EUROPEAN CHEMICALS AGENCY

Helsinki, 21 August 2018

Addressee: [redacted]

Decision number: CCH-D-2114440479-42-01/F
Substance name: N,N-dimethyldecan-1-amide
EC number: 238-405-1
CAS number: 14433-76-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 28/08/2015
Registered tonnage band: Over 1000

DECISION ON A COMPLIANCE CHECK

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

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (rabbit), oral route with the registered substance;**

2. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) in rats, oral route with the registered substance specified as follows:**

   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**

3. **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;**

4. **Biodegradation:**

   - **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: DOC die-away test, OECD TG 301A) or**
   - **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or**

- **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or**
- **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or**
- **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Modified OECD screening test, OECD TG 301E) or**
- **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or**
- **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310))**

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 to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by ***1 March 2021***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Kevin Pollard, Head of Unit, Evaluation E1

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

Appendix 1: Reasons

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

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

Pre-natal developmental toxicity studies (test method EU B.31./OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The information provided

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the oral route using the analogue substance Decanamide, N,N-dimethyl-, mixt. with N,N-dimethyloctanamide (CAS 67359-57-3) as test material.

You have sought to adapt this information requirement. While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision.

You have provided the following justification for the adaptation: *"Results from a developmental toxicity study and a subchronic toxicity study did not reveal any reason of concern for offspring and for parent animals with respect to developmental toxicity or fertility. Since significant scientific evidence for a lack of reprotoxic effects of the substance is drawn from these results and an additional developmental study is not expected to add any further relevant knowledge on this endpoint. Due to animal welfare aspects and/or laws, an additional study is therefore not warranted. Further there is a rabbit study available showing no more detrimental result which is therefore not bought from the owner but underlinining the waiver."*

To support your weight of evidence adaptation you have provided the following sources of information:

- Key study: Sub-chronic repeated dose toxicity study in non-rodents (beagle dogs) by the oral route (OECD TG 409; GLP) with the analogue substance Decanamide, N,N-dimethyl-, mixt. with N,N-dimethyloctanamide (CAS 67359-57-3), [redacted], 2000 (study report), rel. 1,
- Key study: Pre-natal developmental toxicity study in a first species (rats) by the oral route (OECD TG 414; GLP) with the analogue substance Decanamide, N,N-dimethyl-, mixt. with N,N-dimethyloctanamide (CAS 67359-57-3), [redacted], 1991 (study report), rel. 1.

Evaluation approach/criteria

An adaptation pursuant to Annex XI, Section 1.2. requires 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 with respect to the information

requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to pre-natal developmental toxicity study in a second species as requested in this decision, i.e. information on species differences regarding to prenatal developmental toxicity.

Evaluation outcome/conclusion

The available pre-natal developmental toxicity study with an analogue substance covers only the information requirement of pre-natal developmental toxicity study in the first species. The available sub-chronic repeated dose toxicity study in beagle dogs according to OECD TG 409 using an analogue substance does not provide the information covered by a pre-natal developmental toxicity study, such as investigations of offspring concerning effects on skeletal and visceral pre-natal development.

You further refer to a "*rabbit study available showing no more detrimental result*" without providing supporting evidence in the form of a robust study summary. Therefore, ECHA is not in a position to assess that evidence.

Hence, the individual sources of information you provided, together with your justification for the adaptation, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

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

In your comments according to article 50(1) of the REACH Regulation, you state that "*a pre-natal developmental study in a second species, (rabbit) which was conducted with the close analogue substance* Reaction mass of N,N-dimethyloctanamide and N,N-dimethyldecan-1-amide *(EC 909-125-3) is available.*", and that you "*would like to submit the results of this existing pre-natal developmental toxicity study in rabbits, instead of conducting a new animal study*". ECHA reminds you of the "Notes for consideration", below. In addition, to your intention to address the information requirement, ECHA notes you have submitted a dossier update, stating the reason for updating as "*Other: Additional news in chapter 7.8.2*". However, you are reminded that this decision does not take into account any updates submitted after the notification of the draft decision to you. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

The test in the first species was carried out by using a rodent species (rat). According to the test method EU B.31./OECD 414, the rabbit is the preferred non-rodent species. On the basis of this default assumption, ECHA considers that the test should be performed with rabbit as a second species.

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

Notes for your consideration

You refer to an existing pre-natal developmental toxicity study in rabbits available, which you did not include in the technical dossier to fulfil the information requirement. Testing must be conducted only as a last resort (REACH article 25(1)). Therefore, the results of this existing study should be submitted instead of the results of a new study provided that this existing study is available, of sufficient quality and adequate to fulfil the information requirements of Annex X, Section 8.7.2.

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).

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

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

The basic test design of an extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

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

The information provided

You have not provided any study record of an extended one-generation reproductive toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.3.

You have sought to adapt this information requirement. While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision.

You have provided the following justification for the adaptation:
"Results from a developmental toxicity study and a subchronic toxicity study did not reveal any reason of concern for offspring and for parent animals with respect to developmental toxicity or fertility. Since significant scientific evidence for a lack of reprotoxic effects of the substance is drawn from these results and an additional fertility or two generation study is not expected to add any further relevant knowledge on this endpoint. Due to animal welfare aspects and/or laws, an additional study is therefore not warranted."

To support your weight of evidence adaptation you have provided the following sources of information:

- Key study: Sub-chronic repeated dose toxicity study in non-rodents (beagle dogs) by the oral route (OECD TG 409; GLP) with the analogue substance Decanamide, N,N-dimethyl-, mixt. with N,N-dimethyloctanamide (CAS 67359-57-3), [redacted], 2000 (study report), rel. 1,
- Key study: Pre-natal developmental toxicity study in a first species (rats) by the oral route (OECD TG 414; GLP) with the analogue substance Decanamide, N,N-dimethyl-, mixt. with N,N-dimethyloctanamide (CAS 67359-57-3), [redacted], 1991 (study report), rel. 1,

Evaluation approach/criteria

An adaptation pursuant to Annex XI, Section 1.2. requires 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 with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to an extended one-generation reproductive toxicity study (EU B.56./OECD TG 443) as requested in this decision. ECHA considers that this study provides, in addition to information on general toxicity, information in particular on two aspects, namely on sexual function and fertility in P1 and F1 generations (further referred to as 'sexual function and fertility') and on development and toxicity of the offspring from birth until adulthood due to pre- and postnatal and adult exposure in the F1 generation (further referred to as 'effects on offspring'). In addition, 10 weeks premating exposure duration in P0 generation is required.

Relevant elements for 'sexual function and fertility' are in particular functional fertility (oestrous cycle, sperm parameters, mating behaviour, conception, pregnancy, parturition, and lactation) in the P0 parental generation after sufficient pre-mating exposure and histopathological examinations of reproductive organs in both P and F1 generations. Relevant elements for 'effects on offspring' are in particular peri- and post-natal investigations of the F1 generation up to adulthood including investigations to reveal potential endocrine modes of action. Also the sensitivity and depth of investigations to detect effects 'sexual function and fertility' and 'effects on offspring' need to be considered.

Evaluation of the provided information

The quality (reliability, relevance and adequacy) of the provided information on sexual function and fertility for P0/F1 generation is considered low, since neither of the provided studies include exposure regimes and mating to investigate all of the exposure durations and key parameters of an EOGRTS. There is no information on fertility and sexual function available from the OECD TG 408 and OECD TG 414.

Further, the quality (reliability, relevance and adequacy) of the provided information on post-natal developmental toxicity (F1 generation) from OECD TG 408 is inadequate, since it does not provide information on developmental toxicity. The adequacy of the provided information from OECD TG 414 is limited, since it does not investigate post-natal developmental toxicity. This information would include litter size, growth, survival/mortality, some external malformations, sexual maturation (e.g. AGD, VO, PPS, time from vaginal opening to first oestrous) and histopathology of gonads and accessory sex organs in adulthood.

In addition, the statistical power regarding the dog study is low reducing the confidence, particularly since half the number of animals in the high dose group (2 of 4) died before the study was completed. Thus, the sensitivity to detect reproductive toxicity is not similar to that provided by the extended one-generation reproductive toxicity study reducing the confidence.

Conclusion

In light of limited investigations/information and lower sensitivity to detect hazardous properties as indicated above, ECHA considers that the available information, considered individually or together, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to sexual function and fertility, and post-natal developmental toxicity.

Hence, the sources of information you provided, together with your justification for the adaptation, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Annex X, Section 8.7.3.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

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

a) The specifications for the study design

Premating exposure duration and dose-level setting

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

folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017). Ten weeks exposure duration is supported also by the lipophilicity of the substance (log Kow 3.4) to ensure that the steady state in parental animals has been reached before mating.

The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

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

Species and route selection

According to the test method EU B.56./ OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

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

b) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;

When you update your registration dossier with the new endpoint study record for the extended one-generation reproductive toxicity study, you shall include the scientific reasoning for 1) length of the premating exposure duration and dose level selection, as explained in the ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.7a, Section R.7.6.2.3.2, Stage 4.4 (iii) under the header "Study design for the extended one-generation reproductive toxicity study.

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented.

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

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

"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.

You have sought to adapt this information requirement by applying a read-across approach in accordance with Annex XI, Section 1.5.

You have provided a study record for an Alga, Growth Inhibition Test on *Pseudokirchnerella subcapitata* according to OECD test guideline 201 (, 1993)[2] with an analogue substance consisting of a mixture of (ca.), (ca.), (ca.), and (ca.).

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled when applying a read-across approach. Firstly, there needs to be structural similarity between the registered substance and the analogue substance(s) which results in a likelihood that the substances have similar physicochemical, fate, toxicological and ecotoxicological properties so that the substances may be regarded 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 analogue substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a read-across approach is reliable and should be based on recognition of the structural similarities and differences between the analogue and registered substances[3]. This hypothesis explains why the differences in the chemical structures should not influence their properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in

[2] , 1993. . Report number: . Report date:

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

the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

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

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[4]- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common (bio)transformation compounds).

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

You consider to achieve compliance with the REACH information requirements for the registered substance, i.e. N,N-dimethyldecan-1-amide, using data for an analogue substance consisting of a mixture of [redacted] (ca. [redacted]), [redacted] (ca. [redacted]), [redacted] (ca. [redacted]), and [redacted] (ca. [redacted]).

However, you have provided no documentation for this read-across.

By comparing study results available in ECHA's dissemination portal from the registration dossiers for N,N-dimethyldecan-1-amide (EC: 238-405-1), for N,N-dimethyloctanamide (214-272-5) and for a reaction mass of N,N-dimethyldecan-1-amide and N,N-dimethyloctanamide (EC: 909-125-3), ECHA notes that N,N-dimethyldecan-1-amide seems to be more toxic to *Daphnia* than the reaction mass[5]. Due to insufficient data, the comparison is not possible for fish or algae.

Furthermore, based on the information available in ECHA's dissemination portal from the registration dossier for the reaction mass (EC: 909-125-3), ECHA notes that the sensitivity of algae is of the same order of magnitude than for fish or for *Daphnia*[6].

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

[5] For N,N-dimethyldecan-1-amide: 21d-NOEC: 0.079 mg/L – 0.37 mg/L; for the reaction mass (EC: 909-125-3): 21d-EC10: 1.3 mg/L, 21d-NOEC: 1 mg/L.

[6] For short-term toxicity to fish: 96h-LC50: 14.8 mg/L, 19 mg/L, 21.1 mg/L. For short-term toxicity to *Daphnia*: 48h-LC50: 7.7 mg/L. For long-term toxicity to *Daphnia*: 21d-EC10: 1.3 mg/L, 21d-NOEC: 1 mg/L. For algae: 72h-ErC50: 16.06 mg/L, 72h-NOErC: 1.8 mg/L, 72h-ErC10: 4.17 mg/L.

Therefore, the information available does not rule out, firstly, that the study provided for algae with the read-across substance underestimates the toxicity of the registered substance, and secondly, that algae could be more sensitive than fish and *Daphnia* which would imply that the current PNEC values and the classification and labelling of the registered substance would be incorrect.

Hence, ECHA considers that you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. Since your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5., it is rejected and it is necessary to perform testing on the registered substance.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) 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).

4. Ready biodegradability (Annex VII, Section 9.2.1.1.)

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

"Ready biodegradability" is a standard information requirement as laid down in Annex VII, section 9.2.1.1. 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 by applying a read-across approach in accordance with Annex XI, Section 1.5.

You have provided a study record for a ready biodegradability test according to OECD test guideline 301 B (CO2 Evolution Test) with an analogue substance consisting of a mixture of N,N-dimethyldecan-1-amide and N,N-dimethyloctanc-1-amide ([redacted], 2009)[7]. The exact composition of the test material, i.e. the proportion of each constituent, is not specified.

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled when applying a read-across approach. Firstly, there needs to be structural similarity between the registered substance and the analogue substance(s) which results in a likelihood that the substances have similar physicochemical, fate, toxicological and ecotoxicological properties so that the substances may be regarded 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 analogue substance(s) within the group (read-across approach). ECHA considers that the

[7] [redacted] 2009. [redacted] Report number: [redacted] Report date: [redacted].

generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a read-across approach is reliable and should be based on recognition of the structural similarities and differences between the analogue and registered substances[8]. This hypothesis explains why the differences in the chemical structures should not influence their properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests.

Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent.
Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[9] - (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common (bio)transformation compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.
You consider to achieve compliance with the REACH information requirements for the registered substance, i.e. N,N-dimethyldecan-1-amide, using data for an analogue substance consisting of a mixture of N,N-dimethyldecan-1-amide and N,N-dimethyloctanc-1-amide.

However, you have provided no documentation for this read-across.

From the study of [redacted] (2009), 63.63% mineralisation (meeting the 10-day window) was observed after 29 days. The test material is said to be a mixture of N,N-dimethyldecan-

[8] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.
[9] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

1-amide and N,N-dimethyloctanc-1-amide but the proportion of each component is not available.

Firstly, ECHA notes that no information is available on the ready biodegradability of N,N-dimethyldecan-1-amide (EC: 238-405-1) or of N,N-dimethyloctanamide (214-272-5) considered separately.

Secondly, ECHA notes that the result of the study of [redacted] (2009) is just over the pass-level of 60% biodegradation. The test material used for that study can therefore be regarded as formally readily biodegradable, but only by a narrow margin, and no conclusion can be drawn on the readily biodegradability of each constituent.

Therefore, the information available does not rule out, firstly, that the registered substance could be less biodegradable than N,N-dimethyloctanamide and than a mixture of N,N-dimethyloctanamide and N,N-dimethyldecanamide, and secondly, that the registered substance could not meet the formal criterion for ready or rapid biodegradability which would imply that the current classification and labelling of the substance would be incorrect.

Hence, ECHA considers that you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. Since your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5., it is rejected and it is necessary to perform testing on the registered substance.

Regarding the test method, depending on the substance profile, you may conclude on ready biodegradability, by applying the most appropriate and suitable test guideline among those listed in the ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) and in the paragraph below. The test guidelines include the description of their applicability domain.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to perform one of the following tests with the registered substance subject to the present decision:

- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: DOC die-away test, OECD TG 301A), or
- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B), or
- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C), or
- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D), or
- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Modified OECD screening test, OECD TG 301E), or
- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F), or
- Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310)

with the registered substance.

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 26 October 2017.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took your comments into account and did not amend the request(s).

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

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

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

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

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

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