~~Confidential~~

Helsinki, 04 October 2021

Addressees
Registrants of Joint_PIP_110-85-0 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
11/12/2014

Registered substance subject to this decision ("the Substance")
Substance name: Piperazine
EC number: 203-808-3
CAS number: 110-85-0

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***10 July 2023***.

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

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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

B. Information required from all the Registrants subject to Annex IX of REACH

1. In vivo genotoxicity study:

   Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2; test method OECD TG 488[1] from 2020) in transgenic mice or rats, oral route on the following tissues: liver, and glandular stomach, with the Substance; germ cells and duodenum must be harvested and stored for up to 5 years. The duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive.

   OR

   In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum, with the Substance.

2. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

[1] The updated OECD TG 488, adopted on 26 June 2020, is available on OECD website at https://www.oecd-ilibrary.org/docserver/9789264203907-en.pdf?expires=1596539942&id=id&accname=guest&checksum=D552783C4CB0FC8045D04C88EFFBFA66

Reasons for the request(s) are explained in the appendices entitled "Reasons to request information required under Annexes VII to X of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

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

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

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

How to comply with your information requirements

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

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

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

Failure to comply

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

Authorised[2] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[2] 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 to request information required under Annex VII of REACH

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

In your dossier, you have provided a key study, and three supporting studies on the Substance in your dossier:

i. [redacted] 1983, with the following strains, TA 98, TA 100, TA 1535, TA 1537, and TA 1538 which all gave negative results.
ii. [redacted] 1986, with the following strains, TA 98, TA 97, TA 100, TA 1535, which all gave negative results.
iii. Haworth et al. 1983, with the following strains, TA 98, TA 100, TA 1535, TA 1537 which all gave negative results.
iv. [redacted] 1980, with the following strains, TA 98, TA 100, TA 1535, TA 1537, and TA 1538 which all gave negative results.

We have assessed this information and identified the following issue:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[3] (1997). One of the key parameters of this test guideline includes that 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).

The reported data for the studies you have provided do not include the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

The information provided does not cover one of the key parameters required by OECD TG 471.

In your comments on draft decision you argue that "*Piperazine is not a hydrazine. In addition, mechanistic profiling (QSAR Toolboxversion 4.4.1) does not show alerts for DNA reactivity pointing at possible oxidizing mutagenic or crosslinking effects*".

In support of your comments you have provided the following information:

- A QSAR prediction for Piperazine ([redacted].pdf)
- Data Profile for a single molecule: CAS 110-85-0 ([redacted].pdf)
- C-4a 110-85-0_The predicted relevant metabolites from the [redacted].pdf

We have assessed this information and identified the following issue:

Annex XI, Section 1.3. specifies that the following conditions must be fulfilled whenever a (Q)SAR approach is used:

1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and

[3] ECHA Guidance R.7a, Table R.7.7–2, p.557

4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issue(s):

Under ECHA Guidance R.6.1.7.3. a prediction is adequate for the purpose of classification and labelling and/or risk assessment if the following condition is met:

- different metabolites of the same substance are predicted individually.

You provided predictions for the substance and found that piperazine triggers DNA alert Ethylenediamines (including piperazine) "*DNA binding by OECD: Schiff base formers - Chemicals Activated by P450 to Glyoxal".* However, you argue that "*The relevance of this alert is limited because ADME data on Piperazine are indicating that most of the substance is excreted unchanged. (Study in pigs: "the major part of the resorbed compound is excreted as unchanged piperazine during the first 48 h"; EU RAR, 2005).*"

ECHA notes that other softwares, such as Meteor, do predict the formation of one metabolite: 1-Piperazinecarboxaldehyde, which triggers genotoxicity alerts in Toolbox and which is predicted as equivocal in Sarah software. You also acknowldeged that Glyoxal may be a possible metabolite of concern. For glyoxal, OECD QSAR Toolbox found study showing positive results with and without activation in TA 102 (reliability 1). Glyoxal is also subject to harmonised classification as Muta.2.

Taking into account available information either provided by you or available in the public domain, ECHA considers that the metabolic bioactivation of piperazine cannot be ruled out.

Therefore, you have not demonstrated that the prediction is adequate for the purpose of classification and labelling and/or risk assessment.

Therefore, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) should be performed using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

Appendix B: Reasons to request information required under Annex IX of REACH

1. ***In* vivo genotoxicity study (Annex IX, Section 8.4, column 2)**

Under Annex IX, Section 8.4, column 2 of REACH, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study.

In your comments to draft decision you raised the question "*why the in vivo genotoxicity study (Annex IX, section 8.4,column 2) was categorized under Appendix C: Reasons to request information required under Annex IX of REACH, as according to Annex VIII (section 8.4), appropriate in vivo mutagenicity studies shall be consideredin case of a positive result in any of the genotoxicity studies in Annex VII or VIII*". Indeed if this information is missing either at Annex VIII or Annex IX it can be requested. The reason it was requested under Annex IX is justified by the tonnage band of the adressees in this joint submission.

In relation to the first condition, your dossier contains positive results for the *in vitro* gene mutation study in mammalian cells ([redacted] 1980) which raise the concern for gene mutation.

In your comments to draft decision you argue that "*positive result was only obtained with metabolic activation at the highest evaluable concentration showing clear cytotoxicity*, *which was most probably pH-related*". Nevertheless, both in the study provided in the submission used for evaluation as well as in the version submitted during the comments, it is noted that there are positive findings at concentrations below cytotoxicity threshold. Therefore, the argument of pH influence is not sufficient to invalidate the outcome of the study.

We acknowledge the provided information related to the possible influence of cytotoxicity on pH and consequently on the reading outcome. However, from the data provided it seems that this condition may be hypothesised only for the highest concentration used in the study of [redacted], 1980 (key study reliability 1, equivalent to OECD 476 in the dossier on which the evaluation was based, renamed Myhr (1980) reliability 2, non-testing guideline in the comments).

In the comments you also proposed to elevate the supporting study of [redacted] 1987 with piperazine phosphate (reliability 2, no-guideline followed) which did not have a robust study summary in the evaluated dossier, to key study reliability 1, equivalent or similar to OECD 476 (while keeping in principle of method other than guideline: "Mouse lymphoma L5178Y fluctuation assay; based on Cole J and Arlett CF (1976). Ethyl methanesulphonate mutagenesis with L5178Y mouse lymphoma cells: a comparison of ouabain, thioguanine and excess thymidine resistance.Mutat. Res. 34, 507-526."). In your comments you also provided the robust study summary for this study showing negative results. However, as positive results were obtained in another reliable study with the substance, an in vivo gene mutation study is still triggered.

In relation to the second condition, your dossier contains the following *in vivo* study:

i. In vivo cytogenicity study ([redacted] 1987) with piperazine phosphate

We have assessed this information and identified the following issues:

ECHA Guidance R.7a clarifies that in order to justify that an *in vivo* somatic cell genotoxicity study does not need to be performed in accordance with Annex IX, Section 8.4, column 2,

the results of the available *in vivo* study must address the specific concern raised by the *in vitro* positive result.

However, the *in vivo* study provided is not addressing the gene mutation concern raised by the *in vitro* data.

The provided *in vivo* tests is not appropriate to address the concern identified by the *in vitro* gene mutation study in mammalian cells. Therefore, the conditions set out in Annex IX, Section 8.4, column 2 are met and the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered.

Test selection

The present decision requests the registrants concerned to generate and submit a reliable *in vivo* somatic cell study.

According to the ECHA Guidance Chapter R.7a[4], the transgenic rodent somatic and germ cell gene mutation assays ("TGR assay", OECD TG 488) and the in vivo mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up a positive *in vitro* result on gene mutation.

Test design

In case you decide to perform the comet assay according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s), performance of the test by the oral route is appropriate.

In line with the OECD TG 489, the test must be performed by analysing tissues from the liver, as primary site of xenobiotic metabolism, glandular stomach and duodenum, as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

In case the TGR assay is appropriate and you decide to conduct this test, according to the test method OECD TG 488, the test must be performed in transgenic mice or rats and the Substance is usually administered orally.

Based on the recent update of OECD TG 488 (2020), you are requested to follow the new 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals. This updated version provides for a transitional period for the new version. However, ECHA is aware that testing according to the updated OECD TG is already available from CROs and the new study design would provide meaningful germ cell data, so this decision requires the application of the new version.

According to the test method OECD TG 488, the test must be performed by analysing tissues from the liver, as slowly proliferating tissue and primary site of xenobiotic metabolism, glandular stomach and duodenum, as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-

[4] ECHA Guidance Chapter R.7a, Section R.7.7.6.3

chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70ºC) until the analysis of the liver and glandular stomach is completed; the duodenum must then be analysed only if the results obtained for the glandular stomach and the liver are negative or inconclusive.

Germ cells

A subsequent germ cell genotoxicity study (TGR/OECD TG 488, or CA on spermatogonia/OECD TG 483) may still be required under Annex IX of REACH, in case 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

> Therefore, in case you decide to perform the comet assay, you may consider to collect the male gonadal cells collected from the seminiferous tubules in addition to the other aforementioned tissues, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the slides prepared with gonadal cells.
>
> In case you decide to perform the TGR, you must collect the male germ cells at the same time as the other tissues, in order to limit additional animal testing. According to the OECD 488 the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA, in accordance to Annex IX, Section 8.4., column 2, to decide on the need for assessment of mutation frequency in the collected germ cells.
>
> This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

As described above, the TGR or the comet assay include testing at the site of contact for potential genotoxic effects, as well as after systemic exposure. Both tests are considered suitable to follow up the concern on gene mutation for the Substance.

2. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have omitted this information and you provided the following justification: *"Based on acute toxicity studies, aquatic invertebrates are seen to be the most sensitive species."*

We have assessed this information and identified the following issue:

A registrant may adapt this information requirement only on the basis of the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.1 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

Therefore, it is unclear whether your argument refers to any legal ground for adaptation and you have not demonstrated that this information can be omitted.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, while you recognize the rejection of the adaptation of the information requirement, you also specify that you intend to adapt this information requirement under Annex XI, Section 1.2. ('Weight of evidence'). You intend to provide the following justification:

i. The structure as well as the physico-chemical properties of the Substance are clearly identified. The Substance is found not to persist in a acclimated ready biodegradation test showing the likelihood of non persistence in water and soil;
ii. The substance does not produce an alert for protein binding in the schemes by OECD and OASIS (OECD QSAR Toolbox v4.3; see Chapter 2.5 of the updated Read-Across Justification). According to the modified classification scheme of Verhaar, the mode of action of the Substance is narcosis of baseline toxicity. Therefore, it can be concluded that the Substance has no specific mode of action and critical long-term effects are not to be expected;
iii. You specify that no information on long-term toxicity to fish is available for the substance and that no reliable QSAR predictions or in-vitro results for long-term toxicity to fish are available;
iv. Fish are not the most sensitive aquatic trophic level;
v. The Substance is neither acutely nor chronically hazardous to the aquatic environment according to the CLP-Regulation (EC) No 1272/2008. You based your reasoning on aquatic chronic classification on the result of the data currently available on short-term toxicity to fish and the concept of acute-to-chronic ratio;
vi. You further consider that this information is not needed for the PBT assessment of the Substance as it is concluded no B/vB based on some QSARs estimations;
vii. You refer to Article 25 to REACH to specify that vertebrate animal testing should be undertaken as a last resort.

We take note of your intention to submit an adaptation. However, we emphasize that the justification above does not rely on any source of information that could be used to conclude on long-term fish toxicity.

Relevant information that can be used to support weight of evidence adaptation for long-term toxicity to fish includes similar information that is produced by the OECD TG 210. The following aspects need to be covered: Parameters related to the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage following exposure to the test substance are measured, including:

1) the stage of embryonic development at the start of the test, and
2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3) the appearance and behaviour of larvae and juvenile fish, and
4) the weight and length of fish at the end of the test.

As you did not submit such information, ECHA concludes that there is, in the justification provided in your comments, no weight of evidence adaptation to be assessed. Finally, the use of the acute-to chronic ratio concept on its own is not regarded as providing sufficient weight of evidence to conclude on chronic toxicity (ECHA Guidance R.7.8.5.).

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

OECD TG 210 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[5].

B. Test material

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

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ 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.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[6].

[5] https://echa.europa.eu/practical-guides
[6] https://echa.europa.eu/manuals

Appendix D: Procedure

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

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

The compliance check was initiated on 27 March 2020.

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

You have provided comments during the decision-making phase which were found to be compliant with the information required in the draft decision. Therefore the following requests were removed:

- Short-term toxicity testing on aquatic invertebrates
- Growth inhibition study aquatic plants
- Short-term toxicity testing on fish
- Long-term toxicity testing on aquatic invertebrates
- Ready biodegrability
- Simulation testing on ultimate degradation in surface water
- Identification of degradation
- Bioaccumulation in aquatic species
- In vitro cytogenicity study in mammalian cells or In vitro micronucleus study
- Pre-natal developmental toxicity study (first and second species)

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 amendments and referred the modified draft decision to the Member State Committee.

You provided comments only on the draft decision. Your comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee unanimously agreed on the draft decision in its MSC-75 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

Appendix E: List of references - ECHA Guidance[7] and other supporting documents

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 where relevant.

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 where relevant.

Read-across assessment framework (RAAF, March 2017)[8]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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
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.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[9]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[7] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[8] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[9] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

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

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix F: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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

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