~~Confidential~~

Helsinki, 15 November 2022

Addressees
Registrant(s) of JS_4065-45-6_[redacted] as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
11/05/2018

Registered substance subject to this decision ("the Substance")
Substance name: Sulisobenzone
EC number: 223-772-2

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 ***20 August 2024***.

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

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

1. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202);

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201 or EU C.26./OECD TG 221).

Information required from all the Registrants subject to Annex VIII of REACH

3. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490).

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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

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 requirements for testing and reporting new tests under REACH, see Appendix 4.

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[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

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

Appendix 1: Reasons for the decision

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Reasons related to the information under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

1.1 Information provided

2 You have provided an OECD TG 202 key study with the Substance (Data from peer reviewed journal, 2010).

1.2 Assessment of the information provided

3 We have assessed this information and identified the following issues:

1.2.1. The provided study does not meet the information requirement

4 To fulfil the information requirement, a study must comply with the OECD TG 202 (Article 13(3) of REACH). Therefore, the following specifications must be met:

5 Technical specifications impacting the sensitivity/reliability of the test

a) young daphnids, aged less than 24 hours at the start of the test, are used;

b) at least 20 animals are used at each test concentration and for the controls.

6 Characterisation of exposure

c) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

7 Reporting of the methodology and results

d) the test design is reported (*e.g.* static or semi-static test, number of replicates);

e) the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation.

8 Your registration dossier provides an OECD TG 202 key study showing the following:

9 Technical specifications impacting the sensitivity/reliability of the test

a) the age of the test animals was not specified and therefore it is not known if the test was conducted on neonates, i.e. animals aged less than 24 h at the start of the test;

b) the number of animals at each test concentration and for the controls was not reported.

10 Characterisation of exposure

c) no analytical monitoring of exposure was conducted.

11 Reporting of the methodology and results

d) you have not specified the test design or the number of replicates;

e) tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported.

12 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the reported study was based on the data from peer reviewed journal and the reporting of the study was not sufficient to conduct an independent assessment of its reliability. For example, the age of the test animals, test design, number of replicates and the tabulated data on the observed effects were not reported and the test concentrations were not monitored.

13 Therefore, the requirements of OECD TG 202 are not met. On this basis, the information requirement is not fulfilled.

14 In the comments to the draft decision you agree with the request.

2. Growth inhibition study aquatic plants

15 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

2.1 Information provided

16 You have provided an OECD TG 201 key study with the Substance ([redacted], 2018).

2.2 Assessment of the information provided

17 We have assessed this information and identified the following issues:

2.2.1 Study not conducted according to GLP

18 (Eco)toxicological studies must comply with GLP or another recognised international standard; Art. 13(4) of REACH.

19 You have indicated that the study is "not GLP-compliant", without further explanation.

20 The test does not comply with GLP or another recognised international standard and is therefore rejected.

2.2.2 The provided study does not meet the information requirement

21 To fulfil the information requirement, a study must comply with the OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

22 Key parameter to be measured

a) the concentrations of the test material leading to a [redacted] % and [redacted]% (or [redacted]%) inhibition of growth at the end of the test are estimated.

23 Validity criteria

b) at least 16-fold increase in biomass is observed in the control cultures by the end of the test.

24 Technical specifications impacting the sensitivity/reliability of the test

c) three replicates at each test concentration and at least three replicates for controls (including solvent controls, if applicable) are included;

d) one of the two alternative growth medium (i.e. the OECD or the AAP medium) is used. Any deviations from recommended test media must be described and justified.

25 Characterisation of exposure

e) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided.

26 Your registration dossier provides an OECD TG 201 study showing the following:

27 Key parameter measured

a) the concentration of the test material leading to a [redacted]% (or [redacted]%) inhibition of growth at the end of the test are not estimated.

28 Validity criteria

b) the biomass (based on the cell counts tabulated in the dossier) at the start and end of the test (at 72 hours) was 10000 cells/ml and 42000, 40400 and 41600 (in three control replicates), respectively. This corresponds to a less than 16-fold increase.

29 Technical specifications impacting the sensitivity/reliability of the test

c) the number of replicates was two in each test concentration;

d) the test medium is described as Bold's Basal Medium (BBM). You have not provided a justification as to why you did not use one of the two alternative growth medium of OECD TG 201.

30 Characterisation of exposure

e) no analytical monitoring of exposure was conducted, and no justification was provided for the lacking analytical monitoring of exposure concentrations.

31 Based on the above, the key parameter of OECD TG 201 of the concentration of the test material leading to a [redacted]% (or [redacted]%) inhibition of growth is not covered, and the validity criteria of OECD TG 201 of at least 16-fold increase in biomass is not met.

32 Furthermore there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the number of replicates in each test concentration was too low, the used test medium was different than those recommended in the test guideline, and no analytical monitoring was conducted. These methodological deficiencies decrease the reliability of the study and increase the uncertainty of the reported effect value.

33 Therefore, the requirements of the OECD TG 201 are not met. On this basis, the information requirement is not fulfilled.

34 In the comments to the draft decision you agree with the request.

Reasons related to the information under Annex VIII of REACH

3. In vitro gene mutation study in mammalian cells

35 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

3.1 Information provided

36 Your dossier contains negative results for both an Ames test and an *in vitro* cytogenicity study. Therefore, the information requirement is triggered.

37 In your comments on the draft decision you clarified that you have not opted out of the joint submission for the information requirement of Annex VIII, 8.4.3.

38 The jointly submitted dossier provides an *in vitro* gene mutation study in mammalian cells (OECD TG 476, GLP, 2015) with the Substance, giving negative results without metabolic activation and inconclusive results with metabolic activation.

3.2 Assessment of the information provided

39 We have assessed this information and identified the following issue(s):

3.2.1 The study is not adequate for the information requirements

40 To fulfil the information requirement, the study must meet the requirements of the OECD TG 476 or OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2). Therefore, the following specifications must be, among others:

a) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.

41 The study provided is described as an *in vitro* gene mutation study in mammalian cells. In the robust study summary for the test with metabolic activation you state that "*The metabolic activation system could not be ascertained as the positive control failed to produce a significant increase in the number of revertant colonies*" and you conclude that from this test, no result can be determined "*due to invalid positive control data*".

42 Therefore, the following specification is not according to the requirements of the OECD TG 476:

a) one positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.

43 The information provided does not cover a key parameter required by the OECD TG 476.

44 Therefore, the information requirement is not fulfilled.

3.3 Specification of the study design

45 To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF), ECHA (2017)
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs), ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: 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 19 August 2021.

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

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

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;

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

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. 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[2].

1.2. 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 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[3].

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