~~Confidential~~

Helsinki, 04 December 2020

Addressees
Registrants of 265-196-4/64742-93-4 listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of a decision
12 April 2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Asphalt, oxidized
EC number: 265-196-4
CAS number: 64742-93-4

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

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***13 March 2023*** *from the date of the decision*.

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

Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, inhalation route specified as follows:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity); and
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation which must be followed to weaning; and
- Cohort 3 (Developmental immunotoxicity)
- The highest dose in the study must be above 300 mg/m^3 (6h/day).

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 they are required to submit to fulfil the information requirements for their registration.

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.

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 A: Reasons for the requirement applicable to all the Registrants subject to Annex X of REACH

This decision is based on the examination of the testing proposal you submitted.

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

The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement under Annex X to the REACH Regulation. Furthermore, column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 by the inhalation route in rats with 10-week pre-mating exposure duration, without the extension of Cohort 1B to produce the F2 generation and without Cohorts 2 and 3. You have provided the following justification and specification of the study design according to the criteria described in Column 2 of Section 8.7.3, Annex X, and detailed in ECHA Guidance R.7a:

You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You proposed 10 weeks for premating exposure duration. ECHA agrees with your proposal. 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 R.7a.

You proposed to set the dose levels based on the results from existing repeat dose and developmental studies on the Substance.

The highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects, with the other cohorts being tested at the same dose levels.

ECHA notes that your registration dossier contains results from a Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD TG 422, 2009), and from a pre-natal developmental toxicity study (OECD TG 414, 2018) conducted by inhalation with the Substance.

In the OECD TG 422 study, the doses used were 30, 100 and 300 mg/m^3 (6h/day). The study reports no effects on organ weights and histopathology other than at the site of contact (increase in lung weight and decrease in infiltration of immune cells in the nasal cavity epithelium); and no effects on body weight in any dose-group (a significant decrease in body weight gain was reported).

In the OECD TG 414 study, the doses used were 50, 150 and 500 mg/m^3 (6h/day). The study reports no effects on organ weights and histopathology other than at the site of contact. Squamous cell metaplasia in the larynx as well as the alveolar granulocytic cell infiltration and the mononuclear cell infiltration in the lung were significantly increased in the high dose

(500mg/m3) group. These changes was seen in a single animal at the mid-dose. No effect on terminal body weight and total body weight gain were observed. However net body weight, when taking into account the weight of the gravid uterus, was reduced in all dose groups.

Considering the duration and the doses used for all abovementioned studies, ECHA concludes that the highest dose in the EOGRTS must be above 300 mg/m^3 (6h/day).

Cohort 3

The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity.

A Member State submitted a proposal for amendment (PfA) to include Cohort 3, and provided justification following Column 2 criteria.
ECHA agrees that the criteria to include Cohort 3 are met, because existing information on the Substance itself, and substance(s) structurally analogous to the Substance, derived from available *in vivo* and human studies, shows evidence of immunotoxicity as discussed below.

Annex X, Section 8.7.3., column 2 of REACH defines when the study design needs to be expanded: Cohort 3 (developmental immunotoxicity) may be required by the Agency in case of particular concerns on (developmental) immunotoxicity justified by e.g. existing information on the substance itself, and substance(s) structurally analogous to the Substance, derived from relevant available *in vivo* or non-animal approaches (e.g. evidence of adverse effects on the immune system in studies on adult animals or animals exposed prenatally). ECHA Guidance[3] further specifies that Cohort 3 can be triggered based on "*Information on changes in immune function involving innate (e.g. NK-cell function, phagocytosis and oxidative burst) or acquired immunity (e.g. generation of immunological memory, cytotoxic T-cells and antibody production)*".

In vivo

In the study by Anderson *et al.* (2008)[2], mice were exposed to whole asphalt fumes (35 mg/m^3) or the vapor component of asphalt fumes (11 mg/m^3) for 3.5 hr/d, 5 d/wk. Following exposure, the Immunoglobulin (Ig) M response to T-dependent antigen was measured as plaque forming cells in spleen. When compared to air controls, the exposure to whole asphalt fumes and the vapor component of asphalt fumes resulted in a significant suppression of the IgM antibody response to the antigen challenge: the IgM response (plaque-forming cells in spleen) was suppressed by 53% and 30%, after one week of exposure to whole fumes and vapor component respectively, compared to controls. A significantly reduced ability to produce antibodies in response to antigen challenge is an adverse change in immune function, i.e. immunotoxicity. Immunotoxicity observed in adult animals may also have an impact on the developing immune system[3]. ECHA notes that the measurement of IgM antibody response is not a standard parameter in any of the existing studies provided in the dossier. The study by Anderson *et al.* (2008) provides new information on immunotoxicity of asphalt fumes and the vapor component of asphalt fumes. The concern for (developmental) immunotoxicity can be followed up in the Cohort 3 of OECD TG 443 which is specifically measuring the IgM antibody response.

The study by Anderson *et al.* (2008) uses fumes from a specified asphalt (PG 64-22), which is not the Substance. However, oxidised asphalt is produced from asphalt and the boundary composition for the Substance identifies constituents such as [redacted]

[2] Anderson SE, Munson AE, Tomblyn S, Meade BJ, Diotte NM. The humoral immune response of mice exposed to simulated road paving-like asphalt fumes. Journal of Immunotoxicology. 2008 Jul;5(3):307-313.
[3] ECHA Guidance R.7a, Section R.7.6.

[redacted], all with a range of [redacted] by 'LCC'. This range shows considerable overlap with the values for asphalt. Specific PAH constituents, such as fluorene, naphthalene and pyrene, are in common. There is thus considerable overlap in the constituents, to the extent that these are described, and asphalt is structurally analogous to the Substance. Moreover, the generation of fume in Anderson *et al.* (2008), and for the PNDT study in the dossier, yields similar properties for the condensate, with e.g. boiling point 50% value at 364 and 345C, respectively. Thus there is reason to believe that the fume derived from asphalt and from oxidised asphalt shares corresponding commonality in constituents, and so the fumes also are structurally analogous.

Moreover, in the range-finding study for the rat inhalation (nose only) repeat dose and reproduction/developmental screening study, the test material for the Substance causes decreased thymus weight, and this decreased thymus weight indicates overt immunotoxicity (page 23-25 of your [redacted] Importantly, the reduced thymus weight is evident at a concentration of 1000 mg/m^3: absolute thymus weight is reduced by 44% in males and 52% in females, compared to controls. You consider that there is no significant effect at 300 mg/m^3, however ECHA notes that at this dose level, the thymus weight was significantly reduced in females by 24% compared to controls, and by 13% in males (although it did not reach statistical significance). Although you have concluded that there is a "lack of dose-response for thymus effects" in this study, there is a large and statistically significant decrease in thymus weight in both males and females at 1000 mg/m^3, and at 300 mg/m^3, male and female thymus weights are considerably lower than control values, although only the absolute female weight is statistically significant. ECHA considers that there is a dose response relationship, and that the decrease in thymus weight seen at 300 mg/m^3 is biologically significant. Given that the top dose concentration for the EOGRTS (OECD TG 443) study will be in excess of 300 mg/m^3, there is a reasonable expectation that there will be a significant decrease in thymus weight in the treated animals. In view of your hypothesis of PAH-mediated toxicity, and the known involvement of thymic atrophy within this hypothesis, the decreased thymic weight (56 or 48% of absolute control values at high dose) is a severe finding related to an immune organ.

Human study

The study by Karakaya *et al.* (1999)[4] investigated rakermen in road paving operations. In this study, a significant increase of the percentage of CD4+ cells (46% vs. 35% in unexposed controls) and of the CD4+/CD8+ ratio (1.9 vs. 1.47 in controls) as well as enhanced levels of monocytes (9.1% vs. 5.1% in controls) and serum IgG (1464 mg/dl vs. 1288 mg/dl in controls) were observed in the asphalt fume exposed group. In line with the *in vivo* data (Anderson *et al.*, 2008), a reduction in IgM level was observed in the exposed group (144 mg/dl vs. 179 mg/dl in controls) also in this study, although it did not reach statistical significance. These changes in the innate immune system (increased number of monocytes) and acquired immunity (T cell number and ratio, changes in antibody production) are signs of altered immune function, indicating a concern for (developmental) immunotoxicity[3]. The workers were exposed to unspecified asphalt (also referred to as bitumen), and exposure to pyrene (a known constituent of the Substance) was measured via a metabolite. ECHA considers that the workers were exposed to substances which were structurally analogous to the Substance, for the reasons as set out for Anderson *et al.* (2008) above. ECHA considers that this study is methodologically robust, but that the experimental design must be taken into account; for this reason, ECHA considers that this study is only supporting information

[4] Karakaya A, Yücesoy B, Turhan A, Erdem O, Burgaz S, Karakaya AE. Investigation of some immunological functions in a group of asphalt workers exposed to polycyclic aromatic hydrocarbons, Toxicology, Volume 135, Issue 1, 1999, Pages 43-47

for the concern.

Your comments on the PfA

In your comments to the PfA, you consider that the substances tested in the studies by Anderson *et al.* (2008) and Karakaya *et al.* (1999) are not specified, and thus performing read-across to the Substance without any justification is invalid. You also consider that the validity of the Karakaya *et al.* (1999) study is questionable as it does not take into account known confounders (e.g. diesel exhausts and tool cleaning solvents), and it did not show that smoking would have any impact on the biomarkers of exposure or immune effects.

ECHA has amended the decision to take into account your comments.

For the range-finding study on the Substance, you consider that there was lack of dose-response for thymus effects. The thymus weights were significantly reduced at 300 mg/m^3 and 1000 mg/m^3, and ECHA considers this is a dose-dependent manner (males from -13% to -44% and females from -24% to -52%, respectively). ECHA has amended the reasoning above.

Finally, you consider that the above-mentioned studies report transient effects which do not imply an adverse immunotoxic effect. In the absence of any explanation for why you consider the effects seen to be transient, ECHA considers that the effects on immune system, as described above, are not demonstrably transient. Further ECHA notes that transience is a factor to be considered in the judgment on adversity and is not necessarily dispositive. ECHA's reasoning on adversity is set out above.

Constituents of the Substance

The test material for the registered substance contains [redacted]). It is known that specific PAHs can cause immunotoxicity. For example, benzo(a)pyrene is known to cause developmental immunotoxicity (Urso & Gengozian 1980, 1984)[5],[6]. This adds to the concern that the Substance may be immunotoxic, since it contains a constituent, [redacted] which is known to cause (developmental) immunotoxicity, and the Substance contains many constituents which are structurally related; these structurally related PAHs may also cause immunotoxicity. Moreover, the test material for the Substance causes toxicity in the thymus at 300 and 1000 mg/m^3. This is also typical immunotoxicity caused by benzo(a)pyrene. In line with your hypothesis that 3/4-7 ring PAHs are responsible for the reprotoxic effects of the substance, the toxicity seen with the test material of the registered substance is consistent with toxicity from PAHs, which are known to be immunotoxic.

Your comments on the PfA

In your comments, you refer to publications from Kriech *et al.* (2007)[7] and Preiss *et al.*

[5] Urso P & Gengozian N (1980) Depressed humoral immunity and increased tumor incidence in mice following in utero exposure to benzo[a]pyrene, Journal of Toxicology and Environmental Health, 6:3, 569-576
[6] Urso P & Gengozian N (1984) Subnormal expression of cell-mediated and humoral immune responses in progeny disposed toward a high incidence of tumors after *in utero* exposure to benzo[a]pyrene, Journal of Toxicology and Environmental Health, 14(4), 569-584
[7] Anthony J. Kriech, Linda V. Osborn, Herbert L. Wissel, Adam P. Redman, Lisa A. Smith & Todd E. Dobbs (2007) Generation of Bitumen Fumes Using Two Fume Generation Protocols and Comparison to Worker Industrial Hygiene Exposures, Journal of Occupational and Environmental Hygiene, 4:sup1, 6-19, DOI: 10.1080/15459620701358102

(2006)[8]. Based on these publications, you conclude that the PAH content, especially BaP, in oxidised asphalt and bitumen fume is very low or undetectable. Due to lack of constituents, you consider that there is no need for developmental immunotoxicity testing.

In the PNDT study on the Substance, the fume from the Substance has total PAH content > 400 µg/g (not including naphthalene) and BaP was routinely detected. As explained above, specific PAHs are known to cause immunotoxicity and BaP is one example of those PAHs. The toxicity seen with the test material of the registered substance is consistent with toxicity from PAHs, and therefore there is a concern for developmental immunotoxicity.

In your comments, you state that "Urso & Gengozian published in 1980 and 1984 studies dosing mice extremely high levels of benzo(a)pyrene (BaP) in utero." ECHA considers this observation does not detract from the results obtained.

Conclusion

As explained above, there is information showing that the Substance causes adverse effects in immune organs. Furthermore, constituents of the Substance are known to cause (developmental) immunotoxicity. Further, as explained above, there is information on substance(s) structurally analogous to the Substance derived from available *in vivo* studies showing evidence of changes in immune response and, as supporting evidence, from epidemiological studies showing changes in number and ratio of T cells. Therefore, the developmental immunotoxicity Cohort 3 must be conducted because there is a particular concern on (developmental) immunotoxicity.

Species and route selection

You proposed testing by inhalation route in rats. ECHA agrees with your proposal.

In your comments to the draft decision, you agreed to the need to conduct an EOGRT study with the Substance.

You further noted that you proposed to test the Substance via inhalation route. ECHA acknowledged that and corrected an administrative mistake in its draft decision.

In your comments to the draft decision, you also noted a lack of clarity regarding dose level setting. ECHA confirms that, regarding dose level, the other cohorts have to be tested at the same dose level as that where fertility effects are expected to be found.

Outcome
Under Article 40(3)(b) of REACH, you are requested to carry out the proposed test under modified conditions, as explained above with the Substance.

Further expansion of the study design

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) were identified. However, you may expand the study by including the extension of Cohort 1B as well as Cohorts 2A and 2B if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and

[8] Preiss A, Koch W, Kock H, Elend M, Raabe M, Pohlmann G. Collection, validation and generation of bitumen fumes for inhalation studies in rats Part 1: Workplace samples and validation criteria. Ann Occup Hyg. 2006 Nov;50(8):789-804. doi: 10.1093/annhyg/mel047. Epub 2006 Jul 13. PMID: 16840433.

conditions which are described in Column 2, Section 8.7.3., Annex IX/X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[9].

[9] ECHA Guidance R.7a, Section R.7.6.

Appendix B: Procedural history

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 4 June 2019.

ECHA held a third party consultation for the testing proposals from 25 June 2019 until 9 August 2019. ECHA did not receive information from third parties.

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.

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

In your comments you agreed to the draft decision. 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.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-72 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix C: Observations and technical guidance

1. This testing proposal examination decision does not prevent ECHA from initiating compliance checks at a later stage on the registrations present.

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(s).

3. 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 must 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'[10].

4. Test material

Selection of the test material(s) for UVCB substances

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.

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 relevant

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

constituents of the test material and their concentration values and other parameters relevant for the property to be tested, as specified below. 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.

You have provided the following relevant documents in your registration dossier:

In IUCLID section 7.8.1:

Oxidised asphalt testing proposal for the extended one generation reproductive toxicity study (EOGRTS), November 2017;

In IUCLID section 7.8.2:

Oxidised asphalt PNDT Fume Collection and Validation report, January 2018;
Oxidised asphalt PNDT Test Item Certification report (Final Report 12G17009);
Appendix K1: Overview of Analytical data (Final Report 12G17009).

Considering the specific characteristics of the registered substance, in identifying each constituent, the following characteristics must be reported, to the extent of the level of details in *"Oxidised Asphalt: Fume Collection and Validation"* and *"Oxidised Asphalt: PNDT Test Item Certificate Report 12G17009*" documents, provided by you and mentioned above:

1) Total Hydrocarbon Content (THC) / Total Organic Matter (TOM): the amount of actual fume concentration in the exposure atmosphere (can be converted to THC by application of a conversion factor obtained by analysing against a reference oil). IR analysis of aliphatic CH groups according to BIA method 6305 quantified by a standard reference oil (mg THC in Mineral Oil Equivalents (ME) / m^3;

2) Boiling Point Distribution (BPD):
Compared favourably to work place samples to show that this test material provided a conservative worst case testing sample;

3) Fluorescence:
Total polycyclic aromatic hydrocarbon (PAH) content calibrated against diphenylanthracene (DPA);

4) PAH profile, as minimum, the following constituents, in µg/g, and their alkylated derivatives:

- Naphthalene,
- Acenaphthylene,
- Acenaphthene,
- Fluorene,
- Phenanthrene,
- Anthracene,
- Fluoranthene,
- Pyrene,
- Benz(a)anthracene,
- Triphenylene,
- Chrysene,
- Benzo(b)fluoranthene,
- Benzo(k)fluoranthene,
- Benzo(e)pyrene,
- Benzo(a)pyrene,
- Indeno(1,2,3-cd)pyrene,
- Dibenz(ah)anthracene,

- Benzo(ghi)perylene.

5) typical concentrations per hydrocarbon classes of the bulk material, as minimum, wt%:
- Saturated hydrocarbons;
- Aromatic hydrocarbons;
- Polar hydrocarbons;
- Asphaltenes.

6) Additional details on the test material characterisation, to the extent of the level reported in *"Oxidised Asphalt: Fume Collection and Validation"* and *"Oxidised Asphalt: PNDT Test Item Certificate Report 12G17009*" documents, provided by you and mentioned above.

7) Full reports for fume collection and validation, addressing the composition of the condensate collected at the manufacturing site against actual workplace fume samples through a workplace monitoring campaign to ensure that the tested material is representative of real-life exposures, must be provided together with the EOGRTS study results in the updated dossier.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[11].

5. List of references of the ECHA Guidance and other guidance/ reference documents[12]

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)[13]

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
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.

[11] https://echa.europa.eu/manuals
[12] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[13] 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.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

OECD Guidance documents
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Appendix D: Addressees of this decision and the corresponding information requirements applicable to them

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

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