~~Confidential~~

Helsinki, 12 October 2023

Addressees
Registrants of AAPS_C12-18 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
01 April 2021

Registered substance subject to this decision ("the Substance")
Substance name: 1-Propanaminium, N-(3-aminopropyl)-2-hydroxy-N,N-dimethyl-3-sulfo-, N-(C12-18(even numbered) acyl) derivs., hydroxides, inner salts
EC/List number: 939-457-4

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***17 January 2025***.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471)

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

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. C/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310) on relevant constituent(s)/fraction(s) of the Substance, as described under the corresponding appendix on reasons for the request.

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes

to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 for the request(s)

Reasons common to several requests

0.1. Read-across adaptation rejected

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

2 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

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

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Predictions for (eco)toxicological properties

5 You provide a read-across justification document in IUCLID Section 13.2.

6 You predict the properties of the Substance from information obtained from the following source substance(s):

- C8-18 AAPHS, Propanaminium, N-(3-aminopropyl)-2-hydroxy-N,N-dimethyl-3-sulfo-, N-(C8- 18(even numbered) acyl) derivs., hydroxides, inner salts name of the source substance 1, List 939-455-3 (source substance 1).

7 You provide the following reasoning for the prediction of (eco)toxicological properties:

- "*the source and target substances have toxicological, ecotoxicological and environmental fate properties likely to be similar (i.e. analogue approach = different compounds having qualitatively similar properties) as a result of structural similarity due to common functional groups, common precursors, likelihood of common breakdown products, and a constant pattern in the changing of the potency of the properties between substances*"
- "[…] *the constituents of the target substance are all included in the source substance composition in very close proportions. Other constituents of the target substance, not represented in the source substance (short C chain sultaines, i.e. C8 and C10, and corresponding breakdown products) are not expected to display significantly different toxicokinetic or toxicological properties than the main constituents (C12 and C14).*"
- "*Should the short C-chain constituents be associated with a significant toxicity, this would be taken into account in the classification and labelling or the risk assessment, as a worst-case for the target substance resulting from the read-across based on the target substance data.*"
- "*Both substances have been tested for their acute toxicity to freshwater and/or marine fish and invertebrates: both substances exhibited toxicity in the range*

*>1-10 mg/L, whatever the trophic level considered. The source substance is the only one which has been tested for its toxicity to algae (acute and chronic), invertebrates (chronic) and toxicity to aquatic microorganisms. Regarding the toxicity to algae, the acute toxicity value obtained on the source substance is consistent with the ones obtained on fish and invertebrates (i.e. falls in the range >1-10 mg/L). In the end, no trophic level appears to be more sensitive than another and it is not expected that the target substance deviates from this pattern considering its closeness of composition with the source substa*nce".

8 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the toxicological properties of your Substance based on a worst-case approach and the ecotoxicological properties of your Substance to be quantitatively equal to those of the source substance.

0.1.1.1. Inadequate or unreliable source studies

9 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

(1) be adequate for the purpose of classification and labelling and/or risk assessment;

(2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement.

10 Specific reasons why the studies on the source substance(s) do not meet these criteria are explained further below under the applicable information requirement sections 1 to 3. Therefore, no reliable predictions can be made for these information requirements.

0.1.2. Conclusion

11 Based on the above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

12 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

1.1. Information provided

13 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) an *in vitro* gene mutation study in bacteria (1997) with the source substance 1 (C8-18 AAPHS), List 939-455-3.

1.2. Assessment of the information provided

1.2.1. Read-across adaptation rejected

14 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

1.2.1.1. Inadequate or unreliable study (i) on the source substance(s)

15 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 471. Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101);

b) at least 5 doses are evaluated, in each test condition;

c) a concurrent negative control is included in each assay and the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;

d) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

16 In study (i):

a) the test was performed with *S. typhimurium* strains TA 1535, TA 1537, TA 98, TA 100 and TA 1538 (i.e., *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) strain is missing);

b) only 3 and 4 doses were evaluated in absence and in presence of metabolic activation (i.e., less than 5 doses) in experiments 1 and 2, respectively;

c) you have not reported whether the number of revertant colonies per plate for the concurrent negative control was inside the historical control range of the laboratory;

d) no repeat experiment was performed to confirm the negative results and no justification was provided.

17 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) required by the OECD TG 471.

18 Therefore, the information requirement is not fulfilled.

2. Growth inhibition study aquatic plants

19 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

2.1. Information provided

20 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substance:

(i) Growth inhibition study on algae (2009) with the source substance 1 (C8-18 AAPHS), List 939-455-3

2.2. Assessment of the information provided

2.2.1. Read-across adaptation rejected

21 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

2.2.1.1. Inadequate or unreliable study (i) on the source substance(s)

22 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 201, and meet the specifications of OECD GD 23 if the substance is difficult to test. Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) three replicates at each test concentration and at least three replicates for controls (including solvent controls, if applicable) are included;

Characterisation of exposure

b) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided.

23 In study (i):

Technical specifications impacting the sensitivity/reliability of the test

a) the number of replicates was two in each test concentration;

Characterisation of exposure

b) no analytical monitoring of exposure was conducted and no justification was provided why analytical monitoring of test concentrations is not technically feasible.

24 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the reported effect values are based on nominal concentrations but in the absence of analytical monitoring it is not demonstrated that the test concentrations have maintained within ±20 % of the nominal or mean measured initial concentrations throughout the test. Further, the number of replicates in each test concentration is lower than the number of replicates required in the OECD TG 201 algae growth inhibition test.

25 On this basis, the specifications of OECD TG 201 are not met.

26 Based on the above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

27 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. On this basis, your read-across approach under Annex XI, Section 1.5. is rejected.

28 Therefore, the information requirement is not fulfilled.

2.3. Study design

29 The Substance is difficult to test due to the surface active nature of the Substance (surface tension 37.5 mN/m). OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

30 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

31 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (*i.e.* loading rate) and in a consistent manner.

3. Ready biodegradability

32 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

3.1. Information provided

33 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following experimental data:

(i) an OECD TG 310 ready biodegradability study (2010) with the Substance;
(ii) an OECD TG 310 ready biodegradability study (2010) with the analogue substance C8-18 AAPHS (no CAS RN or EC number provided);
(iii) an OECD TG 306 biodegradability in seawater study (2009) with the analogue substance (no CAS RN or EC number provided).

3.2. Assessment of information provided

3.2.1. Weight of evidence adaptation rejected

34 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

35 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

36 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

3.2.1.1. Lack of documentation justifying the weight of evidence adaptation

37 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach.

38 You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

39 Beside this critical deficiency, ECHA has also assessed the other aspects of your adaptation.

40 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 9.2.1.1 includes similar information that is produced by the OECD TG 301 or 310. OECD TG 301/310 requires the study to investigate the following key parameter:

(i) the ultimate aerobic biodegradation (as measured by parameters such as DOC removal, CO2 production and oxygen uptake) of the test material under low inoculum concentration measured at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation

41 The sources of information (i) to (iii) may provide relevant information on the above key parameter.

42 However, the reliability of these sources of information is affected by the following deficiency:

3.2.1. Ready biodegradation tests are normally intended for pure substances

43 The revised introduction to the OECD Guidelines For Testing Of Chemicals, Section 3 Part I states that ready biodegradability tests are intended for pure substances but may also be relevant, on a case-by-case basis, to mixtures of structurally similar chemicals (i.e. which are composed of constituents expected to show similar degradation kinetics). However, such tests are not generally applicable for complex mixtures or substances (i.e. UVCB or multi-constituent substances) containing different types of constituents. For complex substances, a single ready biodegradability test does not allow to conclude on the ready biodegradability of all constituents and therefore, does not fulfil the information requirement. In this case, the ready biodegradability test must be performed on relevant constituent(s)/fraction(s) of the Substance.

44 You have provided studies (i) to (iii) conducted on the Substance and an analogue substance as a whole. In your read-across justification document, you describe the Substance and the analogue substances as UVCB substance. These substances may contain up to six main constituents (upper limits of the concentration ranges from 3% to 65% and 10% to 65%, for the Substance and the analogue substance, respectively) with a large carbon chain length distribution ranging from C8 to C18. These substances also contain Disodium 2-hydroxypropane-1,3-disulfonate (1.2% and 3.8%, for the Substance and the analogue substance, respectively) and Sodium (±)-2,3-dihydroxypropanesulphonate (7.1% and 2.8%, for the Substance and the analogue substance, respectively). The analogue substance also contains glycerol at a concentration of 5.4%. Finally both substances contain traces of Amides, C8-18 even numbered, N-[3-(dimethylamino)propyl] as impurities. Considering the wide range of carbon chain length and the structural variation between constituents, it can be assumed that the constituents of the substance would show varying degradation kinetics.

45 The Substance and selected analogue substances are complex substances and contain constituents with significant structural differences described above. Therefore, the provided study does not provide unequivocal conclusion that all constituents can safely be regarded as readily biodegradable.

46 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for ready biodegradability.

47 Based on the above, your adaptation is rejected.

48 Therefore, the information requirement is not fulfilled.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2023).
***Guidance on intermediates*;** ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 22 February 2023.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA did not receive any comments within the commenting period.

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third-party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1 Test methods, GLP requirements and reporting

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

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

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries (https://echa.europa.eu/practical-guides).

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2 Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).

2. General recommendations for conducting and reporting new tests

2.1 Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in Guidance on IRs & CSA, Section R.11.4.2.2, you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach", (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

References to Guidance on REACH and other supporting documents can be found under Appendix 1.