests is plausible based on the information currently available.

b. Description of the proposed grouping and read-across approach

You have provided the following arguments to justify the read-across approach:

"The similarity of aminofunctional alkoxysilanes analogue group members is justified on basis of representative molecular structure, physico-chemical properties, toxicological profiles and supported by various QSAR methods. There is no convincing evidence that any one of these chemicals might lie out of the overall profile of this analogue group.

The alkoxysilane moiety of the alkyllamine and ethylendiamines undergoes hydrolysis, … In view of the rapid hydrolysis following oral dosing, it is therefore considered appropriate to read-across from one supporting substance (structural analogue or surrogate), which also produces a similar hydrolysis product with similar toxicokinetic properties to address the potential for systemic toxicity after oral exposure.

The analogue group of aminofunctional alkoxysilanes is based on similarities in physico-chemical and toxicological properties".

and

"The physico-chemical data of N-(3-(trimethoxysilyl) propyl) ethylenediamine (CAS No. 1760-24-3) exhibit an adequate average within aminofunctional alkoxysilanes. Furthermore, N-(3-(trimethoxysilyl) propyl) ethylenediamine (CAS No. 1760-24-3) has all relevant structural features or chemical functional groups serving as an appropriate analogue substance. This is supported by the fact that based on the toxicological properties the readacross from the supporting substance N-(3-(trimethoxysilyl) propyl) ethylenediamine (CAS No. 1760-24-3) does not underestimate possible hazards but rather can be seen as a conservative estimate".

c. Information submitted to support the grouping and read-across approach

You have provided the following documents as separate attachments in IUCLID, Section 13, relevant to the testing proposed:

1. [redacted]. The document is summarising the available physico-chemical and toxicological data relevant of the read-across approach used for the substance subject of the current decision.

2. [redacted]. The document is an overview of the grouping and read-across methods of Reconsile REACH submissions. The document describes the general principles applied but does not provide any substance-specific information. According to the report, "*each CSR needs to describe clearly whether Category, Analogue or QSAR methods have been applied, and which endpoints they are applied to, and the IUCLID entries must be consistent with this*"... Based on this document, ECHA understands that you intend to apply analogue approach as a basis for data gap filling which are further justified in each registration dossier and CSR.

3. [redacted] The document is an overview of the grouping of organosilicon substances with a half-life of < 12 hours and which are known to generate silanol hydrolysis product", and how the dissociation constant is determined/predicted.

4. [redacted] The document "*outlines the approach*" to mammalian

toxicity of aminofunctional alkoxysilanes and silanols. It is explained that individual substances have been grouped for the "*purposes of strategy and read-across approaches*". A summary of mammalian toxicity and data matrix is provided. It is stated that "*where there are data gaps, read-across will be performed from the closest available structurally related substance*". The document does not provide information on the (read-across) approach used for individual substances, but states that "*Details of test proposals and justification of read-across are given in individual Chemical Safety Reports*".

In addition, you have provided a "[redacted]" document describing substance-specific read-across hypothesis and justification attached in section 7.5.1 of the IUCLID. ECHA notes that in this read-across justification document you have provided information also on other aminofunctional alkoxysilanes and silanols without explaining how this data is relevant for the testing proposed for the substance subject to the current decision.

In addition, you have provided the following studies relevant to the testing proposed:

For the registered substance:
- Acute oral toxicity (equivalent or similar to OECD 401)
- Acute dermal toxicity (equivalent or similar to OECD 402)

For the source substance:
- Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422).

d. ECHA analysis of the grouping approach and read-across hypothesis in light of the requirements of Annex XI, 1.5.

ECHA notes that the registrants of Aminofunctional alkoxysilanes and silanols have grouped the substances in 'Analogue group', including the substance subject to the current decision, but the category approach is not proposed. Based on the substance specific justification for read-across approach and supporting information provided by you, ECHA understands that no category hypothesis /justification has been included and the proposed prediction is based on the analogue approach using N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6) as a source substance.

According to ECHA's understanding the proposed read-across hypothesis is based on:

- structural similarity,
- similar physico-chemical and toxicokinetic properties, and
- similar toxicological properties.

ECHA understands that the basis of your hypothesis is also based on rapid and complete hydrolysis of the parent substances leading to the formation of the structurally similar silanol hydrolysis products, which are claimed to drive the toxicity of the parent substances.

In the following, ECHA examines whether the substances have indeed similar properties or that they would follow a regular pattern in their properties, before assessing the scientific validity of your postulation regarding the formation, presence and stability of the proposed hydrolysis products.

(i) Structural (dis)similarities and their impact on prediction

Structural similarity is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that structural similarity *per se* is sufficient to enable the prediction of human health properties of a substance, since structural similarity does not always lead to predictable or similar human health properties. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

In your read-across justification document you provide an overview of the aminofunctional alkoxysilanes analogue group and explain that the members of this group (including the target and source substances) have alkoxysilane moiety, primary and secondary amine and alkylamine or ethylendiamine moiety.

ECHA observes that based on the structures provided in the document, both substances contain three methoxy groups in the Si atom, and an alkylamine and an ethylenediamine moiety in the target and the source substance, respectively. Due to structural differences of the target and source substances, the hydrolysis products formed are also structurally different.

ECHA notes that you have not provided any information on how these structural differences in the parent substances and in the silanol hydrolysis products may impact the toxicokinetic behaviour and toxicity of the substances and thus affect the possibility to predict properties of the target substance from the data obtained with the source substance.

The provided explanation is therefore not sufficient to establish a scientifically credible link between the structural similarity and the prediction.

(ii) Similar properties or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances*". One prerequisite for a prediction based on read-across therefore is that the substances involved are structurally similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.

Physico-chemical properties

In your read-across justification you state that the substances have "*Similar physico-chemical properties (high water solubility, log Pow between -0.8 and 2.2, low vapour pressure, molecular weight between 190-265 g/mol)*".
ECHA observes that the physico-chemical properties of target and source substances are in the same/similar range.

Toxicokinetics

Additionally, in your read-across justification document you claim that the "*systemic exposure is supposed to be mainly to the hydrolysis products. Based on the physico-chemical data oral absorption is possible for the substances and its hydrolysis products by passive diffusion.*"
and
"*In view of the rapid hydrolysis following oral dosing, it is therefore considered appropriate to read-across from one supporting substance (structural analogue or surrogate), which also produces a similar hydrolysis product with similar toxicokinetic properties to address the potential for systemic toxicity after oral exposure*".

ECHA observes that your toxicokinetic predictions rely upon the assumed rapid and complete hydrolysis of the target and source substances to the final silanol hydrolysis products. You also state that the parent substances may also absorb. As pointed out under (iii) section of the current decision, there is insufficient evidence supporting the formation, presence and stability of the ultimate silanol hydrolysis products.

Therefore based on the available information, the toxicokinetic profile of target and source substances and/or their hydrolysis and/or condensation products cannot be compared and the similarity in their toxicokinetic profile cannot be confirmed.

In addition, ECHA notes that there is no information on whether other metabolic pathways of the parent substances and/or its hydrolysis products would occur and thus play a role in the systemic toxicity of the substances.

ECHA therefore considers that it is not possible to verify whether the proposed source and the target substances are likely to have similar toxicity profiles as a result of similar toxicokinetic profile. In the absence of such information there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substance.

Toxicological data

Furthermore, you have proposed that the source substance has similar toxicity regarding sub-chronic toxicity and pre-natal developmental toxicity and therefore the properties of the target substance can be predicted from data obtained from the source substances.

ECHA observes that both substances have low acute oral and dermal toxicity. ECHA notes that you have provided a combined repeated dose toxicity with reproduction developmental toxicity screening test via oral route (OECD 422) conducted with the source substance. No higher tier studies are available for the target substance.

ECHA notes that acute toxicity data alone is not sufficient to establish the toxicological profile of a substance with regard to repeated dose and pre-natal developmental toxicity. As no higher tier studies are available for the target substance, comparison of toxicological profiles of the substances is not possible.

Therefore ECHA concludes that based on the presented information it is not possible to confirm that the substances would have similar properties or they would follow a regular pattern in their properties. In the absence of such information there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substance.

(iii) Hydrolysis

You claim that "*In view of the rapid hydrolysis following oral dosing, it is therefore considered appropriate to read-across from one supporting substance (structural analogue or surrogate), which also produces a similar hydrolysis product with similar toxicokinetic properties to address the potential for systemic toxicity after oral exposure.*"

You further explain that "*At pH 7 the time for hydrolysis ranges from 1 min up to 3.5 h. Under conditions given in the gastrointestinal tract and representing the conditions after oral exposure (pH 2) the alkoxysilane moiety hydrolyses more rapidly. In case of the analogue group members half-lives of approx. 5 s are calculated*".

ECHA notes that there is no hydrolysis data available in the registration dossier for pH 2 (neither for the target nor for the source substance) but that you have postulated that the rate of the hydrolysis reaction is dependent on hydronium ion concentration and that there will be a 100 fold increase in hydrolysis rate on going from pH 4 to pH 2. ECHA accepts that the hydrolysis is catalysed by the hydronium ion, however there is no evidence provided to suggest such a dependence on the hydronium ion concentration and consequently ECHA considers the assumption of a 100 fold increase in hydrolysis rate on going from pH 4 to pH 2 as not supported by scientific evidence.

ECHA further notes that the ultimate hydrolysis of the target and source substances involves several hydrolysis steps. In the hydrolysis studies provided in the registration dossier there is no evidence of the formation of the ultimate silanol hydrolysis products so it is not possible to verify that ultimate hydrolysis has indeed occurred within the timeframe of the test. Furthermore, there is no discussion or analysis of the possible intermediate hydrolysis products and the final products expected to be present upon hydrolysis and subsequent/concurrent condensation.

Furthermore, you have not substantiated your assumption of a complete hydrolysis. In fact, the hydrolysis process which involves several steps may produce also other substances, whose possible presence and effects on your hypothesis you have not addressed.

Hence, ECHA considers that you have not provided sufficient evidence to demonstrate the formation, presence and stability of the similar silanol hydrolysis products.

<u>Condensation of the silanols</u>

Your assumption that the silanols are exclusively relevant in terms of bioavailability and hence would drive the systemic toxicity is not supported by data. In fact you acknowledge the occurrence of condensation reaction following the hydrolysis of the parent substances but you did not consider the implication of such reaction on the prediction. You explain that the silanol hydrolysis products may undergo condensation reactions leading to the formation of siloxane dimers, oligomers and polymers and state that:

Further to the silanol hydrolysis products you also explain that "*Silanetriols may undergo condensation reactions to give siloxane dimers, oligomers and polymers.... A highly cross-linked gel may form. The degree of condensation that will occur may vary with:*

- *Concentration of the silanol; the greater the initial concentration, the greater the degree of condensation. Significant condensation is not expected at concentrations less than approximately 100 mg/l, but is dependent on specific conditions.*
- *pH; the condensation reaction may be either acid or base catalysed.*
- *Temperature.*
- *Other species present.*

- *The nature of the R group*
- *The number of Si-OH groups; silanetriols condense more rapidly than silanediols".*

ECHA notes that you have not specified the conditions (e.g. substance specific concentration limit, specific pH, temperature, impact of the groups bound to the Si atom etc.) neither for the target nor for the source substance under which the condensation occurs and how the condensation products of the target and source substances may impact the toxicity of the substances. In consequence, the nature of the condensation products and their rate of formation under conditions relevant to the proposed test(s) are not clear. Thus exposure to condensation products cannot be ruled out following administration of the source and target substances but you have not addressed how and in which manner the condensation products of the source and target substances would affect the systemic toxicity.

e. Conclusion on the read-across approach

Based on the above considerations ECHA concludes that you have not provided adequate and reliable information to demonstrate that the proposed read-across approach is plausible for the endpoint(s) in consideration.

ECHA therefore concludes that the criteria of Annex XI, Section 1.5, are not met, and consequently the testing proposed on the read-across substance(s) is not appropriate to fulfil the information requirement(s)of the substance subject to the present decision.

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

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to (OECD TG 408) with the analogue substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6).

ECHA has evaluated your proposal to perform the test with the source substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6). As explained in Section 0 "Read-across approach" of this decision, your adaptation of the information requirement cannot be accepted. Hence there is a need to test the registered substance.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration.

More specifically, the substance is a liquid of low vapour pressure. Uses with industrial spray application are reported in the chemical safety report. However, the reported concentrations are low (<[redacted]%). Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

b) Outcome

In your comments on the draft decision you did not provide considerations to this specific endpoint. As you did not update the registration dossier submitted for the substance subject to the present decision, ECHA did not modify the draft decision.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26./OECD TG 408)

while your originally proposed test for sub-chronic toxicity (90-day) study (OECD 408) with the source substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6) is rejected according to Article 40(3)(d) of the REACH Regulation.

Notes for your consideration

ECHA notes that a revised version of OECD TG 408 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

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

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a pre-natal developmental toxicity study according to EU B.31./OECD TG 414 in rats by the oral route with the source substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6).

ECHA has evaluated your proposal to perform the test with the source substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6). As explained in Section 0 "Read-across approach" of this decision, your adaptation of the information requirement cannot be accepted. Hence there is a need to test the registered substance.

ECHA considers that the proposed study performed with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

According to the test method EU B.31./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 the rat or rabbit 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) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

b) Outcome

In your comments on the draft decision you did not provide considerations to this specific endpoint. As you did not update the registration dossier submitted for the substance subject to the present decision, ECHA did not modify the draft decision.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the study with the registered substance: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31./OECD TG 414)

while your originally proposed test for pre-natal developmental toxicity study (OECD 414) with the source substance N-(3-(trimethoxysilyl)- propyl)ethylenediamine (CAS No 1760-24-3, EC No 217-164-6) is rejected according to Article 40(3)(d) of the REACH Regulation.

Notes for your consideration

ECHA notes that a revised version of OECD TG 414 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 28 May 2014.

ECHA held a third party consultation for the testing proposal(s) from 18 September 2014 until 3 November 2014. ECHA did not receive information from third parties.

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.

You were notified that the draft decision does not take into account any updates after **11 July 2016**, 30 calendar days after the end of the commenting period.

However, following your request and justification provided (including interlinked read-across testing strategy on several supposedly related registered substances) ECHA has exceptionally granted you additional time until 30 June 2017 for the update.

You did not update the dossier by the given deadline.

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 took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) 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 test(s) 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 test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.