Helsinki, 13 May 2020

Addressees
Registrants of SIEF CAS 85586-35-2 listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
18/01/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Soybean oil, epoxidized, reaction products with methanol
EC number: 287-837-7
CAS number: 85586-35-2

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 ***18 August 2022***.

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

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method OECD TG 408) in rats with the Substance;

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance.

Conditions to comply with the requests

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 Annexes VII, VIII and IX of REACH, if you have registered a substance at 100-1000 tpa;

Registrants are only required to share the costs of information that they must submit to fulfil the information requirements for their registration.

The Appendix on general considerations addresses issues relevant for several requests 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 Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference

documents.

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.

Authorised[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

(i) Assessment of the Grouping of substances and read-across approach under Annex XI, Section 1.5.

You seek to adapt the information requirements for the following standard information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- Sub-chronic toxicity study (90-day)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. 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 (addressed under 'Scope of the grouping'). 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 (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you have formed a group, which consists of the Substance and two source substances of the read-across, i.e. Fatty acids, tall-oil, epoxidized, 2-ethylhexylesters (ETP), and Epoxidized Soybean oil (ESBO).

You have provided a read-across justification document in IUCLID Section 13.

For the purpose of this decision, the following abbreviations are used for the group members:

1. The Substance,

2. Fatty acids, tall-oil, epoxidized, 2-ethylhexylesters (**ETP**), EC No. 263-024-4, (CAS No. 61789-01-3),

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

[3] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[4] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

3. Epoxidised Soybean oil (**ESBO**), EC No. 232-391-0, (CAS No. 8013-07-8),3. The Substance.

You provide the following reasoning for the grouping the substances: "*The category definition is valid for substances which are epoxidized oils and derivatives of epoxidized fatty acid esters. The oils from which these products are derived are naturally occurring long chain fatty acids, and there is considerable overlap in the composition of the fatty acid portion of these products. They are primarily the C18 acids: oleic, linoleic, and linolenic acid. The alcohols are primary alcohols, diols or triols. This category consists of related fatty acid esters. Fatty acids, tall-oil, epoxidized, 2-ethylhexyl esters (ETP), Epoxidized soybean oil (ESBO), Soybean oil, epoxidized, reaction products with methanol.*" This is also the applicability domain of the category that you have indicated.

Thereby you have also defined the structural basis for the grouping.

ii. Assessment of the grouping

ECHA notes the following shortcomings with regards to your grouping approach.

Characterisation of the composition of the group members

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of chemical similarity may be considered as group.*"

According to the ECHA Guidance, "*in identifying a category, it is important that all potential category members are described as comprehensively as possible*", because the purity profile and composition can influence the overall toxicity/properties of the potential category members.[5] Therefore, qualitative and quantitative information on the **compositions** of the category members, also including considerations of differences, when applicable, should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities, and hence to confirm the category membership.

Furthermore, the provided information for categories consisting of UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances needs to include qualitative compositional information of the individual constituents of the category members; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.[6]

You have defined the applicability domain of the category as explained above. Your read-across justification document contains compositional information for the members of your category. The category members are UVCBs.

You have described the composition these substances as follows: *The substances are triglycerides based on either soybean - or tall oil. Soybean oil contains* [redacted] *stearic,* [redacted] *oleic,* [redacted] *linoleic, and* [redacted] *linolenic fatty acid while tall oil contains mostly palm (C16), oleic (C18:1) and linoleic fatty acid (C18:2) and are thus comparable in composition.*

[5] Guidance on information requirements and chemical safety assessment Chapter R.6, Section R.6.2.4.1
[6] Guidance on information requirements and chemical safety assessment Chapter R.6, Section R.6.2.5.5

Your read-across justification document contains only this basic compositional information for the members of your category, i.e. generic description of "raw materials". You have not listed the constituents of the category members, but only the constituents of the "raw materials", soybean oil and white tall oil. You have not provided any comparison of the composition of the three members of the category.

In addition, you have indicated that "*ESBO, ETP and Soybean oil, epoxidized, reaction products with methanol are comparable in composition* ***except*** *for the presence of the methylether moieties in the latter after ring opening of some of the epoxides with* ***methanol.***"

Without detailed information of the composition of the member substances of the category, qualitative or quantitative comparative assessment of the structural and chemical differences between the members cannot be made. Therefore, the category membership cannot be confirmed.

A. Predictions for properties

a. Prediction for toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: "*Read-across from ESBO and ETP to Soybean oil epoxidized, reaction products with methanol is based on similarities in constituents between the three compounds and* ***similarities*** *in physical-chemical and* ***toxicological data.***"

ECHA understands that you predict the properties of the Substance using a read-across hypothesis, which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be qualitatively and quantitatively equal to those of the source substance.

You intend to predict the properties Sub-chronic toxicity study (90-day) and Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) for the Substance from information obtained from the two source substances, as specified below in Appendix A.

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

Missing supporting information on the target substance

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*"[7]. 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 other category members.

Supporting information must include bridging studies to compare properties of the category members and to support your prediction, which is based on similarity of the relevant toxic properties.

[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

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

The data set reported in the technical dossier includes the following toxicological studies for the source and target substance to support your read-across hypothesis: acute toxicity, skin and eye irritation/corrosion, skin sensitisation and genotoxicity. You have not provided sub-acute toxicity studies or reprotoxicity (screening) studies for the target substance, which could be considered as bridging studies to demonstrate toxicological similarity among the members of the category.

In the absence of such information, you have not established that the target and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

In your comments to the draft decision, you expressed your intention to update the dossier, in particular the read-across justification in accordance to RAAF and provide detailed information on the composition of the source substances to compare the structural and chemical properties of the target and source substances. You also indicate that you intend to provide studies on sub-acute and pre-natal developmental toxicity made with a new source substance fatty acids, C16-18 and C18-unsaturated, methyl esters, epoxidized (FAME) and to perform a bridging study (OECD 422) with the Substance.

ECHA acknowledges that you intend to fulfil the information requirements with an updated read-across justification. You may, under your own responsibility, carry out your testing programme. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline.

Inadequate or unreliable information
The information provided does not meet the requirement for adequate and reliable documentation under Annex XI, Section 1.5 for the reasons set forth in Appendix A, Section 1.

B. Conclusions on the read-across approach

As explained above, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, your adaptation is it is rejected and it is necessary to perform testing on your Substance.

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

In accordance with Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII-IX to REACH.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

A Sub-chronic toxicity study (90 days) is a standard information requirement listed in Annex IX, Section 8.6.2. of REACH.

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 studies:

i. Combined repeated dose toxicity study, OECD TG 422 with the reproduction/developmental toxicity study provided with source substance ETP;
ii. Study equivalent to Combined Chronic Toxicity/Carcinogenicity Study OECD TG 453 made with source substance ESBO;
iii. Non-guideline chronic toxicity oral study, with source substance ESBO

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

A. Read-across

As explained in the Appendix on general considerations your adaptation is rejected.

In addition, the endpoint-specific deficiencies described below have been identified in your read-across adaptation.

B. Quality and parameters of the studies

To be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the following key parameters of OECD TG 408:

- 90-day exposure duration
- At least 10 female and 10 male animals should be used at each dose level (including control group)
- Clinical observations, clinical biochemistry, and urinalysis

The Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) has the exposure duration of a screening test, i.e. approximately 39 days (for females) and 42 days (for males). Furthermore the organ weight and histopathological investigations in OECD TG 422 are only conducted using 5 animals per sex per group.

In the non-guideline chronic toxicity study, clinical biochemistry and urinalysis were not performed.

Based on the above, the information you provided in study i and iii do not fulfil the key parameters of the OECD TG 408 and thus do not fulfil the information requirement. Study ii cannot be used to meet the information requirement, because the read-across adaptation is not found acceptable as explained in chapter A above.

According to your comments to the draft decision, your intention is to perform a screening study on the Substance and to provide a sub-acute study made with a new source substance FAME. As already explained in the Appendix on general consideration you may, under your own responsibility, carry out your testing programme. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline.

Consequently, there is a data gap and you need to generate the missing information on your Substance.

For an oral Sub-chronic toxicity study, the OECD TG 408 is the appropriate test method. According to the ECHA Guidance[8] and the OECD TG 408, the rat is the preferred species for the study.

Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity[9]. As the substance is a liquid with low vapour pressure the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) 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 adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5 by providing a PNDT study, OECD TG 414 with source substance ESBO.

As explained in the Appendix on general considerations your adaptation is rejected.

According to your comments to the draft decision, your intention is to perform a screening study on the Substance and to provide a pre-natal developmental toxicity study made with a new source substance FAME.

As already explained in the Appendix on general consideration you may, under your own responsibility, carry out your testing programme. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline.

Therefore, the information requirement is not fulfilled.

A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species with oral[10] administration of the Substance.

---

[9] ECHA Guidance R.7a, Section R.7.5.4.3.
[10] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix B: 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 REACH.

The compliance check was initiated on 30 April 2019.

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).

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 C: Observations and technical guidance

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

2. 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.

3. 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'[11].

4. 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.

   Any constituents that have harmonised classification and labelling according to the CLP Regulation (Regulation (EC) No 1272/2008) must be identified and quantified using the appropriate analytical methods. In addition, the OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 11 [ENV/MC/CHEM(98)16] requires a careful identification of the test material and description of its characteristics. The Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a* [...] *UVCB* [...] *sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*".

   In order to meet this requirement, all the constituents of the test material used for each

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

test must be identified as far as possible. For each constituent the concentration value in the test material must be reported in the Test material section of the endpoint study record.

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. 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.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[12].

5. List of references of the ECHA Guidance and other guidance/ reference documents[13]

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.

ECHA Read-across assessment framework (RAAF, March 2017)[14]

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

[12] https://echa.europa.eu/manuals
[13] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[14] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

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.

OECD Guidance documents[15]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

[15] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix D: 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.