EUROPEAN CHEMICALS AGENCY

Helsinki, 19 February 2020

Addressees
Registrants of [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
19/12/2018

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: N-[4-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthryl)-amino]phenyl]acetamide
EC number: 267-636-0
CAS number: 67905-17-3

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

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***24 November 2021***.

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

1. Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105) with the Substance

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201) with the Substance

3. Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2; test method: EU C.20./OECD TG 211) 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 study under request B.1 has negative results, 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

3. and 4. Combined Repeated Dose Toxicity Study with the reproduction/Developmental Toxicity Screening Test (Annex VIII, Section 8.7.1.; test method: OECD TG 422) in rats, oral route with the Substance

5. Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2; test method: OECD TG 210) with the Substance

6. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.; test

method: OECD TG 209) with the Substance

7. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111) with the Substance

8. Adsorption/desorption screening (Annex VIII, Section 9.3.1.; using an appropriate test method) with the Substance

Conditions to comply with the requested information

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 Annex VII of REACH, if you have registered a substance at 1-10 tonnes per annum (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- you have to comply with the requirements of Annexes VII and VIII of REACH, if you have registered a substance at 10-100 tpa;

The Appendix on general considerations addresses common arguments that are applicable throughout the present decision 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 test material used to perform the required studies must be selected and reported in accordance with the specifications prescribed in the Appendix entitled Observations and technical guidance.

The data sharing obligations of REACH require registrants to ensure that the costs of sharing information are determined in a fair, transparent and non-discriminatory way. Registrants are only required to share the costs of information that they must submit to fulfil the information requirements for their registration.

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. The timeline has been set to allow for sequential testing where relevant.

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 on general considerations

The ECHA Guidance documents referred to in this decision are listed in Appendix F of this decision.

(i) Assessment of the weight-of-evidence adaptations, in light of the requirements of Annex XI, Section 1.2.

You have adapted the following standard information requirements by applying weight-of-evidence (WoE) approaches in accordance with Annex XI, Section 1.2:

- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.);
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.);
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);
- Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2);
- Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.);
- Adsorption/desorption screening (Annex VIII, Section 9.3.1.).

We have assessed this information and identified the following general issue:

ECHA Guidance R.4.4. specifies that a weight-of-evidence adaptation must involve an assessment of the relative values / weights of the several pieces of available information. This assessment must consider for instance the relevance and reliability of the information, the consistency of results/data, the nature and severity of effects. The lines of evidence should be integrated considering their relative values or weights in order to draw a conclusion. The assessment should be documented and included in your technical dossier.

You have not provided documentation in support of any of your weight-of-evidence adaptations. In particular an assessment of the relevance of the selected source of information is lacking.

Hence, as your weight-of-evidence adaptations are not supported by adequate documentation, they do not comply with the general rules of adaptation as set out in Annex XI, Section 1.2. Therefore, your adaptations are rejected.

Specific considerations for the individual endpoints also result in a failure to meet the requirement of Annex XI, Section 1.2. These are set out under the endpoint concerned.

(ii) Assessment of the Qualitative or quantitative structure-activity relationships adaptations, in light of the requirements of Annex XI, Section 1.3.

You have adapted the following standard information requirements by using data derived from Qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3.:

- Water solubility (Annex VII, Section 7.7.);
- Partition coefficient n-octanol/water (Annex VII, Section 7.8.);
- Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.);
- Adsorption/desorption screening (Annex VIII, Section 9.3.1.).

We have assessed this information and identified the following general issue:
Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when the following cumulative conditions are met, in particular:

- the substance falls within the applicability domain of the QSAR model;
- adequate and reliable documentation of the applied method is provided; and
- the results are adequate for classification and labelling and/or risk assessment.

According to ECHA's Practical guide "How to use and report (Q)SARs", section 3.4., a QSAR Model Reporting Format (QMRF) and a QSAR Prediction Reporting Format (QPRF) are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.

Your dossier does not contain QMRF and/or QPRF. In your comments on the draft decisions for the endpoints listed above, you state the following: "*As per the ECHA requirements, we have attached the QMRF report for the predictions attached in these sections to support the results*". However, we note that no QMRF and/or QPRF is attached to your comments on the draft decision.

Because you have not included QMRFs and a QPRFs in your dossier, there is no adequate and reliable documentation for the QSAR predictions. Hence ECHA cannot verify whether the cumulative conditions of Annex XI, Section 1.3. listed above are met.

Your adaptations do not comply with the general rules of adaptation as set out in Annex XI, Section 1.3. Therefore, your adaptations are rejected.

(iii) Assessment of the read-across adaptations, in light of the requirements of Annex XI, Section 1.5.

You have adapted the following standard information requirements by applying read-across approaches in accordance with Annex XI, Section 1.5.:

- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.);
- Short-term repeated dose toxicity (28 day) (Annex VIII, Section 8.6.1.);
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);
- Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.);
- Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.);
- Adsorption/desorption screening (Annex VIII, Section 9.3.1.).

Annex XI, Section 1.5. specifies three conditions which must be fulfilled whenever a read-across approach is used:

(i) 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;
(ii) 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;
(iii) adequate and reliable documentation of the applied method must be provided.

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

For the endpoints listed above, you initially used in your dossier subject to the compliance check data from the following substances:

- (2-hydroxy-4-(octyloxy)phenyl)(phenyl)methanone (EC No 217-421-2);
- Acetanilide (EC No 203-150-7);
- 1,4-Bis(p-tolylamino)anthraquinone (EC No 204-909-5);

- 1-N,4-N-diphenylbenzene-1,4-diamine; N,N'-diphenyl-p-phenylenediamine (EC No 200-806-4);
- sodium 4-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthryl)amino]toluene-3-sulphonate (EC No 224-618-7);
- Disodium 2,2'-(9,10-dioxoanthracene-1,4-diyldiimino)bis(5-methylsulphonate) (EC No 224-546-6);
- 1,4-diamino-9,10-anthraquinone (EC No 204-922-6);
- 1,2-diamino-9,10-dihydroanthracene-9,10-dione (EC No 217-156-2);
- 1-(2-hydroxyethylamino)-4-(methylamino)anthracene-9,10-dione (EC No 219-604-2);
- 1,4-anthraquinone (EC No 211-228-7).

In the draft decision notified to you, we identified the following issue:

> For each of the source of information provided on the source substances, you need to provide a justification that it is relevant to predict the properties of the Substance. You also need to provide an adequate robust study summary of the selected studies to allow an independent assessment of their adequacy, their results and their use for hazard assessment.
>
> However, you had not provided any documentation, in Section 13 of your IUCLID dossier nor in the CSR, to explain your read-across hypothesis and to support that it may provide a reliable basis to predict the properties of the Substance.
>
> Hence, as your read-across adaptations were not supported by adequate documentation, the draft decision indicated that they do not comply with the general rules of adaptation as set out in Annex XI, Section 1.5.

As part of your comments on the draft decision, you provide a document entitled "[redacted]". The justification document includes information on various new source substances with varying degree of structural similarity to the Substance. You justify the reliability of the read-across predictions based on:

- structural similarity (Tanimoto score, common organic functional groups),
- similar physico-chemical properties,
- some similarity in "*mechanistic triggers*" assessed using the OASIS v1.4. and the OECD QSAR Toolbox v3.4,
- fate properties (hydrolysis using the Hydrowin QSAR),
- similar "*market sector uses* [...] *which confirms their similarity thereby use for different toxicity values as they are expected to behave similarly*".

In the attached read-across justification document, you provide two data matrices (one for environmental fate and ecotoxicological endpoints and one for human health endpoints) with the information listed above.Whenever grouping and read-across is used under REACH, Section 1.5 of Annex XI requires explicitly that "*adequate and reliable documentation of the applied method shall be provided*". According to the ECHA Guidance Section R.6.2.3.1 "*the approach should be documented according to an appropriate format in order to justify that the approach may be used instead of testing. The justification for the read-across should include an explanation of the rationale, as well as the assessment including all relevant supporting information*". The Guidance also specifies the following elements that must be included in the documentation of the adaptation:

1. A read-across hypothesis, establishing why a prediction for a toxicological or ecotoxicological property is reliable;
2. Scientific information substantiating that the prediction of the properties is justified for each relevant endpoint, taking into account the structural differences between

the substances;
3. Robust study summaries of the source studies.

We have assessed the information provided in your comments on the draft decision and identified the following issues:

1. *"Adequate and reliable documentation of the applied method"* in the form of a read-across hypothesis establishing why a prediction of property is reliable

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. 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 (read-across approach). A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the substances[2]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

In your read-across justification you state that *"the read across substances are selected based on structural as well as functional similarity of the substances. Similarity were checked on the base moiety of the read across substance and based on these different categorization approaches, they are expected to perform similarly".*

However, similarity in chemical structure, in physico-chemical properties and functional similarity do not necessarily lead to predictable or similar human health and ecotoxicological properties in other endpoints. As described above, a well-founded hypothesis is needed to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities and differences between the source substance(s) and your Substance.

2. *"Adequate and reliable documentation of the applied method"* in the form of scientific information substantiating that the prediction of the properties is justified for each relevant endpoint

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. Thus, in addition to the property/endpoint being read-across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals"."* (ECHA Guidance R.6, Section R.6.2.2.1.f). 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 must include relevant and reliable information (experimental studies or reliable predictions) to support the claimed similarity in physico-chemical, ecotoxicological and toxicological properties of the Substance and source substances. Variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g.

[2] ECHA Guidance R.6

interactions with receptors and enzymes). Therefore the information provided to support the predictions must explain why the differences in the chemical structures should not influence their toxicological, ecotoxicological and fate properties or should do so in a regular pattern (ECHA Guidance R.6., Section 6.2.1.).

To support similarity of properties of the Substance and source you have provided:

a) some information on physico-chemical characteristics of the Substance and the source substances. However, you have not provided reliable information (experimental studies or reliable predictions) on basic physico-chemical properties (e.g. water solubility, Log Kow) for all source substances and no reliable information on these physico-chemical properties is available for the Substance. Therefore, no comparison of the physico-chemical properties of the substance can be made.

b) an assessment of the impact of the structural differences using QSAR models. However, whilst the reported QSAR predictions may constitute relevant information in support of the read-across approach, considering the complexity of the (eco)toxicological endpoints under consideration, these QSAR predictions cannot be seen, on their own, as sufficient evidence to support similarity in toxicological and ecotoxicological properties. Therefore, you have not characterised the structural differences between the substances and demonstrated that these differences will not impact the predictions.

c) a statement that the source substances are used in the same market sector which, according to you, "*confirms their similarity thereby use for different toxicity values as they are expected to behave similarly*". Similarity in market sector uses do not inform on the toxicological or ecotoxicological properties of the Substance and the selected source substances and consequently do not constitute relevant supporting information.

The technical dossier does not include any other relevant, reliable and adequate information on the properties under consideration for your Substance and the source substances, e.g. bridging studies of comparable design and duration.

In the absence of relevant, reliable information, you have not established that the Substance and of the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

3. "*Adequate and reliable documentation of the applied method*" in the form of a robust study summary of each source study

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*". When properties of a substance are read-across from a source study conducted with an analogue substance to fulfil an information requirement, this source study provides key data for the hazard assessment. Therefore a robust study summary providing information allowing to make an independent assessment of the study must be provided for each source study used in read-across approaches.

In the document attached to your comments to the draft decision you have identified the studies conducted with analogue substances that you intend to use as source studies in your read-across approach.

You have not provided robust study summaries for any for these source studies. In particular you have not provided detailed information on the methods, results and conclusions of these studies allowing for an independent assessment of the studies. In the absence of such information, we cannot assess the reliability of the information used to predict the properties of the Substance.

Conclusion

For all the reasons presented above, the information included in your technical dossier and provided in your comments to the draft decision taken together does not meet the requirements of Annex XI, 1.5 of the REACH Regulation.

The deficiencies identified above are manifest breaches of the obligation to submit "*adequate and reliable documentation of the applied method*" set out in Section 1.5 of Annex XI. While the required documentation is simply missing, ECHA is not in a position to verify if any documentation would be adequate and reliable.

If, in reply to the present decision, you still submit a read-across adaptation without:

1. an hypothesis establishing why a prediction for a toxicological or ecotoxicological property is reliable for each relevant endpoint; and
2. scientific information substantiating that the prediction of the properties is justified for each relevant endpoint; and
3. a robust study summary of each source study;

your adaptation will be considered manifestly unreasonable. In this case, the adaptation will not be subject to the follow-up compliance check process set out in Articles 42 and 41 of the REACH Regulation.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, 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 the REACH Regulation.

1. Water solubility (Annex VII, Section 7.7.)

Water solubility is a standard information requirement in Annex VII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.3. You have provided a water solubility estimate predicted using the WSKOW model (v1.42) (2017), which indicates that the substance is poorly water soluble.

For the reasons explained in the Appendix on General considerations regarding Qualitative or quantitative structure-activity relationships (QSARs), your adaptation is rejected. Therefore, the information requirement is not fulfiled.

In your comments on the draft decision, you specify that you intend to update your dossier with experimental data using an appropriate technical guideline for this endpoint.

In a later update of your dossier, you have provided a robust study summary for a water solubility study according to OECD TG 105 with the shake-flask method. The concentration of the test substance was determined using UV spectrophotometry. The water solubility was determined to be 0.21 mg/L at pH 6.85.

We have assessed this information and identified the following issue:

> EU test method A.6 and OECD TG 105 establish the requirements for the data to be reported for a water solubility study. These test guidelines describe two methods (the column elution method and the flask method) for conducting the study. The test method must be selected based on a water solubility estimate obtained in a preliminary study. For substances with preliminary water solubility below 10 mg/L the column elution method must be used.
>
> The water solubility was determined to be 0.064 mg/L in the preliminary study, which indicates that the substance is poorly water soluble. The full test was performed using the shake flask method.
>
> The reported result falls outside of the applicability domain of the flask method and the test should have been conducted with the column elution method.

Therefore the information requirement is not fulfilled.

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

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:

(i) a weight-of-evidence record including a summary of the studies (ii) and (iii) below;
(ii) a study by [redacted] (2002) with the source substance 1,4-diamino-9,10-

anthraquinone (EC No 204-922-6);

(iii) a study by [redacted] (2002) with the source substance 1,2-diamino-9,10-dihydroanthracene-9,10-dione (EC No 217-156-2).

We have assessed the information you provided in your dossier and identified the following issues:

A. For the reasons explained in the Appendix on General considerations regarding weight-of-evidence and read-across, your adaptations are rejected.

B. Annex XI, Section 1.1.2. imposes a number of cumulative conditions for a non-guideline study to be considered equivalent to a guideline study. In particular, the study must provide an adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3). EU C.3 and OECD TG 201 are the preferred guidelines to fulfil this information requirement. These guidelines in combination with the revised OECD Guidance Document 23 (ENV/JM/MONO(2000)6/rev1) requires that the following conditions are met (among others):
   - the test endpoint is inhibition of growth, expressed as the logarithmic increase in biomass during the exposure period;
   - effect concentrations based on the measured values rather than nominal values unless the test concentrations are maintained within 20% of the measured initial concentrations throughout testing;
   - a reliable monitoring of exposure concentrations must be available. For difficult to test substances, including poorly water soluble substance, a sufficiently sensitive analytical method is particularly necessary for the analysis of the test substance in the test solution. The possibility of losses during sampling, sample treatment and analysis must be considered and documented.

   The study by [redacted] (2002) was not conducted according to any recommended guideline and the parameter monitored is the percentage inhibition of yield. This parameter is only rergarded as an additional endpoint in recommended guidelines. Furthermore, no analytical monitoring of exposure concentrations was performed.

   Therefore the study by [redacted] (2002) does not comply with the specific rules of adaptation as set out in Annex XI, Section 1.1.2. as it does not provide a reliable coverage of the key parameter foreseen to be investigated in an OECD TG 201 study and it does not fulfil the information requirement.

In your comments on the draft decision you specify that you have self-classified the substance as Aquatic Acute 1 based on the results of the study by [redacted] (2002). You further explain that you intend to include in your dossier information on additional source substances. You provide a brief summary of the following studies:

(i) a study according to OECD TG 201 on *Selenatrum capricornutum* cited from the OECD SIDS (1996) on 1-Aminoanthraquinone (EC No 201-423-5);

(ii) a study according to OECD TG 201 on *Selenatrum capricornutum* cited from the Gsbl database (2017) on 2-Ethylanthraquinone (EC No 201-535-4).

We have assessed this additional information from your comments and identified the following issues:

C. Self-classification as aquatic 1 is not regarded as a valid justification to adapt this information requirement.

D. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

E. To fulfil the information requirement, the study has to be growth inhibition study on aquatic plants in accordance with OECD TG 201. The key parameters of the OECD TG 201 include:
   - a description of the test design including the spacing factor of test concentrations,
   - details on sampling and on analytical monitoring of the test concentrations,
   - the parameter monitored (reduction of cell density or specific growth rate compared to control),
   - The reporting of raw data to allow verifying that the validity criteria of OECD TG 201 were met.

   In your comments on the draft decision, you provide brief summaries from secondary sources on the growth inhibition studies on 1-Aminoanthraquinone (EC No 201-423-5) and 2-Ethylanthraquinone (EC No 201-535-4). You did not provide the information listed above. Therefore the documentation of these studies is insufficient and does not allow an independent assessment of their adequacy, the reliability of the reported results and their use for hazard assessment. The study summaries cannot therefore be considered as reliable information in support your read-across adaptation.

Therefore, the information requirement is not fulfiled.

3. Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2).

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII to REACH. However, pursuant to Annex VII, section 9.1.1., column 2, for poorly water soluble substances (i.e. water solubility below 1 mg/L) long-term toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5.) must be considered instead of an acute test.

You have provided a key study performed according to OECD TG 202 (2005). You have not provided any data on long-term toxicity to aquatic invertebrates.

We have assessed the information from your dossier and additionnal considerations you provided in your comments and we note the following issue:

Annex VII, section 9.1.1., column 2, requires to perform a long-term toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5.) instead of an acute test when the substance concerned is poorly water soluble (*i.e.* water solubility below 1 mg/L). Poorly water soluble substances require longer time to reach steady-state conditions. Hence, the short-term tests may not give a true measure of toxicity for this type of substances.

Based on the new water solubility study provided in an update of your dossier the Substance is regarded as poorly water soluble.

In your comments on the draft decision, you consider that "*as per Annex VIII, long-term toxicity data on aquatic invertebrates is not the standard* [information] *requirement*" and that "*since the Short-term toxicity to aquatic invertebrate has the GLP study to fulfil the classification for aquatic invertebrate end point*".

As explained under request A.1., the new water solubility study is not compliant with the recommended test guideline as the full test was not performed according to the appropriate method. However, this study includes a valid preliminary test which already allows to conclude that the Substance is poorly water soluble (i.e. water solubility < 1 mg/L). Hence, we disagree with your comment that the short-term study provided in your dossier is adequate to fulfil this information requirement. Therefore, we conclude that a long-term toxicity test must be conducted in lieu of the short-term test.

Therefore the information requirement is not fulfilled.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, 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 the REACH Regulation.

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. To fulfil the information requirement, the study has to be an in vitro chromosomal aberration test or an in vitro micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively (ECHA Guidance R.7a, Table R.7.7-2).

Your dossier does not include a key study providing equivalent information to an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study (OECD TG 473 or OECD TG 487). In the endpoint summary section for genetic toxicity, you provide a brief summary of an *in vivo* micronucleus study in mice.

We understand that you have sought to adapt the information requirement according to Annex VIII, Section 8.4.2., column 2.

We have assessed the information you provided in your dossier and identified the following issues:

A. According to Annex VIII, Section 8.4.2., column 2, a "*study does not usually need to be conducted if adequate data from an in vivo cytogenicity test are available*". The *in vivo* study must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively (ECHA Guidance R.7a, Table R.7.7-3). To be considered adequate, an *in vivo* micronucleus study must meet the requirements of OECD TG 474, and more specifically:
   - the study must include a minimum of three dose levels for the treated groups;
   - at least 4000 immature erythrocytes per animal must be scored for the incidence of micronucleated immature erythrocytes.

   In the brief summary of an *in vivo* micronucleus study reported in your dossier, you indicated that "*mice were treated [...] at a dose level of 0 or 3000 mg/kg bw*" and that "*1000 polychromatic erythrocytes were counted for each animal*".

   Therefore the study provided does not fulfil the conditions for adapting the information requirement with an *in vivo* micronucleus study.

B. Furthermore, for any study used to conclude on a given intrinsic property of the Substance, a robust study summary must be provided (Articles 3(28) and 10(a)(vii) and Annex I, Section 1.1.4. of REACH). A robust study summary must cover critical information and allows for an assessment of the validity and reliability of the study. For an *in vivo* micronucleus study in mice, it must include:
   - the technical guideline followed, if any;
   - the GLP compliance of the study;
   - a clear description of the identity and composition of the test material;
   - if a positive control group (or scoring control) was included and a statistically significant increase in the induced response compared with the concurrent

negative control was observed;
- the raw data of the study in a tabulated form (i.e. proportion of immature among total (immature + mature) erythrocytes determined for each animal by counting a total of at least 500 erythrocytes for bone marrow and 2000 erythrocytes for peripheral blood; results of the scoring of at least 4000 immature erythrocytes per animal for the incidence of micronucleated immature erythrocytes).

The robust study summary submitted in your technical dossier does not contain the information listed above. Therefore the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

Therefore, the provided information is not adequate to adapt the information requirement according to Annex VIII, Section 8.4.2., column 2 and your adaptation is rejected.

In your comments on the draft decision, you did not provide comments on the above assessment of the information currently included in your dossier. Instead you provide brief summaries of the following studies:
- an *in vitro* mammalian chromosome aberration study (guideline not specified) mentioned in an authoritative database (J-check 2010) on 1-amino-9,10-dihydroanthracene-9,10-dione (EC No 201-423- 5);
- an *in vitro* mammalian chromosome aberration study according to OECD TG 473 mentioned in an authoritative database (J-check 2010) on 1-chloro-9,10-dihydroanthracene-9,10-dione (EC No 201-421-4).

We have assessed this additional information from your comments and identified the following issues:

C. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

D. To fulfil the information requirement, the study has to be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively (ECHA Guidance R.7a, Table R.7.7-2). The key parameters for the OECD TG 473 include:
   - that at least 300 well-spread metaphases must be scored per concentration;
   - information on cell cycle length, doubling time or proliferation index is provided;
   - a rationale for selection of concentrations and number of cultures including, cytotoxicity measurements;
   - historical negative (solvent) and positive control data (with ranges, means and standard deviations and 95% control limits for the distribution, as well as the number of data).

   In your comments on the draft decision, you provide brief summaries from secondary sources of the studies listed above. You report that for these two studies only 200 metaphases were scored per concentration. Furthermore you have not provided the information listed above. Therefore these studies do not provide equivalent information to OECD TG 473 studies.

Therefore, the information requirement is not fulfilled.

2. Only if the study under section B.1. has a negative result: 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.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:

(i) a weight-of-evidence record including a summary of the studies (ii) and (iii) below;
(ii) a study performed according to OECD TG 476 (4 hr treatment) from a secondary source with the source substance sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate (EC No 224-618-7);
(iii) a study performed according to OECD TG 476 (24 hr treatment) from a secondary source with the source substance sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate (EC No 224-618-7).

We have assessed the information you provided in your dossier and identified the following issues:

A. For the reasons explained in the Appendix on General considerations regarding weight-of-evidence and read-across, your adaptations are rejected.

B. For any study used to conclude on a given intrinsic property of the Substance, a robust study summary must be provided (Articles 3(28) and 10(a)(vii) and Annex I, Section 1.1.4. of REACH). A robust study summary must cover critical information and allows for an assessment of the validity and reliability of the study. For an *in vivo* mammalian gene mutation study, it must include:
   - adequate information that the maximum concentration tested induced 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;
   - the response for the concurrent negative control showing it was inside the historical control range of the laboratory;
   - the number of cells treated and number of cells sub-cultured for each culture;
   - cytotoxicity measurements and other observations if any;
   - the number of colonies in non-selective medium and number of resistant colonies in selective medium, and related mutant frequencies.

   The robust study summary for the OECD TG 476 study on the source substance sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate (EC No 224-618-7) included in your technical dossier does not include the information listed above.

   Therefore the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments on the draft decisions, you further explain that you intend to support the lack of mutagenic potential of the Substance using additional data on a source substance and you provide a brief summary of an *in vitro* mammalian cell gene mutation test (no guideline

specified) cited from a SCCS Report (2013) on Disodium 2,2'-(9,10-dioxoanthracene-1,4-diyldiimino)bis(5-methylsulphonate) (EC No 224-546-6). Finally, you also state that "*in annex VIII OECD 476 is not a standard data requirement*".
We have assessed this additional information from your comments and identified the following issues:

C. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

D. To fulfil the information requirement, the study has to be an in vitro gene mutation study in mammalian cells in accordance with OECD TG 490. The key parameters of the OECD TG 490 include:
   - an adequate description of the test material (i.e. purity, chemical identification of impurities);
   - an adequate number of cells treated and of cells sub-cultured for each culture;
   - information on historical negative (solvent) and positive control data (concentrations and solvents);
   - an adequate reporting of the test results (i.e. raw data in a tabulated form).

   In your comments on the draft decision, you provide a brief summary of the above study. However, this summary does not cover any of the key elements listed above. Hence, without this information, the documentation submitted does not allow for an assessment of validity and reliability of the study.

Therefore the information requirement is not fulfilled.

3. Short-term repeated dose toxicity (28 day), oral route (Annex VIII, Section 8.6.1.)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:
(i) a weight-of-evidence record including a summary of the studies (ii) and (iii) below;
(ii) a reference to a secondary source (SCCS report, 2013) summarizing a 13-week oral study in Sprague-Dawley rats with the source substance sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate (EC No 224-618-7);
(iii) a reference to a secondary source (SCCS report, 2013) summarizing a 13-week oral study in Wistar rats with the source substance sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate (EC No 224-618-7).

We have assessed the information you provided in your dossier and identified the following issues:

A. For the reasons explained in the Appendix on General considerations regarding weight-of-evidence and read-across, your adaptations are rejected.

B. For any study used to conclude on a given intrinsic property of the Substance, a robust study summary must be provided (Articles 3(28) and 10(a)(vii) and Annex I, Section

1.1.4. of REACH). A robust study summary must cover critical information and allows for an assessment of the validity and reliability of the study. For a repeated dose toxicity study, it must include:

- details on sampling and on analytical monitoring of the test concentrations, details on the preparation of the test solutions, description of the test design and test conditions, and identification of the test material and a specification of organs examined for histopathology.

Your technical dossier does not include the information listed above. In your comments on the draft decisions, you provide further details on the preparation of the test solutions, the test design and the test conditions. However, this additional information does not cover all elements listed above, including adequate information on the identification of the test material and a specification of organs examined for histopathology.

Therefore the documentation of these studies is insufficient and does not allow an independent assessment of their adequacy, their results and their use for hazard assessment.

Furthermore in your comments on the draft decision you have provided a brief summary of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) cited from the J-CHECK online database (2010) with the source substances 1,8-Dihydroxy–4-nitro-5-(phenylamino)anthracene-9,10-dione (EC No 243-632-4).

We have assessed this additional information from your comments and identified the following issues:

C. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

D. To fulfil the information requirement, the study has to be a short-term repeated dose toxicity (28 day) study in accordance with OECD TG 407/422. The key parameters of the OECD TG 407 and 422 include:
   - adequate information on the chemical identity of the test material (i.e. purity, chemical identity of impurities), and
   - adequate reporting of the results as described in "Test report" of the corresponding OECD TG.

   However, you have not provided the information listed above. Therefore the documentation of this study is insufficient and does not allow an independent assessment of its adequacy, its results and its use for hazard assessment.

Therefore, the information requirement is not fulfiled.

Information on the design of the study to be performed

Following the criteria provided in Annex VIII, Section 8.6.1., Column 2, the oral route is the most relevant route of administration to investigate repeated dose toxicity (ECHA Guidance R.7a, Section R.7.6.2.3.2.). As the substance is a solid the sub-acute toxicity study must be performed according to OECD TG 407, in rats and *via* oral administration, because no oral repeated dose toxicity study is available to evaluate systemic toxicity following oral

administration and no specific information on uses indicating inhalation exposure has been provided.

When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407) nor for the screening study for reproductive/developmental toxicity (OECD TG 421) (see request B.4. below), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to avoid unnecessary animal testing and because it fulfils the information requirement in both Annex VIII, Section 8.6.1. and 8.7.1. of REACH (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

A Screening for reproductive/developmental toxicity study is a standard information requirement in Annex VIII of REACH, if there is no evidence from source substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:

(i) a weight-of-evidence record including a summary of two "*reproductive toxicity studies on rats*";
(ii) a study summary record cited from a SCCS report (secondary literature, 2013) for a prenatal developmental toxicity study (OECD TG 414) with the source substance sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate (EC No 224-618-7) in female rat;
(iii) a study summary record cited from a SCCS report (secondary literature, 2012) for a prenatal developmental toxicity study (OECD TG 414) with the source substance Disodium 2,2'-(9,10-dioxoanthracene-1,4-diyldiimino)bis(5-methylsulphonate) (EC No 224-546-6) in female rat.

We have assessed the information you provided in your dossier and identified the following issue:

A. For the reasons explained in the Appendix on General considerations regarding weight-of-evidence and read-across, your adaptations are rejected.

Furthermore in your comments on the draft decisions, you specify that you have adapted this information requirement based on a weight-of-evidence supported by data on source substances. You also provide a brief summary of an additional study according to OECD TG 422 cited from the J-CHECK online database (2010) on 1,8-Dihydroxy–4-nitro-5-(phenylamino)anthracene-9,10-dione (EC No 243-632-4).

We have assessed this additional information from your comments and identified the following issues:

B. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

C. To fulfil the information requirement, the study has to be screening study for

reproductive/developmental toxicity in accordance with OECD TG 421/422. The key parameters of the OECD TG 421 and 422 include dosing of the Substance for a minimum of approx. 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation.

However, in the additonnal study you have provided as part of your comments on the draft decision, females were dosed for 41-45 days. Therefore the study does not have a required exposure duration. Therefore it does not fulfil the criteria set in OECD TG 421 OECD TG 422.

D. Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

In order to allow concluding on no developmental toxicity for the Substance in a weight of evidence adaptation, the justification must cover the key elements (parameters) foreseen to be investigated in an OECD TG 421/422 study.

To support your adaptation you have provided in your dossier and in your comments on the draft decision information on:

i. an adaptation according to Annex XI, Section 1.2 (weight of evidence) based on the following studies:
ii. a prenatal developmental toxicity study (OECD TG 414) on sodium 2-[(4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yl)amino]-5-methylbenzenesulfonate with EC No 224-618-7 (SCCS, 2013),
iii. a prenatal developmental toxicity study (OECD TG 414) on Disodium 2,2'-(9,10-dioxoanthracene-1,4-diyldiimino)bis(5-methylsulphonate) with EC No 224-546-6 (SCCS, 2013),
iv. a screening study for reproductive/developmental toxicity (OECD TG 422) on 1,8-Dihydroxy–4-nitro-5-(phenylamino)anthracene-9,10-dione (EC No 243-632-4).

The studies provided (ii, iii, iv), alone or together, do not inform on property for reproductive toxicity for the Substance because they were conducted on analogues substances and as explained in the Appendix on General considerations the proposed rea-across adaptations are rejected. Furthermore regarding (iii), as explained in issue C above, this study does not provide an adequate coverage of the key parameters foreseen to be investigated in a screening study for reproductive/developmental toxicity.

In conclusion, none of the pieces of information alone or together, and taking into account your justification for the weight of evidence adaptation, allows to conclude whether the Substance has or has not hazardous properties related to screening for reproductive/developmental toxicity. Therefore, your adaptation according to Annex XI, Section 1.2. is rejected.

Therefore, the information requirement is not fulfiled.

Information on the design of the study to be performed

The study must be performed according to the test method OECD TG 422, in rats, and with oral route administration of the Substance (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407) nor for the screening study for reproductive/developmental toxicity (OECD TG 421) (see request B.4 below), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to avoid unnecessary animal testing and because it fulfils the information requirement in both Annex VIII, Section 8.6.1. and 8.7.1. of REACH (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

5. Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2).

Short-term toxicity testing on fish is a standard information requirement in Annex VIII to REACH. However, pursuant to Annex VIII, section 9.1.3., column 2, for poorly water soluble substances (i.e. water solubility below 1 mg/L) long-term toxicity study on fish (Annex IX, Section 9.1.6.) must be considered instead of an acute test.

In your dossier, you have not provided any data on long-term toxicity to fish.

We have assessed the information from your dossier and additionnal considerations you provided in your comments and we note the following issue:

> Annex VII, section 9.1.1., column 2, requires to perform a long-term toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5.) instead of an acute test when the substance concerned is poorly water soluble (*i.e.* water solubility below 1 mg/L). Poorly water soluble substances require longer time to reach steady-state conditions. Hence, the short-term tests may not give a true measure of toxicity for this type of substances.
>
> Based on the new water solubility study provided in an update of your dossier the Substance is regarded as poorly water soluble.
>
> In your comments on the draft decision, you consider that "*as per Annex VIII, long-term toxicity data on aquatic invertebrates is not the standard* [information] *requirement*" and that "*Since we have short term toxicity fish, predicted data for the* [Substance] *was supported by another two supporting studies for* [source substances] *which supports the classification of target chemical*".
>
> As explained under request A.1., the new water solubility study is not compliant with the recommended test guideline as the full test was not performed according to the appropriate method. However, this study includes a valid preliminary test which already allows to conclude that the Substance is poorly water soluble (i.e. water solubility < 1 mg/L). Hence, we disagree with your comment that the short-term study provided in your dossier is adequate to fulfil this information requirement. Therefore, we conclude that a long-term toxicity test must be conducted in lieu of the short-term test.

Therefore the information requirement is not fulfilled.

6. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.)

Activated sludge respiration inhibition testing is a standard information requirement in Annex VIII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:

(i) a study with the source substance 1-(2-hydroxyethylamino)-4-(methylamino) anthracene-9,10-dione (EC No 219-604-2) with an IC50 on *Tetrahymena pyriformis* of 0.5 mg/L;
(ii) a study with the source substance 1,4-anthraquinone (EC No 211-228-7) with a 48h-IC50 on *Tetrahymena pyriformis* of 0.228 mg/L.

We have assessed the information you provided in your dossier and identified the following issue:

A. As explained in the Appendix on General considerations on weight-of-evidence and read-across, your adaptations are rejected.

In your comments on the draft decision, you explain that "*as the test conducted was not based on the recommended guidelines, thus, earlier used read across analogue 1,4-anthraquinone, CAS no. 635-12-1 (EC No 211-328-7) was further strengthened with new read across analogue 2-Ethylanthraquinone, CAS no. 84-51-5 (EC No 201-535-4) whose study was performed as per the standard method*". You refer to a study cited from the Gsbl database (2017) with the source substance 2-Ethylanthraquinone and according to DIN 38412 Part 34.

We have assessed this additional information from your comments and identified the following issue:

B. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

Therefore, the information requirement is not fulfiled.

7. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.)

Hydrolysis as a function of pH is a standard information requirement in Annex VIII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.3. of REACH, and have provided a key study using HYDROWIN v2.00 to predict the hydrolysis of the Substance. You have reported a hydrolysis half-life of 3950 years at 25°C and pH 7.0.

In addition, you have adapted the standard information requirement according to Annex XI, Section 1.5. and have provided:

(i) a supporting study with the source substance (2-hydroxy-4-(octyloxy)phenyl) (phenyl)methanone (EC No 217-421-2);
(ii) a supporting study with the source substance Acetanilide (EC No 203-150-7).

We have assessed the information you provided in your dossier and identified the following issue:

A. As explained above in the Appendix on General considerations regarding qualitative or quantitative structure-activity relationships (QSARs) and read-across, your adaptations are rejected.

In your comments on the draft decision, you state that you intend to strengthen the proposed

read-across adaptation with information on 1-Aminoanthraquinone (EC No 201- 423-5) and Acetanilide (EC No 203-150-7). You refer to OECD TG 111 studies conducted with these source substances and cited from handbooks and other secondary sources. You state that "*other supporting details regarding the read across adaptation will be provided in the document of RA justification*". You consider this information supportive of the fact that the Substance is hydrolytically stable.

We have assessed the information you provided in your dossier and identified the following issue:

B. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

Therefore the information requirement is not fulfilled.

8. Adsorption/desorption screening (Annex VIII, Section 9.3.1.)

Adsorption/desorption screening is a standard information requirement in Annex VIII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:

(i) a QSAR prediction based on KOCWIN (v 2.00);
(ii) a QSAR prediction using the ACD/PhysCHem suite;
(iii) a QSAR prediction from the SciFinder database;
(iv) a QSAR prediction based on OPERA (OPEn (quantitative) structure-activity Relationship Application, v 1.02);
(v) a read-across adaptation based on 1,4-Bis(p-tolylamino)anthraquinone (EC No 204-909-5);
(vi) a read-across adaptation based on 1-N,4-N-diphenylbenzene-1,4-diamine (EC No 200-806-4).

We have assessed the information you provided in your dossier and identified the following issue:

A. As explained above in the Appendix on General considerations regarding weight-of-evidence, qualitative or quantitative structure-activity relationships (QSARs) and read-across, your adaptations are rejected.

In your comments on the draft decision, you state that "*read across analogue 1-N,4-N-diphenylbenzene-1,4-diamine; N,N'-diphenyl-p-phenylenediamine, CAS no. 74-31-7 (EC no. 200-806-4) has been removed from the dossier and further strengthened with the read across analogue 1-Amino-2-methylanthraquinone, CAS no. 82-28-0 (EC No 201-408-3)*" and that you intend to provide "*supporting data (from authoritative database HSDB, 2017) of the read across analogues 1,4-Bis(p-tolylamine)anthraquinone, CAS no. 128-80-3 (EC No 204-909-5) and 1-Amino-2-methylanthraquinone, CAS no. 82-28-0 (EC No 201-408-3) which are structurally and functionally similar with* [the Substance]".

We have assessed the information you provided in your dossier and identified the following issue:

B. The reasons explained in the Appendix on General considerations justifying the rejection of the read-across adaptation provided in your dossier also apply to your comments on the draft decision.

Therefore the information requirement is not fulfilled.

Guidance for determining appropriate test methods for the adsorption/desorption screening is available in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.1.15.

Appendix C: 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 the REACH Regulation.

The compliance check was initiated on 18 January 2019.

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and amended 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 D: Observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2019.

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[3]'.

5. Test material

Selection of the test material(s)

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.

Technical reporting of the test material

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 particle size distribution of the powder. 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.

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

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

6. List of references for the Guidance documents[4]

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.

Read-Across Assessment Framework (RAAF) (March 2017), available at https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

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.

Environmental toxicology and fate
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.

Technical guidance
OECD Guidance document on aqueous-phase aquatic toxicity testing of difficult test chemicals, Series on Testing and Assessment No. 23, Second Edition (ENV/JM/MONO(2000)6/REV1, 8 February 2019) available at http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2000)6/REV1&doclanguage=en

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment

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]