~~Confidential~~

Helsinki, 15 March 2022

Addressees
Registrant(s) of JS_Bismuth_Subsalicylate as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
17/09/2018

Registered substance subject to this decision ("the Substance")
Substance name: Bismuth oxide salicylate
EC number: 238-953-1

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 ***21 December 2022***.

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. Ready biodegrability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301B or OECD TG 310)

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

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

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

- Appendices entitled "Reasons to request information required under Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

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

- the information specified in Annex VII to REACH, for registration at [redacted] or as a transported isolated intermediate in quantity [redacted];
- the information specified in Annexes VII, VIII and IX to REACH, for registration at [redacted].

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

Appeal

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

Failure to comply

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

Authorised[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. Ready biodegradability

Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

You have provided an adaptation under Annex XI, Section 1.5 (read-across approach). In support of your adaptation you provided an inherent biodegradability EU Method C.9 (Biodegradation: Zahn-Wellens Test) study with salicylic acid (EC 200-712-3) as source substance.

You have provided a read-across justification in the section 5.2.1 of IUCLID and in the CSR.

You read-across between the structurally similar substance salicylic acid (EC 200-712-3) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties:
- in section 5.2.1 of IUCLID, "*Read-across is considered justified based on the similarity between salicylic acid and the subsalicylate component of bismuth subsalicylate. […] The concept of biodegradability does not apply to the bismuth component of bismuth subsalicylate.*"
- in the CSR "*A read-across approach is followed based on all information available for bismuth compounds. This grouping of bismuth compounds for estimating their properties is based on the assumption that properties are likely to be similar or follow a similar pattern as a result of the presence of the common bismuth component. The potential effects of the non-bismuth component of these substance are also considered under the relevant sections of this CSR".*

It is not clear if you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products or assume that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

We have assessed this information and identified the following issues:

Supporting information

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*" (Guidance on IRs and CSA 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).

a) Hypothesis based on the formation of common transformation products

Supporting information must include information (e.g. on dissociation and/or on hydrolysis at different pHs) on the formation of the common compound(s) to compare properties of the Substance and source substance(s).

If your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s), in this context, information characterising the rate and extent of the (bio)transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common

(bio)transformation product and to assess the impact of the exposure to the parent compounds.

In the section 5.1.2 of IUCLID (Hydrolysis), you claim that testing for the hydrolysis as function of pH is not scientifically necessary, because "*bismuth subsalicylate is expected to dissociate to form bismuth ions, salicylate ions and hydroxide ions.*" However, in the section 4.21 of IUCLID (Dissociation constant) you conclude that "*Dissociation constant cannot be calculated because of low solubility. As the substance does not dissolve, it cannot dissociate in water.*"

Thus, you have not provided any experimental information, about the transformation (via dissociation or hydrolysis at different pHs) of the Substance to support your claims regarding formation of a common compound.

In the absence of this information, you have not provided supporting evidence establishing that the proposed common (bio)transformation product is formed as assumed in your read-across hypothesis.

b) Hypothesis based on assumption that different compounds have the same type of effects

If your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s), in this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

For the source substance, you provided a study investigating inherent biodegradability of this substance. The Substance differs from the source substance by the presence of bismuth atom in the molecule of the Substance. There is no information provided in the dossier which would address the impact of bismuth present in the molecule of the Substance on the ready biodegradability when compared to the source substance, for instance on the bioavailability of the Substance molecule or availability of the carboxyl and hydroxy groups for the (bio)transformation, both in comparison to the source substance.

Furthermore, ECHA Guidance R.7b (section R.7.9.1.1) notes that "*ultimate biodegradation describes the (multistep) degradation process leading to inorganic endproducts and biomass*". Therefore, the formation of inorganic endproduct(s) containing bismuth is part of the degradation process which is investigated by the biodegradability studies measuring ultimate biodegradation, including ready biodegradability studies.

In the absence of such supporting information, you have not established that the Substance and the source substance(s) are likely to have similar properties.

Therefore, you have not provided sufficient supporting information on the rationale for the read-across.

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).

  Under Annex XI, Section 1.5., the results to be read across must 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 301 (or 310). Therefore, for a study according to OECD TG 301 (or 310), the following requirements must be met:

- Key parameter to be measured: the ultimate aerobic biodegradation (as measured by parameters such as DOC removal, CO_2 production and oxygen uptake) of the test material under relatively low inoculum concentration[2] is measured at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation.

  The ECHA Guidance R.7b (section R.7.9.1.1) explains that inherent biodegradability tests are "*Tests inoculated with a high concentration of microorganisms carried out under aerobic conditions in which biodegradation rate and/ or extent are measured. The test procedures offer a higher chance of detecting biodegradation compared to tests for ready biodegradability*".

  Your registration dossier provides an inherent biodegradability study which measures biodegradation of the source substance under relatively high[3] inoculum concentration.

  Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter of the corresponding OECD TG and consequently, the results of this study are not adequate for the purpose of classification and labelling and/or risk assessment.

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Due to the relatively low solubility of the Substance in water ("*0.19 to 22.83 mg/L (mean = 9.2 mg/L) at 20 ± 0.5 °C*", OECD TG 105) and presence of bismuth atom in the molecule of the Substance, ECHA considers methods measuring CO_2 production, i.e. OECD TGs 301B and 310, as the most appropriate to investigate ready biodegradability of the Substace.

[2] Concentration ranges of test substance and of inoculum to be used are given in OECD TG 301 (Table 12) and in OECD TG 310. Furthermore, in the *OECD REVISED INTRODUCTION TO THE OECD GUIDELINES FOR TESTING OF CHEMICALS, SECTION 3* it is explained that ready biodegradability tests are similar in respect of "*a relatively low concentration of biomass*".

[3] Concentration ranges of test substance and of inoculum to be used are given in EU method C.9. Furthermore, in the *OECD REVISED INTRODUCTION TO THE OECD GUIDELINES FOR TESTING OF CHEMICALS, SECTION 3* it is explained that the inherent biodegradation test "*procedures allow … a low ratio of test substance to biomass, which offers a better chance to obtain a positive result compared to tests for ready biodegradability.*"

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

1. Hydrolysis as a function of pH

Hydrolysis as a function of pH is a standard information requirement in Annex VIII to REACH (Section 9.2.2.1.).

You have adapted the information with reference to Annex XI with the following justification: "*According to Annex XI of regulation (EC) 1907/2006, testing for a specific endpoint may be omitted if testing does not appear to be scientifically necessary or if it is technically not possible to conduct the study as a consequence of the properties of the substance. Under REACH (ECHA 2008, Chapter R.7B – Endpoint Specific Guidance), the term 'Hydrolysis' refers to the "Decomposition or degradation of a chemical by reaction with water", and this as a function of pH (i.e., abiotic degradation). In water, bismuth subsalicylate is expected to dissociate to form bismuth ions, salicylate ions and hydroxide ions. The bismuth component of the substance cannot be transformed by reaction with water therefore this test is not considered relevant.*"

We have assessed this information and identified the following issue:

While an adaptation was not specifically indicated by you, ECHA has evaluated the provided information according to Annex XI, Section 1.2 of REACH (weight of evidence).

Annex XI, Section 1.2 states that there may be sufficient weight of evidence 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.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, Section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.2.2.1. at Annex VIII includes similar information that is produced by the OECD TG 111. This includes:

- determination of the rate of hydrolysis of the test substance as a function of pH; and
- determination of the identity or nature and rates of formation and decline of hydrolysis products.

In the section 4.21 of IUCLID (Dissociation constant) you conclude that "*Dissociation constant cannot be calculated because of low solubility. As the substance does not dissolve, it cannot dissociate in water.*" Thus, you note that the Substance does not dissociate and therefore, your provided justification does not allow to conclude neither on the rate of hydrolysis nor on the identity and rates of formation/decline of hydrolysis products.

Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[4].

B. Test material

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

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

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

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

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

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

Appendix D: Procedure

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

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

The compliance check was initiated on 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 E: 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 F: Addressees of this decision and their corresponding information requirements

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

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

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.