~~Confidential~~

Helsinki, 15 March 2022

Addressees
Registrant(s) of CAS 53770-52-8 JS as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
23/03/2015

Registered substance subject to this decision ("the Substance")
Substance name: Zinc 3,5-bis(α-methylbenzyl)salicylate
EC number: 258-753-8

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 ***22 June 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)

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

B. Information required from 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)

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

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

2. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

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

Reasons for the request(s) are explained in the following appendices

- Appendices entitled "Reasons to request information required under Annexes VII, VIII and IX 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 Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil 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[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

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

Appendix A: Reasons 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.).

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

i. OECD TG 471, in vitro gene mutation study in bacteria (1992) with the following strains, TA 98, TA 100, TA 1535, TA 1537, and TA 1538 which all gave negative results, (Test material: Mixture containing zinc 3,5-bis(α-methylbenzyl)salicylate 38%).

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

Adequacy and reliability of source studies

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

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3)m in this case OECD TG 471.

Some of the key parameters of this test guideline include:

a) 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)
b) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
c) Triplicate plating must be used at each dose level.

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

a) The required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).
b) a maximum dose of 5 mg/plate or 5 ml/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance.
c) triplicate plating at each dose level.

In particular, since the test material is only a 38% or 30% (differing reporting in the ESR and CSR) solution, you have not explained how, taking into account the condition for the High dose as explained under b), the information can be used for predicting the property of the Substance itself and, therefore, how the study is adequate for the purpose of classification and labelling and/or risk assessment. Furthermore, not all key parameters are fulfilled (a to c above).

Therefore, the study submitted in your adaptation, as currently reported in your dossier, study is not adequate for the purpose of classification and labelling and /or risk assessment and does not provide an adequate and reliable coverage of the key parameter as specified in the corresponding OECD TG and the information requirement is not fulfilled.

Therefore, your adaptation is rejected.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

2. Short-term toxicity testing on aquatic invertebrates

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

You have provided an adaptation under Annex VII, Section 9.1.1., Column 2 with the following justification: "*Zinc 3,5-bis(α-methylbenzyl)salicylate was tested for inhibition of reproduction of Daphnia Magna in a long-term toxicity test therefore it is not considered scientifically justified to conduct a short-term toxicity test.*"

We have assessed this information and identified the following issue:

Under Section 9.1.1., Column 2, second indent, Annex VII to REACH, the study may be omitted if a long-term aquatic toxicity study on invertebrates is available.

As explained under Appendix C, Section 2, the provided long-term aquatic toxicity study on invertebrates is rejected. Therefore your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the potential volatility (due to high vapour pressure of 270 Pa at 20 °C and moderate water solubility of 90 mg/L at 20 °C) and its ready biodegradability (84% degradation (OECD 301B, CO2 Evolution Test), 10d window met). OECD TG 202 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. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

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

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

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

i. OECD TG 473, in vitro cytogenicity/ chromosome aberration study in mammalian cells, 1992 (Test material: Mixture containing zinc 3,5-bis(α-methylbenzyl)salicylate, 38%).

We have assessed this information and identified the following issue:

As explained under section A1, under Annex XI, Section 1.5., the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment and have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 473 or OECD TG 487[2]. The key parameters of these test guidelines include:

a) The maximum concentration tested must induce 55+5% 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 reported data for the study you have provided did not include:

a) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.

In the provided study the test material is a solution of the substance with a concentration of 38 % (info from the ESR). In the CSR you report the test material is a mixture containing [redacted]. Therefore, it is unclear if the final concentration of the substance in the high dose is causing the cytotoxicity or if one of the other listed substances are responsible for the detected cytogenicity. Furthermore, no percentage of cytotoxicity is reported for the highest concentration. Taking this into account, you have not explained how the information can be used for predicting the property of the Substance itself and, therefore, how the study is adequate for the purpose of classification and labelling and/or risk assessment.

Conclusion

Therefore, the study submitted in your adaptation, as currently reported in your dossier, is not adequate for the purpose of classification and labelling and /or risk assessment and does not provide an adequate and reliable coverage of the key parameter as specified in the corresponding OECD TG and the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, either *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) are considered suitable.

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

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

1. Pre-natal developmental toxicity study in one species

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

You have provided the following information:

i. A screening for reproductive / developmental toxicity study (OECD TG 421), 2008, with the Substance

ii. A data waiver:
"It is considered to be unjustified to conduct this study for the following reasons: Reproductive effects were only observed at maternally toxic doses in the reproductive/developmental toxicity screening study. No developmental abnormalities were detected in the reproductive/developmental toxicity screening study despite maternal toxicity. No evidence was found in the pathology (either at necropsy or histopathology) of the reproductive/developmental toxicity screening or the 90-day repeat dose studies of treatment-related effects on the reproductive organs."

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

In order to be considered compliant and enable assessing if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in one species, e.g external, skeletal and visceral malformations and variations has to be investigated as described in OECD TG 414.

You have not provided information following OECD TG 414. Instead, you have provided a "reproduction/ developmental toxicity screening test" (OECD TG 421). This study does not inform on skeletal and visceral malformations and variations as required by OECD TG 414.

Therefore, this study does not fulfil the information requirement.

You have not provided a legal reference to your data waiver under point ii). We understand this as a Column 2 adaptation.

There are three conditions for adapting based on Annex IX Section 8.7 column two, one of which must be met:

- classification as genotoxic carcinogen, or
- classification for germ cell mutagen, or
- low toxicological activity.

As you have not self-classified your substance we understand that you are trying to base the column 2 adaptation on low toxicity of the Substance.

According to Annex IX, Section 8.7., Column 2, third indent, the study does not need to be conducted if the substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria:

- that there is no evidence of toxicity seen in any of the tests available and
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure and
- that there is no or no significant human exposure.

However there are effects observed in the available repeated dose toxicity and screening studies (e.g. in the subchronic repeated dose toxicity study (2000) a NOAEL of 8 mg/kg bw/d: based on lower body weight, adverse clinical signs and mortality, and in the screening study

(2008), a NOAEL of 50 mg/kg bw/day based on increased post-implantation loss, reduced litter size, pup viability and pup body weight).

In addition, you have not provided any toxicokinetic data to show that there is no systemic absorption and absorption is demonstrated by the effects described above.

Furthermore, the uses of the Substance indicate that there is human exposure based on industrial uses (e.g. PROC 4, PROC 7) and Service life of paper articles including paper recycling.

Therefore, your adaptation is rejected.

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

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[3] administration of the Substance.

2. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have provided the following information:

i. Key study noting that the "*method followed the recommendations of the OECD Guidelines for Testing of Chemicals (1984) No. 202 "Daphnia Sp., Acute Immobilisation Test and Reproduction Test.""*, [redacted], 1990.

We have assessed this information and identified the following issue[s]:

To fulfil the information requirement, a study must comply with the OECD TG 211 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

- in semi-static tests, if the concentration of the test material:
  - is not expected to remain within ± 20 % of the nominal concentration, then all test concentrations must be determined when freshly prepared and at the time of renewal on one occasion during each week of the test.

Your registration dossier provides *Daphnia* reproduction test showing that no analytical monitoring of exposure was conducted.

Further, the Substance is readyly biodegradable, has relatively high vapour pressure with moderate solubility (90 mg/L), so it may be volatile.

Additionally, the provided NOEC (based on nominal concentrations with 0.32 mg/L) is close to the 0.1 mg/L cut off for more stringent classification.

Based on the above, the Substance is difficult to test (see Appendix A, Section 3) and there are critical methodological deficiencies resulting in the rejection of the study results. More, you have not demonstrated that the substance is not expected to remain within ± 20 % of the nominal concentration considering the properties of the Substance suggesting the contrary. Therefore, analytical monitoring is considered to be necessary

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

to provide hazard values base on measured concentrations instead of nominal exposure concentrations for reliable determination of ECx/NOEC.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 211 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A, Section 3.

3. 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 provided the following information:

i. a justification to omit the study with following justification: "*The results of short-term toxicity studies in fish, algae and Daphnia Magna showed that Daphnia Magna is the most sensitive species. A long-term toxicity test has been conducted in Daphnia Magna therefore it is considered unjustified to conduct a long-term toxicity study in fish based on animal welfare considerations.*"

We have assessed this information and identified the following issues:

A registrant may only adapt this information requirement based on 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.

Furthermore, for the reasons explained under Appendix C, section 3, your dossier does not include reliable information on the hazardous properties of the substance on aquatic invertebrates and therefore, comparison of species sensitivity between species from three trophic levels is not possible.

Therefore, you have not demonstrated that this information can be omitted. Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

On this basis, the information requirement is not fulfilled.

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 OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A, Section 3.

Appendix D: 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[4].

B. Test material

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 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[5].

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

Appendix E: 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 07 December 2020.

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

ECHA did not receive any comments within the commenting period.

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

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

Appendix F: List of references - ECHA Guidance[6] 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)[7]

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]

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[9] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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 G: 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]

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.