Helsinki, 03 July 2020

Addressees
Registrants of 941-364-9 (RFC) listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
21 August 2015

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Petroleum gas oil fraction, co-processed with renewable hydrocarbons of plant and/or animal origin
EC number: 941-364-9
CAS number: NS

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed in A.1, B.1 and C.1, below by ***8 October 2021*** and all other information listed below by the deadline of ***10 October 2022***.

A. Requirements applicable to all the Registrants subject to Annex VII of REACH

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method EU B.13/14. / OECD TG 471) with the Substance;

B. Requirements applicable to all the Registrants subject to Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) with the Substance;

2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method OECD TG 476 or TG 490) with the Substance;

C. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method OECD TG 408) in rats with the Substance;

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance;

D. Requirements applicable to all the Registrants subject to Annex X of REACH

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

Conditions to comply with the requests

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.
To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annexes VII to X of REACH, if you have registered a substance at above 1000 tpa.

Registrants are only required to share the costs of information that they must submit to fulfil the information requirements for their registration.

The Appendix on general considerations addresses issues relevant for several requests while the other Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

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.

Failure to comply

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

Approved[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[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 on general considerations

(i) Assessment of the Grouping of substances and read-across approach, in light of the requirements of Annex XI, Section 1.5.

You seek to adapt the following standard information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.)

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

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

A. Predictions for toxicological properties

In your comments to the draft decision, you have provided an updated read-across justification document.

You propose to read-across from the following similar substances (source substances): fuels, diesel (EC No. 269-822-7, CAS No. 68334-30-5), fuel oil, No 2 (EC No. 270-671-4, CAS No 68476-30-2), fuel oil, No 4 (EC No. 270-673-5, CAS No 68476-31-3), and fuels, diesel, No 2 (EC No 270-676-1, CAS No 68476-34-6).

In your comments to the draft decision you have provided the following reasoning for the prediction of toxicological properties: *" The composition and the physico-chemical properties of the target substance Petroleum gas oil fraction, co-processed with renewable hydrocarbons of plant and/or animal origin (EC No. 941-364-9) and source substances from the Concawe VHGO Category are very similar. It is planned to conduct new Annex VII and Annex VIII (OECD 471, 473/487 and 476/490 and 422) studies on the target substance to fulfil the information requirements. It is expected that this will provide further information to support the hypothesis that the target substance is very similar from a hazard (as well as*

[2] ECHA Guidance R.6
[3] ECHA Read-across assessment framework (March 2017)
[4] ECHA Read-across assessment framework (March 2017) - considerations on multi-constituent substances and UVCBs

compositional) perspective to members of the VHGO category, and to reinforce the read-across approach employed in the IUCLID dossier. This approach will then be applied to the endpoints related to toxicity, specifically the Annex IX and X information requirements for sub-chronic toxicity, developmental and reproductive toxicity". "

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcomings with regards to predictions of toxicological properties.

Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information should include toxicokinetic information on the substances, and supporting information/bridging studies to compare properties of the Substance and source substances.

You have not provided any study results conducted with the Substance (target substance). In the absence of such information, it is not possible to compare the toxicological profiles of the target and source substances. Therefore, it is not possible to establish similarity of toxicological properties and your grouping and read-across approach does not provide a reliable basis for prediction.

In your comments to the draft decision, you acknowledge the current lack of supporting information to compare toxicological profiles of target and source substances. You indicate your plans to remedy that by generating experimental toxicological data on the Substance for the applicable Annex VII and Annex VIII information requirements (OECD 471, 473/487 and 476/490 and 422) and you consider that this information will provide further information to support your hypothesis for the higher tier endpoints.

ECHA notes, that the testing plan may or may not confirm your hypothesis.

Currently, as there is no data to confirm similarity of toxicological properties of the target and source substances, your grouping and read-across approach does not provide a reliable basis for prediction.

Characterisation of the source substance(s)

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of chemical similarity may be considered as group.*"

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s). Therefore, qualitative

and quantitative information on the compositions of the Substance and of the source substance(s) should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

Furthermore, whenever the Substance and/or the source substances are UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances qualitative compositional information of the individual constituents of the category members needs to be provided; as well as quantitative characterization in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.

For certain studies that you provided for the endpoints genetic toxicity, sub-chronic toxicity, and developmental toxicity in a first species, no information on the identifiers and individual constituents of the source substances or the test material was submitted as outlined below under section 1 of Appendices A, C, and D.

Without any further information on the test materials, the similarity of the compositions of the Substance and of the source substances cannot be assessed. Therefore, ECHA considers that it is not possible to assess whether prediction is possible.

Adequacy and reliability of source studies

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

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

The studies that you provided for the endpoints on genetic toxicity, sub-chronic toxicity, and developmental toxicity in a first species do not provide an adequate coverage of some key parameters expected to be investigated and do not meet the requirement for adequacy and reliability under Section 1.5, Annex XI to REACH for the reasons provided under Appendices A, section 1, B, sections 1 and 2, C, sections 1 and 2, and D, section 1.

In your comments to the draft decision, you indicate that you have identified new existing repeated-dose toxicity and pre-natal developmental toxicity studies conducted with the substance Fuels, diesel (EC 269-822-7) in rats via the dermal route and that you intend to use these studies as source studies in your read-across approach to predict the properties of the Substance.

However, as these studies were not provided by you in your comments, ECHA cannot evaluate them and their adequacy and reliability, for the related information requirements of the Substance, is unconfirmed.

B. Conclusions on the read-across approach

As explained above, you have not established, neither in your dossier nor in your comments to the draft decision, that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Appendix A: Reasons for the requests to comply with Annex VII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 1 to 10 tonnes or more per year must contain, as a minimum, the information specified in Annex VII to REACH.

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An *in vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have provided a key study in your dossier:

- Bacterial Reverse Mutation Test (GLP, 2013), conducted with 14 Gas oils in *Salmonella typhimurium* TA98.

We have assessed this information and identified the following issues:

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected.

Furthermore, your key study contains only identifiers of one from 14 test substances, diesel fuel (EC 269-822-7, CAS RN 68334-30-5) and no further information of the other test materials, except that "*14 gas oils have been tested*". No information on the identifiers and individual constituents of the source substances is provided.

Without any further information on the test materials, the similarity of the compositions of the Substance and of the source substances cannot be assessed. Therefore, ECHA considers that it is not possible to conclude if the test material (the source substances) is similar to the Substance.

In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

Adequacy and reliability of source study

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should:
- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The source study that you have used in your read-across approach, Bacterial Reverse Mutation Test ([redacted], 2013), conducted with 14 Gas oils in *Salmonella typhimurium, strain TA98*, using a modification of the pour-plate assay designed to detect mutagenicity mediated by polynuclear aromatic compounds derived from petroleum,corresponds to a ASTM Standard Test Method E 168 performed similar to the OECD TG 471.

According to the provisions of Annex VII, Section 8.4.1., information on *in vitro* gene mutation study in bacteria as specified in the OECD TG 471 shall be provided. Under OECD TG 471 the following key parameters (among others) are expected to be investigated in a study performed according to this test guideline:

1. The test must be conducted in absence and in presence of metabolic activation.

2. The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)
3. The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
4. The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.

The reported data for the study you have provided did not include:

1. Test in absence of metabolic activation.
2. Results for the appropriate 5 strains, that is in TA98/TA100/TA1535/TA1537 or TA97a or TA97/the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
3. A maximum dose of 5 mg/plate or 5 ml/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance.
4. A negative control with a number of revertant colonies per plate inside the historical control range of the laboratory.

The information provided does not cover some of the key parameters required by OECD TG 471. Therefore, the provided source study could not fulfil the standard information requirement and also for this reason, your read-across is rejected.

In your comments to the draft decision, you agreed to perform the requested test.

Appendix B: Reasons for the requests to comply with Annex VIII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to REACH.

1. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is a standard information requirement in Annex VIII to REACH.

You provided three *in vivo* cytogenicity read-across studies to fulfil this standard information requirement according to Column 2 of Section 8.4., Annex VIII. .

As explained in the Appendix on general considerations your read-across adaptation is rejected. In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

To be considered adequate, the *in vivo* studies submitted have to meet the requirements of OECD TG 475, and the key parameters of this test guideline include the following:

1. The study must include a negative control group and a positive control group.
2. The highest dose studied must be the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow (e.g. a reduction in the proportion of immature erythrocytes among total erythrocytes in the bone marrow or peripheral blood).
3. The proportion of immature among total (immature + mature) erythrocytes must be determined for each animal (by counting a total of at least 500 erythrocytes for bone marrow and 2000 erythrocytes for peripheral blood).
4. The mitotic index must be determined as a measure of cytotoxicity in at least 1000 cells per animal for all treated animals (including positive controls), untreated or vehicle/solvent negative control animals.
5. At least 200 metaphases must be analysed for each animal for structural chromosomal aberrations including and excluding gaps.
6. The mitotic index and the mean number of cells with aberrations per group must be reported for each group of animals.

You have provided a key study and supporting read-across studies in your dossier:

1. Key study, OECD 475, GLP, 1994, conducted with another petroleum substance home heating oil, (CAS No 68476-30-2, EC No 270-671-4;), mouse, oral (gavage), doses 1.0, 2,5, 5,0 g/kg, negative;
2. Supporting study, OECD 475, non GLP, 1978, conducted with another petroleum substance diesel fuel (CAS No 68334-30-5, EC No 269-822-7), rat, intraperitoneal, positive;
3. Supporting study, mouse dominant lethal assay, no guideline, no GLP, 1980, conducted with another petroleum substance diesel fuel No 2 (CAS No 68476-34-6, EC No 270-676-1), inhalation, negative.

The reported data for the *in vivo* studies 1 and 2 did not include:

1. a maximum studied dose that is a MTD or induces toxicity
2. the analysis of the adequate number of cells
3. a negative control with a response inside the historical control range of the laboratory.
4. a positive control group (or scoring control) that produced a statistically significant increase in the induced response compared with the concurrent negative control
5. data on the mitotic index and the mean number of cells with aberrations per group for each group of animals.

ECHA notes that only two doses were used in the supporting (negative) mouse dominant lethal assay, and you also acknowledged that reporting of this study lacks various details. Furthermore, due to the limitations of this assay, this assay is not intended for use as a primary method, but rather as a supplemental test method which can only be used when there is no alternative for regulatory requirements for this endpoint; hence, even a compliant rodent dominant lethal test on its own cannot be considered as sufficient to fulfil the standard information requirement under REACH.

Therefore, the provided *in vivo* tests are not adequate to adapt this standard information requirement according to Column 2 of Section 8.4., Annex VIII.

To fulfil the information requirement for the Substance, both *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) and *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

In your comments to the draft decision, you agreed to perform the requested test.

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

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

The *in vitro* gene mutation study in bacteria and *in vivo* chromosomal aberration studies provided in the dossier do not fulfil this information requirement for the reasons provided in sections A.1 and B.1. The results of the requests for information in sections A.1 and B.1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

You have provided a key study in your dossier:

1. *In vitro* mouse lymphoma assay (not GLP, 1978, OECD 476), conducted with another petroleum substance, diesel fuel No 2 (CAS RN 68476-34-6, EC 270-676-1), negative.

We assessed this information and identified the following issues:

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected. In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

Adequacy and reliability of source study

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

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The source study that you have used in your read-across approach, *in vitro* Mammalian Cell Gene Mutation Test ([redacted] 1978), conducted with another petroleum substance, diesel fuel No 2 (CAS RN 68476-34-6, EC 270-676-1), corresponds to the OECD TG 476.

According to the provisions of Annex VIII, Section 8.4.3., information on *in vitro* gene mutation study in mammalian cells as specified in the OECD TG 476 shall be provided. Under OECD TG 476 the following key parameters (among others) are expected to be investigated in a study performed according to this test guideline:

1. The maximum concentration tested must induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
2. One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
3. The response for the concurrent negative control must be inside the historical control range of the laboratory.
4. Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

The reported data for the study you have provided do not include:

1. a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.
2. one positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
3. a negative control with a response inside the historical control range of the laboratory.
4. data on the cytotoxicity and the mutation frequency for the treated and control cultures.

The information provided does not cover key parameter(s) required by the relevant OECD TG. Therefore, the information requirement is not fulfilled.

In your comments to the draft decision, you agreed to perform the requested test in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

Appendix C: Reasons for the requests to comply with Annex IX of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII to IX to REACH.

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

Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

You have provided two key studies and a supporting study for this endpoint in your dossier:

1. Key, sub-chronic inhalation toxicity study (1984, GLP not specified, OECD 413) conducted with another substance, CAS No 68334-30-6;
2. Key, sub-chronic dermal toxicity study (1994, GLP, OECD 411) conducted with another petroleum substance, diesel, CAS No 68334-30-5.

We have assessed this information and identified the following issues:

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected. Furthermore, your key study contains only a CAS RN of the test substance (68334-30-6). ECHA assumes that it is a reporting mistake and the study was most likely conducted with diesel, CAS No 68334-30-5. However, no further information of the test material is provided. Therefore, it is not possible to conclude on structural similarity and your read-across is also rejected for that reason.

In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

Adequacy and reliability of source study

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

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).;
- - cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

The source studies that you have used in your read-across approach, sub-chronic inhalation toxicity study ([redacted] 1984) and sub-chronic dermal toxicity study ([redacted] 1994) dermal *in vitro* Mammalian Cell Gene Mutation Test [redacted], 1978), correspond to the OECD TG 411 and 413.

According to the provisions of Annex IX, Section 8.6.2., information on sub-chronic toxicity studies as specified in the OECD TG 408, 411 or 413 shall be provided. Under OECD TG 408, 411 or 413 the following key parameters (among others) are expected to be investigated in a study performed according to this test guideline:

- highest dose level should aim to induce some systemic toxicity, but not death or severe suffering;
- dosing of the Substance daily for a period of 90 days until the scheduled termination of the study;
- ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals, haematology and clinical biochemistry;
- pathology of sexual (male and female) organ and full detailed gross necropsy and subsequent histopathology of both types tissues.

The studies you have provided were not performed according to the criteria of the OECD TG 413 or 411 since the following key parameters are missing:

- The highest dose level in both studies did not induce any systemic toxicity. Regarding the dermal study, you defined a systemic LOAEL based on irritating properties of the test substance. You only reported moderate dermal irritation accompanied by decreased body weight (males only), increased food consumption, changes in differential leukocyte counts, decreased albumin (and albumin/globulin ratio), and increased incidence of lymphoid hyperplasia of the auxiliary lymph node. Therefore, the dose level selection was too low, and the studies do not fulfil the criterion set in OECD TG 413 and 411.
- The inhalation study you have provided does not have the required exposure duration of 90 days as required in OECD TG 413, because you indicated an exposure duration of 4 hour per day, two days per week for 13 weeks (total of 26 exposures).
- In both studies, ophthalmological examination was not performed.
- No behaviour examination was conducted in the dermal study.

Based on the above, the information you provided does not fulfil the information requirement.

Information on the design of the study to be performed

The oral route is the default route of administration because it is assumed to maximise systemic availability (internal exposure). In the absence of toxicokinetic data, the physicochemical characteristics of numerous components of the Substance indicate limited dermal absorption. In addition, the Substance is a liquid with low vapour pressure and there is no indication for severe local effects following inhalation exposure. ECHA therefore concludes that the oral route is the most appropriate and the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

In your comments to the draft decision, you acknowledge the current lack of supporting information to compare toxicological profiles of target and source substances. You indicate your plans to remedy that by generating experimental toxicological data on the Substance for the applicable Annex VII and Annex VIII information requirements (OECD 471, 473/487 and 476/490 and 422) and you consider that this information will provide further information to support your hypothesis.

ECHA notes, that the testing plan may or may not confirm your hypothesis.

Currently, as there is no data to confirm similarity of toxicological properties of the target and source substances, your grouping and read-across approach does not provide a reliable basis for prediction.

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

A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

In your dossier you have provided a key study and four supporting studies conducted with other petroleum substances on rats. We have assessed this information and identified the following issues:

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected. In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

Adequacy and reliability of source study

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

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).;
- - cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

The source studies that you have used in your read-across approach, inhalation and dermal prenatal developmental toxicity studies ([redacted] 1979; [redacted] 1993; [redacted] 1994) correspond to the OECD TG 414.

According to the provisions of Annex IX, Section 8.7.2., information on pre-natal developmental toxicity study as specified in the OECD TG 414 shall be provided. Under OECD TG 414 the following key parameters (among others) are expected to be investigated in a study performed according to this test guideline:

- testing of at least three dose levels and a concurrent control,
- highest dose level should aim to induce some developmental and/or maternal toxicity,
- 20 female animals with implantation sites for each test and control group,
- examination of the dams for weight and histopathology of the thyroid gland/thyroid hormone measurements/gravid uterus weight/uterine content/body weight of the dams/clinical signs of the dams,
- examination of the foetuses for sex and body weight/external, skeletal and soft tissue alterations (variations and malformations)/number of resorptions and or live foetuses/ measurement of anogenital distance in live rodent foetuses.

In your dossier you have provided the following studies for this endpoint:

Key study:

- (1) inhalation (whole body) study, conducted with another petroleum substance diesel fuel (CAS No 68334-30-5, EC No 269-822-7) [redacted] 1979), OECD 414, GLP not specified, doses of 0, 101.8, or 401.5 ppm (equivalent to 0, 530, and 2110 mg/m3, respectively), no adverse effects reported;

Supporting studies:

- (2) inhalation, (whole body) study, conducted with another petroleum substance heating oil No 2, a mixture of straight run gas oil and cracked gas oil (CAS No 68476-30-2, EC No 270-671-4; ([redacted] 1979), OECD 414, GLP not specified, doses 0 (control group), 86.9 or 408.8 ppm (equivalent to 460 or 2,150 mg/m3); no adverse effects reported;
- (3) dermal study, conducted with another petroleum substance straight run diesel (CAS No 68334-30-5, EC No 269-822-7), ([redacted] 1994), GLP, dose levels of 0, 125, or 250 mg/kg bw/day; no adverse effects reported;
- (4) dermal study, conducted with another petroleum substance, 'most likely' diesel (CAS No 68334-30-5, EC No 269-822-7), ([redacted] 1994), GLP, dose levels of 0, 125, or 250 mg/kg bw/day; no adverse effects reported;
- (5) dermal study conducted with another petroleum substance straight run diesel (CAS No 68334-30-5, EC No 269-822-7), ([redacted] 1993) GLP, dose levels of 0, 50, 150, or 300 mg/kg bw/day. No treatment-related effects on reproduction or development (number of corpora lutea, implantations, litter size, live fetuses, resorptions, fetal body weight, or sex ratio) reported.

The key (1) study and a supporting (2) study were conducted with two dose levels. Therefore these studies do not fulfil the criterion of at least three dose levels set in OECD TG 414. Furthermore, the highest dose level in these studies did not induce maternal toxicity. Therefore, the dose level selection was too low.

The supporting studies (3) and (4) were conducted with 14 or 15 presumably pregnant females for each test group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 pregnant females for each test group set in OECD TG 414.

Based on the reporting in the registration dossier, in all five studies you have provided the weight and histopathology of the thyroid gland has not been examined in dams, thyroid hormone measurements have not been conducted in dams and gravid uterus weight has not been measured. In the supporting studies (3) and (4) you have provided, the external, skeletal and soft tissue alterations (variations and malformations) have not been examined.

Based on the above, the information you provided does not fulfil the information requirement because the studies are inadequate.

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[5] administration of the Substance.

In your comments to the draft decision, you acknowledge the current lack of supporting information to compare toxicological profiles of target and source substances. You indicate your plans to remedy that by generating experimental toxicological data on the Substance for the applicable Annex VII and Annex VIII information requirements (OECD 471, 473/487 and

[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.

476/490 and 422) and you consider that this information will provide further information to support your hypothesis.

ECHA notes, that the testing plan may or may not confirm your hypothesis.

Currently, as there is no data to confirm similarity of toxicological properties of the target and source substances, your grouping and read-across approach does not provide a reliable basis for prediction.

Appendix D: Reasons for the requests to comply with Annex X of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier at a tonnage above 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to REACH.

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

Pre-natal developmental toxicity study in a second species is a standard information requirement at Annex X unless one or more of the adaptations in Section 8.7 of Annex X or Annex XI apply, taking into account the results of the test in the first species or any other relevant available information.

In your dossier you have not provided a study with the Substance. Instead, you have adapted the information requirement according to Annex XI, Section 1.5. and you have provided the studies listed under Appendix C.2. for the first species prenatal developmental toxicity.

We have assessed this information and identified the following issues:

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected.

In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

All the studies provided and listed in Appendix C.2 were conducted on one species only and with other petroleum substances, and the proposed read-across is rejected. You have not provided information on pre-natal developmental toxicity (PNDT) on a second species.

Based on the above, the information you provided does not fulfil the information requirement.

A PNDT study according to the OECD TG 414 study should be performed in rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (request C.2 in this decision). The study shall be performed with oral[6] administration of the Substance.

In your comments to the draft decision, you acknowledge current lack of supporting information to compare toxicological profiles of target and source substances. You indicate your plans to remedy that by generating experimental toxicological data on the Substance for the applicable Annex VII and Annex VIII information requirements (OECD 471, 473/487 and 476/490 and 422) and you consider that this information will provide further information to support your hypothesis.

ECHA notes, that the testing plan may or may not confirm your hypothesis.

Currently, as there is no data to confirm similarity of toxicological properties of the target and source substances, your grouping and read-across approach does not provide a reliable basis for prediction.

[6] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix E: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The compliance check was initiated on 13 June 2019.

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

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

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

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

Appendix F: Observations and technical guidance

1. The information requirement under Section 8.7.3. of Annex IX/X to REACH (Extended one-generation reproductive toxicity study, EOGRTS) is not addressed in this decision. A testing proposal on the EOGRTS (full study design) was submitted on 21 August 2015. ECHA notes that, based on currently available information, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) were identified. The sub-chronic toxicity study shall be conducted before the extended one-generation reproductive toxicity study, as the results of the former may provide information on neurotoxic effects that is relevant for the including Cohorts 2A and 2B.

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

3. 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 the Member States.

4. Test guidelines, GLP requirements and reporting

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

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

   Under Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries'[7].

5. Test material

   Selection of the test material(s) for UVCB substances

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account the impact of each constituent/impurity on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/impurity. Any constituents that have harmonised classification and labelling according to the CLP Regulation (Regulation (EC) No 1272/2008) must be identified and quantified using the appropriate analytical methods.

[7] https://echa.europa.eu/practical-guides

The OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 11 [ENV/MC/CHEM(98)16] requires a careful identification of the test material and description of its characteristics. In addition, the Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "if the test method is used for the testing of a [...] UVCB [...] sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents".

In order to meet this requirement, all the constituents of the test material used for each test must be identified as far as possible. For each constituent the concentration value in the test material must be reported in the Test material section of the endpoint study record.

Technical Reporting of the test material for UVCB substances

The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers" on the ECHA website8.

6. List of references of the ECHA Guidance and other guidance/ reference documents[9]

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 in this decision.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[10]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate

[8] https://echa.europa.eu/manuals
[9] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

OECD Guidance documents[11]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

[11] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix G: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.