Helsinki, 3 May 2016

Addressee: [redacted]

Decision number: CCH-D-2114330930-57-01/F
Substance name: diisopropylbenzene
EC number: 246-835-6
CAS number: 25321-09-9
Registration number: [redacted]
Submission number: [redacted]
Submission date: 26.03.2013
Registered tonnage band: 100 to 1000 tonnes per year

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. **Name(s) in the IUPAC nomenclature or other international chemical name(s) (Annex VI, Section 2.1.1.), CAS number and CAS name (Annex VI, Section 2.1.4) of the registered substance;**

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

3. **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;**

4. **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/inhalation] route with the registered substance;**

5. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2; test method: Alga, growth inhibition test, EU C.3/OECD TG 201) with the registered substance;**

6. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5; test method: Daphnia magna reproduction test, EU C.20/OECD TG 211) with the registered substance;**

7. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

8. **Classification and labelling in accordance with the CLP Regulation (Annex VI, Section 4.);**

9. **Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2; test method: Earthworm reproduction test (Eisenia fetida/Eisenia andrei), OECD TG 222, or Enchytraeid reproduction test, OECD TG 220, or Collembolan reproduction test in soil, OECD TG 232) with the registered substance;**

10. **Long-term toxicity to plants (Annex IX, Section 9.4.3., column 2; test method: Terrestrial plants, growth test, OECD TG 208), with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species) or, Soil Quality - Biological Methods - Chronic toxicity in higher plants, ISO 22030) with the registered substance;**

11. **Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD TG 216) and carbon transformation test, EU C.22/OECD TG 217) with 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 **10 May 2019**. 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

IDENTIFICATION OF THE SUBSTANCE

In order to ensure that potential hazardous properties of the substance are not underestimated, the substance identification deficiencies must be resolved before identifying the test sample to be used for the testing requested in the present decision.

1. Name(s) in the IUPAC nomenclature or other international chemical name(s) (Annex VI, Section 2.1.1.), CAS number and CAS name (Annex VI, Section 2.1.4)

Pursuant to Article 10(a)(ii) of the REACH Regulation, the technical dossier shall contain information on the identity of the substance as specified in Annex VI, Section 2 of the REACH Regulation. In accordance with Annex VI, Section 2 the information provided shall be sufficient to enable the identification of the registered substance.

According to Annex VI, Section 2.1 of the REACH Regulation, name or other identifier of the substance shall be provided. This includes the name in the IUPAC nomenclature or other international chemical name(s) (Annex VI, Section 2.1.1); as well as CAS name and CAS number (if available) (Annex VI, Section 2.1.4).

In accordance with the Guidance for identification and naming of substances under REACH and CLP (Version: 1.3, February 2014)[2] - referred to as "the Guidance" thereinafter, a well-defined multi-constituent substance is a substance consisting of several main constituents present at concentrations generally ≥ 10% and < 80% (w/w). All constituents (except additives) which are not the main constituents in a multi-constituent substance are considered to be impurities. A multi-constituent substance is named as the reaction mass of two or more main constituents.

ECHA notes that you identified the registered multi-constituent substance with the IUPAC name di(propan-2-yl)benzene and the numerical identifiers (EC number 246-835-6 and CAS number 25321-09-9). The identifiers used for defining the registered substance refer to a substance containing all the possible isomers of diisopropylbenzene (1,2-, 1,3- and 1,4-diisopropylbenzene). However, the composition of the substance provided in section 1.2 of the IUCLID dossier, substantiated by the analytical data provided in section 1.4, shows that 1,2-diisopropylbenzene is present at a typical concentration <10% (w/w). Thus, according to the Guidance, this constituent should be considered as an impurity, and not contribute to the naming of the substance.

As a consequence, ECHA considers that the IUPAC name you provided is not representative of the composition of the registered substance, because the isomer 1,2-diisopropylbenzene should not be reflected in the name of the substance. In addition, ECHA concludes that the numerical identifiers EC/CAS entries are not appropriate to identify the registered multi-constituent substance, as they reflect also a constituent that should be regarded as an impurity.

[2] http://echa.europa.eu/documents/10162/13643/substance_id_en.pdf

Accordingly you are requested to provide a chemical name corresponding to the specific multi-constituent substance covered in this registration. The chemical name shall follow the generic format "Reaction mass of [names of the main constituents]". All main constituents present in the registered substance shall be reflected in the name of the registered substance. All the constituents present at a concentration <10% (w/w) should be listed under the impurities and not be part of the name. You shall also specify any available and appropriate CAS number and CAS name reflecting the identity of the main constituents of the substance. You shall delete from the registration any information referring to different substances than the multi-constituent substance which is the subject of this registration.

As for the reporting of the information in IUCLID, the chemical name shall be indicated in the "IUPAC name" field in IUCLID section 1.1. The CAS number and CAS name shall be reported under the "CAS information" header in IUCLID section 1.1.

For technical reasons, you are requested not to remove or modify at this stage the EC entry currently assigned to this registration, as the registration is linked to that EC entry in REACH-IT. You are requested to include in the "Remarks field" of the reference substance the following: "The EC entry currently assigned does not specifically correspond to the registered substance. This identifier cannot be modified in the present registration at this stage for technical reasons". Please note that ECHA has established a process, subject to certain conditions, enabling registrants to adapt an existing registration, while maintaining the regulatory rights already conferred to the substance concerned.

Furthermore, you shall ensure that the molecular and structural information specified in IUCLID section 1.1 (smiles notation, InChI code and structural formula) are consistent with the chemical name and CAS number and CAS name assigned to the registered substance.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly.

PROPERTIES OF THE SUBSTANCE

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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. 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 study records for a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422, oral route, reliability 1), and an oral subacute toxicity study (OECD TG 407, reliability 1). However, these studies do not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days, respectively of approximately 50 days for the OECD TG 422 study (as it was performed according to the OECD TG 421) and of 28 days for the OECD TG 407 study, hence they do not fulfil all requirements for a RDT-90 study. In addition, the number of animals per dose group is significantly lower in the OECD TG 407 study than in a 90-day study according to OECD TG 408. Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study.

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 has evaluated the most appropriate route of administration for the study. 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 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of vapour pressure of 0.34 hPa at 25°C. Even though the information indicates that human exposure to the registered substance by the inhalation route is likely (PROCs 8a, 8b and 9), the available oral studies indicate the presence of some systemic effects after oral exposure (OECD TG 407) demonstrating that the substance is available after administration by gavage (in corn oil): mydriasis, changes in clinical chemistry, increase in liver (male and female), kidney weight in males, centrilobular hypertrophy of hepatocytes in both male and female, and the incidence of eosinophilic bodies in proximal tubules of the kidney was increased in males. In addition in the OECD TG 422, study, exophtalmos was noted in 2 males at 750 mg/kg bw, and transiently lowered food consumption. At the same dose, mydriasis was noted in females. On histopathological examination in males only at 750 mg/kg bw, vacuolization of lens fibers and hyperplasia of epithelium lentis were noted in 2 and 1 animal, respectively.

Hence ECHA considers that these effects require further investigation on repeated dose toxicity by the oral route.

Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408. 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.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, suggesting that you will *submit an update with information on a read-across substance [...] "1,3-diisopropylbenzene (EC 202-773-1; CAS 99-62-7) for which data will be available by 2 January 2017 [...] when access to the data will be granted"*. You also indicated as another option to [...] *"carry out the required study"*. You added that *"a robust QSAR/ read across document will be prepared to substantiate the planned tox/ ecotox read across, summarizing all available data on DIPB, the pure meta and pure para substances"*.

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: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH 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 some study records for *in vitro* genotoxicity (originating from the CICAD, 2008 on cumene and from the SIAP, 1994 on 1,4-diethylbenzene or DEB), as well as *in vivo* micronucleus (originating from the CICAD, 2008 on cumene) with the analogue substances cumene and DEB, (with EC number 202-704-5 and CAS RN 105-05-5 respectively).

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

Annex XI, Section 1.5. requires a structural similarity among the substances within a group or category such that relevant properties of a substance within the group can be predicted from the data on reference substance(s) within the group by interpolation.

The following analysis presents your justification for the proposed grouping approach and read-across hypothesis, together with ECHA's analysis concerning the justification in both a generic and an property-specific context:

(i) Description of the grouping and read-across approach proposed by the Registrant

ECHA considers the following statement as the description you used to make predictions for the property listed above: "*No other studies are available, but related chemicals like diethyl benzene was also negative* in vitro*, and cumene (isopropyl benzene) was also negative* in vivo", for addressing the requirement of Annex VIII, Section 8.4.3.

(ii) ECHA analysis of the grouping and read-across approach in light of the requirements of Annex XI, 1.5.

You have provided no justification in the endpoint summary of your registration, or elsewhere in the registration dossier, to support your approach for the grouping and read-across.

Accordingly, ECHA considers that you have failed to meet the requirement of Annex XI, 1.5 that adequate and reliable documentation of the applied method shall be provided.

ECHA further notes that you provided a record for the two supporting studies. However, ECHA considers that these records do not meet the requirements of a robust study summary of the experimental data on the source substances, as required under Article 10(a)(vii), and as further described in Practical Guide 3: How to report robust study summaries (http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf), because they do not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. ECHA is therefore unable to verify the adequacy, or otherwise, of the studies. For this reason also, ECHA considers that you have failed to meet the requirement of Annex XI, 1.5 that adequate and reliable documentation of the applied method shall be provided.

(iii) Conclusion on the read-across approach

As set out above, ECHA considers that you have failed to provide adequate and reliable documentation for the read-across, and ECHA is unable to verify that the grouping and read-across is acceptable. ECHA therefore concludes that you have failed to meet the requirement of Annex XI, Section 1.5. that human health effects may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).

Pursuant to Article 41(1) of the REACH Regulation, ECHA concludes that the adaptation of the standard information requirements proposed in the technical dossier and based on the proposed read-across approach fails to predict the properties of the registered substance and therefore does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5.

Therefore, ECHA rejects the adaptation of the information requirement. Consequently, the information provided for this endpoint for the registered substance in the technical dossier does not meet the information requirement andthere is an information gap and it is necessary to provide information for this endpoint.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, suggesting that you will *"submit an update with information on a read-across substance [...] "1,3-diisopropylbenzene (EC 202-773-1; CAS 99-62-7) for which data on In vitro Mammalian Cell Gene Mutation Test (GLP and OECD Guideline 476, reliability 1) is available in the corresponding REACH registration dossier [...], when access to the data will be granted"*. You also indicated as another option to [...] *"carry out the required study"*. You added that *"a robust QSAR/ read across document will be prepared to substantiate the planned tox/ ecotox read across, summarizing all available data on DIPB, the pure meta and pure para substances".*

ECHA considers that the *in vitro* mammalian cell gene mutation test – *hprt* test (OECD TG 476) and the *in vitro* mammalian cell gene mutation test – Mouse lymphoma assay (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.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./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.

You have sought to adapt this information requirement according to Annex XI, Section 1.2. of the REACH Regulation by providing the following statement: *"[T]he repeated NOAEL is of 150 mg/kg bw, while in the OECD 422 assay, the fertility and developmental NOAEL are of 750 mg/kg bw (highest dose tested). As related chemicals like DEP (Diethylbenzene) with a lower repeated NOAEL (30 mg/kg bw) have the same limits for reprotoxicity, and that cumene (isopropylbenzene) is in the same case; it do not seem necessary to run a new animal study, even at the limit dose of 1000 mg/kg, if not toxic for dams. Furthermore DIPB have a low Vapour pressure, and so less volatile"* for the requirement of Annex IX, Section 8.7.2 (Pre-natal developmental toxicity study).

In addition you provided supporting study records for a pre-natal developmental toxicity study, inhalation route (OECD TG 414), in the rat and the rabbit, on isopropylbenzene (or cumene with EC number 202-704-5).

Annex XI, Section 1.2 provides that: *"There may be sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, while the information from each single source alone is regarded insufficient to support this notion."*

ECHA firstly evaluates the individual components of the Weight of Evidence justification. ECHA considers that repeated-dose toxicity studies and OECD 422 studies do not have adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3), i.e. the OECD TG 414, and in particular (a) the examination of uterine contents and foetuses and (b) dose-setting as required by the OECD TG 414 paragraph 13. A comparison of NOAELs of such studies likewise fails to address these key parameters.

ECHA notes that you have suggested read-across for diethylbenzene and isopropylbenzene. ECHA considers that there is no justification provided for this read-across, that there is a failure to provide adequate and reliable documentation, and that consequently it is not possible that human health effects of the registered substance may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach), as specified in Annex XI, Section 1.5. Therefore the read-across data are not sufficient to fulfil the information requirement by themselves.
ECHA considers that low vapour pressure does not provide information about the prenatal developmental toxicity of a substance.

Secondly, ECHA considers the overall weight of evidence. ECHA notes that you have not identified the deficiencies in the individual components of your evidence, and you have not explained why the information from all of these components, when combined, provides a sufficient weight of evidence to overcome the deficiencies that ECHA has identified above. ECHA considers that there is not sufficient weight of evidence from several independent sources of information leading to the assumption and conclusion that a substance has or has not a particular dangerous property (prenatal developmental toxicity).

The proposed adaptation does not meet the requirements of Annex XI, Section 1.2, and hence must be 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.

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 assumption ECHA considers testing should be performed with rats or rabbits as a first species.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, suggesting that you will *"submit an update with information on a read-across substance [...] "1,3-diisopropylbenzene (EC 202-773-1; CAS 99-62-7) for which data will be available by 2 January 2017 [...] when access to the data will be granted"*. You also indicated as another option to [...] *"carry out the required study"*. You added that *"a robust QSAR/ read across document will be prepared to substantiate the planned tox/ ecotox read across, summarizing all available data on DIPB, the pure meta and pure para substances"*.

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 4.1, October 2015) 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.

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: EU B.31./ OECD TG 414) in a first species (rats or rabbits) by the oral route.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. 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.

Column 2 of Annex VII, Section 9.1.2 specifies that the study does not need to be conducted if there are mitigating factors indicating that aquatic toxicity is unlikely to occur for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes.

In the technical dossier you have provided a study record "[redacted] However, this study does not provide the information required by Annex VII, Section 9.1.2., as it was performed using dispersant/solubilising agents and the estimated values were higher than the water solubility. Also, because of the presence of insoluble particles that could affect the results, the validity of this study is doubtful. These are unjustified deviations from the key parameters of the standard test that are, therefore, not adequately and reliably covered.

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.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, indicating that DIPB can be characterized as difficult substance as defined in the OCDE guidance document on aquatic toxicity testing of difficult substances and mixtures (Series on Testing and Assessment n°23, 2000).

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 2.0, November 2014) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

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: Algae growth inhibition test, EU C.3./OECD TG 201).

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. 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 "[redacted]". However, this study does not provide the information required by Annex IX, Section 9.1.5., as it was performed using dispersant/solubilising agents and the estimated values were higher than the water solubility. Also, because of the presence of insoluble particles that could affect the results, the validity of this study is doubtful. These are unjustified deviations from the key parameters of the standard test that are, therefore, not adequately and reliably covered.

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.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, indicating that DIPB can be characterized as difficult substance as defined in the OCDE guidance document on aquatic toxicity testing of difficult substances and mixtures (Series on Testing and Assessment n°23, 2000).

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 2.0, November 2014) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

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: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) 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. You provided the following justification for the adaptation: "*As fish was shown to be less sensitive than Daphnia magna in acute tests, a chronic test in this vertebrate was not considered as necessary, and, as for Daphnia, the NOEC was considered as being above the substance water solubility limit*".

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2. It is because, from the information provided, it is not possible to ascertain whether daphnia is more sensitive than fish in short term studies considering the significant uncertainties which are not addressed in the technical dossier, such as the use of dispersant/solubilising agents, estimated values higher than the water solubility and presence of insoluble particles in short term daphnia studies. Also the long-term aquatic toxicity study on fish (Annex IX, Section 9.1.6.) shall be considered if the substance is poorly soluble as indicated in Annex VII, Section 9.1.3, Column 2 for the short term toxicity on fish.

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.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, indicating that DIPB can be characterized as difficult substance as defined in the OCDE guidance document on aquatic toxicity testing of difficult substances and mixtures (Series on Testing and Assessment n°23, 2000).

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 2.0, November 2014) fish early-life stage toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. /OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

Regarding the long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 2.0, November 2014). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

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: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration

Before conducting any of the tests mentioned above in point 6 and in the current point 7 you shall consult the ECHA *Guidance on information requirements and chemical safety assessment (version 2.0, November 2014)*, Chapter R7b, Section R.7.8.5 to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

8. Classification and labelling (Annex VI, Section 4.1.)

Article 10(a)(iv) of the REACH Regulation requires that the technical dossier shall include the classification and labelling of the substance in accordance with the CLP Regulation, as specified in Annex VI, Section 4 of the REACH Regulation.

In the classification section (IUCLID 2.1.) of the dossier for aspiration hazard, you state "*conclusive but not sufficient for classification*".

A substance must be classified as aspiration toxicity hazard category 1 if it meets the following two criteria: the substance is a hydrocarbon and has a kinematic viscosity of 20.5 mm^2/s or less, measured at 40°C.

ECHA notes that the registered substance is a hydrocarbon, and you have provided in the registration dossier a study with the conclusion "[redacted]". ECHA understands this to be a read-across of the properties of 1,3-diisopropylbenzene to the registered substance. A dynamic viscosity of 1.403 mPa s at 25°C is equivalent to a kinematic viscosity of 1.64 mm^2/s at 25°C. Since viscosity decreases with increasing temperature, the kinematic viscosity value at 40°C will clearly be lower than 20.5 mm^2/s. You have, however, not addressed these criteria in the registration dossier or provided any appropriate justification why the registered substance should not be classified as aspiration toxicity hazard category 1.

As explained above, the information provided for the registered substance in the technical dossier does not meet the information requirement and there is a data gap.

Therefore, pursuant to Article 41(1)(a) and (3) of the REACH Regulation, you are requested to submit the following information for the registered substance subject to the present decision: a classification and labelling in accordance with the CLP Regulation.

This information must be provided in Section 2 of the IUCLID dossier. In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly.

9. Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. Adequate information on effects on short-term toxicity to invertebrates (Annex IX, Section 9.4.1.), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and short-term toxicity to plants (Annex IX, Section 9.4.3.) needs to be present in the technical dossier for the registered substance to meet the information requirements. Column 2 of Annex IX, Section 9.4 specifies that long-term toxicity testing shall be considered by the Registrant instead of short-term, in particular for substances that have a high potential to adsorb to soil or that are very persistent.

You have waived the standard information requirements of Annex IX, section 9.4.1. using the following justification: "*Given very low toxicity in mammals (NOAEL 150 mg/kg bw/d), toxicity in soil compartment is not expected*".

Your justification for waiving does not meet the criteria of either the specific adaptation rules of Column 2 of Annex IX, Section 9.4, or the general adaptation rules of Annex XI. Therefore, the adaptations cannot be accepted.

The substance is not biodegradable, it is adsorptive and it is used as fertilizer additive therefore direct exposure to soil is foreseen and toxicity to terrestrial organisms needs to be investigated.

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

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, indicating that DIPB can be characterized as difficult substance as defined in the OCDE guidance document on aquatic toxicity testing of difficult substances and mixtures (Series on Testing and Assessment n°23, 2000).

According to section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), substances that are ionisable or have a log K_{ow} or log K_{oc} >5 are considered highly adsorptive, whereas substances with a half-life >180 days are considered very persistent in soil. According to the evidence presented within the Registration dossier, the substance has a high potential to adsorb to soil (log K_{ow} 5.23). Therefore ECHA considers that the column II adaptation for Annex IX, section 9.4 regarding long-term testing instead of short-term testing, is applicable to this substance.

According to section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), where there is adequate data available to sufficiently derive a PNEC for aquatic organisms, this PNEC can be used in a screening assessment for soil risks through the use of the Equilibrium Partitioning Method (EPM) approach.

You have considered that it is unfeasible, with the information currently available, to derive a PNEC for aquatic organisms. Consequently, it is not possible to waive the standard information requirements for the terrestrial compartment through an initial screening assessment based upon the EPM, mentioned in Column 2 of Annex IX, section 9.4. Since a screening assessment for terrestrial organisms is not possible, testing for effects on all terrestrial organisms indicated in section 9.4 of Annex IX is considered necessary.

The earthworm reproduction test (OECD TG 222), Enchytraeid reproduction test (OECD TG 220) are each considered capable of generating information appropriate for the fulfilment of the information requirements for long-term toxicity testing to terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol, since this decision is dependent upon species sensitivity and substance properties.

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: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) (test method: OECD TG 222), or Enchytraeid reproduction test (test method: OECD TG 220),

10. Long-term toxicity to plants (Annex IX, Section 9.4.3., column 2)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. Adequate information on effects on short-term toxicity to invertebrates (Annex IX, Section 9.4.1.), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and short-term toxicity to plants (Annex IX, Section 9.4.3.) needs to be present in the technical dossier for the registered substance to meet the information requirements. Column 2 of Annex IX, Section 9.4 specifies that long-term toxicity testing shall be considered by the Registrant instead of short-term, in particular for substances that have a high potential to adsorb to soil or that are very persistent.

You have waived the standard information requirements of Annex IX, section 9.4.3. using the following justification: "*Given very low toxicity in mammals (NOAEL 150 mg/kg bw/d), toxicity in soil compartment is not expected*".

Your justification for waiving does not meet the criteria of either the specific adaptation rules of Column 2 of Annex IX, Section 9.4, or the general adaptation rules of Annex XI. Therefore, the adaptations cannot be accepted.

The substance is not biodegradable, it is adsorptive and it is used as fertilizer additive therefore direct exposure to soil is foreseen and toxicity to terrestrial organisms needs to be investigated.

As established under point 9 above, it is not currently possible to waive the standard information requirements for the terrestrial compartment through an initial screening assessment based upon the EPM, mentioned in Column 2 of Annex IX, section 9.4.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, indicating that DIPB can be characterized as difficult substance as defined in the OCDE guidance document on aquatic toxicity testing of difficult substances and mixtures (Series on Testing and Assessment n°23, 2000).

OECD TG guideline 208 (Terrestrial plants, growth test) considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing shall be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208 guideline. You should consider if testing on additional species is required to cover the information requirement.

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: Terrestrial plants, growth test (test method: OECD TG 208), with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species), or, Soil Quality – Biological Methods – Chronic toxicity in higher plants (test method: ISO 22030).

11. Effects on soil micro-organisms (Annex IX, Section 9.4.2.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

You have waived the standard information requirements of Annex IX, section 9.4.2. using the following justification: "*Given very low toxicity in mammals (NOAEL 150 mg/kg bw/d), toxicity in soil compartment is not expected*".

Your justification for waiving does not meet the criteria of either the specific adaptation rules of Column 2 of Annex IX, Section 9.4, or the general adaptation rules of Annex XI. Therefore, the adaptations cannot be accepted.

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

ECHA notes that the tests requested under points 9 and 10 above are not sufficient to address this standard information requirement. ECHA concludes that the effects on soil microorganisms need to be ascertained by performing a relevant test.

In your comments on the draft decision, ECHA noted that you agreed to update your dossier accordingly, indicating that DIPB can be characterized as difficult substance as defined in the OCDE guidance document on aquatic toxicity testing of difficult substances and mixtures (Series on Testing and Assessment n°23, 2000).

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R.7C, Section R.7.11.3.1., p115, the nitrogen transformation test is considered sufficient for most non-agrochemicals. However, as the substance has known agrochemical uses, ECHA considers that both the nitrogen and carbon transformation tests should be performed simultaneously.

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: Soil microorganisms: nitrogen transformation test (test method: EU C.21./OECD TG 216), and Soil microorganisms: carbon transformation test (test method: EU C.22./OECD TG 217).

Notes for your consideration

ECHA notes that the results from the toxicity tests on fish/ aquatic invertebrates/algae requested under points 5, 6 and 7 of the present Decision may allow the subsequent derivation of a $PNEC_{water}$. Consequently, you may consider the Integrated Testing Strategy as recommended in section R.7.11.6., of the above-mentioned *Guidance* and determine the need for further testing on terrestrial organisms. If you conclude that no further investigation of effects on terrestrial organisms is required, you should update your technical dossier by clearly stating the reasons for adapting the information requirements of section 9.4. of Annex IX, of the REACH Regulation.

ECHA emphasises that the intrinsic properties of soil microbial communities are not addressed through the EPM extrapolation method and therefore the potential adaptation possibility outlined for the information requirement of Annex IX, Section 9.4. does not apply for the present endpoint.

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 3 December 2015.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

ECHA notified you of the draft decision and invited you to provide comments. ECHA took into account your comments, which were sent within the commenting period, and they are reflected in the Reasons (Appendix 1).

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment(s).
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. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2017. Note: the start of the evaluation may be postponed upon the evaluating member state's decision.

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

3. 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 your Member State.

4. 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.