SCIENTIFIC OPINION

efsa JOURNAL

ADOPTED: 8 June 2023

doi: 10.2903/j.efsa.2023.8100

Safety assessment of the substance poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters, for use in food contact materials

EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Claude Lambré, José Manuel Barat Baviera, Claudia Bolognesi, Andrew Chesson, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Evgenia Lampi, Marcel Mengelers, Alicja Mortensen, Inger-Lise Steffensen, Christina Tlustos, Henk Van Loveren, Laurence Vernis, Holger Zorn, Laurence Castle, Emma Di Consiglio, Roland Franz, Nicole Hellwig, Stefan Merkel, Maria Rosaria Milana, Eric Barthélémy, Remigio Marano, Ellen Van Haver and Gilles Rivière

Abstract

The EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) assessed the safety of poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters (OLA8), which is intended to be used as a plasticiser into polylactic acid (PLA) in contact with non-fatty foods. OLA8 is intended to be used at up to 5% and 15% w/w with or without starch, respectively (or with other additives with similar function). The migration for 10 days at 40°C from the film without starch was 0.16 mg/kg in 10% ethanol and 0.01 mg/kg in 3% acetic acid, while from the film with the starch it was well above 0.05 mg/kg food in all simulants. Some of the testing conditions were inconsistently reported. The substance did not induce gene mutations in bacterial cells and did not induce structural chromosomal aberrations or polyploidy in mammalian cells, thus, does not raise concern for genotoxicity. Instead of providing a 90-day oral toxicity study, a hydrolysis study in [redacted] was submitted to read-across from the authorised starting substances, [redacted] and the [redacted]. However, the data provided did not allow to perform the read-across, thus no appropriate toxicological data were provided to support migration above 0.05 mg/kg food (including for contact with 10% ethanol and use in combination with starch). The Panel concluded that OLA8 does not raise a safety concern for the consumer if it is used as an additive at up to 15% w/w in the manufacture of PLA articles that do not contain starch (and other additives with similar function), that are intended to be in contact for 10 days at 40°C with foods simulated by 3% acetic acid and from which the migration does not exceed 0.05 mg/kg food.

© 2023 European Food Safety Authority. *EFSA Journal* published by Wiley-VCH GmbH on behalf of European Food Safety Authority.

Keywords: poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters, plasticiser, polylactic acid, PLA, FCM substance No. 1088, food contact materials

Requestor: Italian competent authority (Ministero della Salute)

Question number: EFSA-Q-2021-00179

Correspondence: fip@efsa.europa.eu

Panel members: José Manuel Barat Baviera, Claudia Bolognesi, Andrew Chesson, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Claude Lambré, Evgenia Lampi, Marcel Mengelers, Alicja Mortensen, Gilles Rivière, Inger-Lise Steffensen, Christina Tlustos, Henk Van Loveren, Laurence Vernis and Holger Zorn.

Note: The full opinion will be published in accordance with Article 10(6) of Regulation (EC) No 1935/2004 once the decision on confidentiality, in line with Article 20(3) of the Regulation, will be received from the European Commission. The following information has been provided under confidentiality and it is redacted awaiting the decision of the Commission: identity of the substance, technological function, manufacturing details, physical properties, specific migration method, toxicological data (except for the summary of the *in vitro* mammalian chromosome aberration test).

Declarations of interest: If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

Suggested citation: EFSA CEP Panel (EFSA Panel on Food Contact Materials; Enzymes and Processing Aids), Lambré C, Barat Baviera JM, Bolognesi C, Chesson A, Cocconcelli PS, Crebelli R, Gott DM, Grob K, Lampi E, Mengelers M, Mortensen A, Steffensen I-L, Tlustos C, Van Loveren H, Vernis L, Zorn H, Castle L, Di Consiglio E, Franz R, Hellwig N, Merkel S, Milana MR, Barthélémy E, Marano R, Van Haver E and Rivière G, 2023. Scientific Opinon on the safety assessment of the substance poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters, for use in food contact materials. EFSA Journal 2023;21(7):8100, 9 pp. https://doi.org/10.2903/j.efsa.2023.8100

ISSN: 1831-4732

© 2023 European Food Safety Authority. *EFSA Journal* published by Wiley-VCH GmbH on behalf of European Food Safety Authority.

This is an open access article under the terms of the Creative Commons Attribution-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.

EFSA may include images or other content for which it does not hold copyright. In such cases, EFSA indicates the copyright holder and users should seek permission to reproduce the content from the original source.

The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.

Table of contents

1. Introduction

1.1. Background and terms of reference as provided by the requestor

Before a substance is authorised to be used in food contact materials (FCM) and is included in a positive list EFSA's opinion on its safety is required. This procedure has been established in Articles 8, 9 and 10 of Regulation (EC) No 1935/2004[1] of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food.

According to this procedure, the industry submits applications to the Member States' competent authorities which transmit the applications to the European Food Safety Authority (EFSA) for their evaluation.

In this case, EFSA received an application from the Spanish Competent Authority (Ministerio de Consumo, Agencia Española de Seguridad Alimentaria y Nutrición), requesting the evaluation of the substance poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters, the FCM substance No. 1088. The dossier was submitted on behalf of Condensia Química S.A.

According to Regulation (EC) No 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food, EFSA is asked to carry out an assessment of the risks related to the intended use of the substance and to deliver a scientific opinion.

2. Data and methodologies

2.1. Data

The applicant submitted a dossier in support of its application for the authorisation of poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters to be used in plastic FCM.

Additional information was provided by the applicant during the assessment process in response to requests from EFSA sent on 7 October 2021 and on 19 July 2022 (see 'Documentation provided to EFSA').

Data submitted and used for the evaluation are:

Non-toxicological data and information

- Chemical identity
- Description of manufacturing process of substance/FCM
- Physical and chemical properties
- Intended use
- Migration of the substance

Toxicological data

- Bacterial gene mutation test
- *In vitro* mammalian chromosomal aberration test
- Hydrolysis study

2.2. Methodologies

The assessment was conducted in line with the principles laid down in Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food. This Regulation underlines that applicants may consult the Guidelines of the Scientific Committee on Food (SCF) for the presentation of an application for safety assessment of a substance to be used in FCM prior to its authorisation (European Commission, 2001), including the corresponding data requirements. The dossier that the applicant submitted for evaluation was in line with the SCF guidelines (European Commission, 2001).

The methodology is based on the characterisation of the substance that is the subject of the request for safety assessment prior to authorisation, its impurities and reaction and degradation products, the evaluation of the exposure to those substances through migration and the definition of minimum sets of toxicity data required for safety assessment.

To establish the safety from ingestion of migrating substances, the toxicological data indicating the potential hazard and the likely human exposure data need to be combined. Exposure is estimated from

[1] Regulation (EC) No 1935/2004 of the European parliament and of the council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC. OJ L 338, 13.11.2004, pp. 4–17.

studies on migration into food or food simulants and considering that a person may consume daily up to 1 kg of food in contact with the relevant FCM.

As a general rule, the greater the exposure through migration, the more toxicological data is required for the safety assessment of a substance. Currently there are three tiers with different thresholds triggering the need for more toxicological information as follows:

a) In case of high migration (i.e. 5–60 mg/kg food), an extensive data set is needed.
b) In case of migration between 0.05 and 5 mg/kg food, a reduced data set may suffice.
c) In case of low migration (i.e. < 0.05 mg/kg food), only a limited data set is needed.

More detailed information on the required data is available in the SCF guidelines (European Commission, 2001).

The assessment was conducted in line with the principles described in the EFSA Guidance on transparency in the scientific aspects of risk assessment (EFSA, 2009) and considering the relevant guidance from the EFSA Scientific Committee.

3. Assessment

According to the applicant, the substance poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters (OLA8) is a polymeric additive intended to be used up to 15% w/w in polylactic acid (PLA) articles as a plasticiser. It can also be used as [redacted]. OLA8 is intended to be used in PLA at a maximum concentration of 5% w/w in combination with other additives, such as starch which aims to increase the biodegradation of the plastic.

PLA final articles containing OLA8 are intended for single use applications (films, trays, containers) to be used for contact at room temperature or below (0–40°C), up to 7 days, with fresh foods such as fruits, vegetables, slightly acidic foods (e.g. pickled vegetables) and watery based materials (e.g. water, non-alcoholic beverages). It is not intended to enter in contact with fatty foods (e.g. oils, foods preserved in oil, high-fat cheese or meats).

The substance was not evaluated by the SCF or by EFSA in the past. However, [redacted] is authorised according to Annex I of Regulation (EU) 10/2011[2] (FCM No [redacted]) to be used as an additive or polymer production aid and as a monomer or other starting substance in plastics, without restrictions. [redacted] are also authorised (FCM No [redacted]) as a monomer or other starting substance in plastics, without restrictions.[3]

3.1. Non-toxicological data

3.1.1. Identity of the substance[4]

Chemical structure and formula:

[redacted]

[2] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food OJ L 12, 15.1.2011, pp. 1–89. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32011R0010.

[3] In the EU, [redacted] is authorised as food flavouring (Commission Regulation (EU) No 1334/200813; FL-no: [redacted]) and as food additive (E [redacted]) (Regulation (EC) No 1333/200810) and it is currently under re-evaluation.

[4] Technical dossier/ADD DATA_MARCH 2023/Appendix B/Section 1, Annexes I and VIII.

The substance is manufactured from [redacted] under controlled conditions to get the target oligomers of lactic acid with a final [redacted]. The oligomer mixture has a number average molecular mass (Mn) = [redacted] and a polydispersity index (Mw/Mn) = [redacted]. The purity of the substance is specified to be > [redacted]%. Low levels of the [redacted] were measured in the substance.

3.1.2. Physical and chemical properties[5]

The applicant claimed that the substance [redacted], however, this was not substantiated by any data.

In the thermogravimetric analysis (TGA) provided, the onset of weight loss of OLA8 ([redacted]%) was [redacted]°C, which, according to the applicant, corresponds to the [redacted]. The TGA analysis of PLA made with 15% w/w of OLA8 to demonstrate thermostability, showed the onset of weight loss at [redacted]°C, above the maximum processing temperature claimed to be 220°C. Therefore, no relevant thermal degradation of the substance is expected under processing conditions.

3.1.3. Specific migration[6]

The specific and overall migrations were tested from two PLA film samples:

a) PLA with 15% w/w OLA8[7];
b) PLA with starch[8] and 5% w/w OLA8.

Tests were performed by total immersion at a surface to volume ratio of 20 dm^2/L using 3% acetic acid and 10% ethanol for 10 days at 40°C. Analysis was performed by [redacted] and the results are expressed as the [redacted] Da. The migration was recalculated for the ratio of 6 dm^2/kg. In 10% ethanol, it was 0.16 mg/kg (film a) and 1.18 mg/kg (film b), while in 3% acetic acid, it was 0.01 mg/kg (film a) and 0.61 mg/kg (film b).

The applicant carried out tests also in 95% ethanol and in isooctane, even though the articles containing the substance are not intended for contact with fatty foods. Migration of oligomers was 5.07 mg/kg (film a) and 3.26 mg/kg (film b) in 95% ethanol, and it was 0.13 mg/kg (film a) and 15.05 mg/kg (film b) in isooctane.

Overall migration[9] was tested using 3% acetic acid, 10% ethanol and olive oil for 10 days at 40°C. The migration in 3% acetic acid was 2.6 mg/dm^2 (film a) and 3.0 mg/dm^2 (film b). In the other two simulants, the overall migration was lower than the respective limits of detection of 2 mg/dm^2 in 10% ethanol and 4 mg/dm^2 in olive oil.

3.2. Toxicological data

A bacterial reverse mutation assay (Ames test) and an *in vitro* chromosomal aberration test, both carried out on OLA8, have been provided. As the migration exceeded 0.05 mg/kg of food, the applicant should have provided, in accordance with the EFSA Note for Guidance for Food Contact Materials (EFSA CEF Panel, 2008), a 90-day oral toxicity study and data to demonstrate the absence of potential for accumulation in humans. Instead, the applicant submitted a hydrolysis test of OLA8 in [redacted] to support a read-across from its authorised starting monomer [redacted] and [redacted].

[5] Technical dossier/ADD DATA_MARCH 2023/Appendix B/Section 2, Annexes I and VIII.
[6] Technical dossier/ADD DATA_MARCH 2023/Appendix B/Section 5 and Annexes II and XII.
[7] The applicant originally reported a thickness of 35 μm, while in the last submission the applicant reported a thickness of 100 μm without supporting explanations.
[8] The applicant originally reported 60% w/w of starch, while in the last submission the applicant reported 20% w/w without supporting explanations. Similarly, as for the sample without starch, the applicant originally reported a thickness of 35 μm, while in the last submission the applicant reported a thickness of 100 μm without supporting explanations.
[9] Technical dossier/ADD DATA_MARCH 2023/Appendix B/Section 5.2 and Annexes III, IV and XIII.

3.2.1. Genotoxicity[10]

3.2.1.1. Bacterial reverse mutation test

The test substance OLA8 (purity [redacted]) was tested in a bacterial reverse mutation assay (Ames test) according to OECD Test Guideline 471 (OECD, 1997) and following Good Laboratory Practice (GLP). [redacted]

The Panel concluded that the substance did not induce gene mutations under the test conditions employed in this study. The study is considered reliable without restrictions and the results of high relevance.

3.2.1.2. *In vitro* mammalian chromosomal aberration test

The test substance OLA8 (purity [redacted]%) dissolved in DMSO was tested in an *in vitro* mammalian chromosomal aberration test carried out in human peripheral blood lymphocytes according to OECD Test Guideline 473 (OECD, 2016) and following GLP. In a preliminary toxicity experiment, [redacted] Precipitation was observed at concentrations of 500 μg/mL or higher with and without metabolic activation by liver S9-mix from phenobarbital-/β-naphthoflavone-induced rats. Based on these results, the cells were exposed to the substance at [redacted] μg/mL in a short-term treatment (4 h) with and without S9-mix, and at 50–500 μg/mL in a continuous treatment (24 h) in the absence of S9-mix.

In Experiment I (short-term treatment), the relative mitotic index was reduced about 30% compared to controls with and without S9-mix at 500 μg/mL, which was the top concentration evaluated due to precipitation. In this experiment, no statistically significant increase in the incidence of cells bearing structural chromosomal aberrations was observed in treated cell cultures compared to solvent controls, at any concentration with and without metabolic activation. In Experiment II (continuous treatment), marked cytotoxicity could be observed at the highest evaluated concentration (500 μg/mL), showing a relative mitotic index of [redacted]% with a marked depression of cell proliferation compared to the solvent control. Therefore, the solely statistically significant increase of cells with structural chromosome aberrations ([redacted]%) observed in this experiment at the highest concentration can be regarded as not biologically relevant, supported by the lack of a concentration-related increase. In addition, the aberration rate was within the historical control range ([redacted]%). In both experiments, no treatment-related increase in polyploid cells was observed. The positive controls induced statistically significant increases of chromosomal aberrations. All values of the negative, solvent and positive controls were within the respective historical control range.

The Panel concluded that the test substance did not induce structural chromosomal aberrations or polyploidy under the test conditions employed in this study. The study is considered reliable without restrictions and the negative results obtained of high relevance.

[10] Technical dossier/ADD DATA_MARCH 2023/Appendix B/Section 8.1 and Annexes V and VI.

3.2.2. Hydrolysis study in gastric juice simulant[11]

In order to support read-across from its starting substances, a hydrolysis study with OLA8 in [redacted] was conducted according to Annex I of the EFSA Note for Guidance (EFSA CEF Panel, 2008). No appropriate analysis able to identify and quantify the oligomers [redacted] was performed. After [redacted] h of incubation at [redacted]°C, the [redacted]. This was accompanied with a [redacted]. However, still [redacted] of the compounds analysed.

The Panel concluded that the results of the hydrolysis study demonstrated only a partial breaking of the polymeric lactate backbone and the hydrolysis of [redacted] was not proven.

3.3. Discussion

The substance OLA8 was tested with negative results in two *in vitro* genotoxicity tests (Ames test, mammalian chromosomal aberration test) with and without metabolic activation up to the limit concentrations. The applicant did not provide an *in vitro* micronucleus test (OECD 487) which is recommended in the current EFSA Note for Guidance (EFSA CEF Panel, 2008) to assess both clastogenic and aneugenic potential. However, in the mammalian chromosomal aberration test, no treatment-related increases in polyploid cells, a hallmark of aneugenic potential, was observed. Furthermore, the polymeric additive is made from the already authorised monomer [redacted], which by reaction loose the reactive functional groups and no further functional groups are generated. Therefore, no mutagenic, clastogenic or aneugenic activity was observed and the CEP Panel concluded that the OLA8 does not raise concern regarding genotoxicity.

The Panel concluded that the results of the hydrolysis study in [redacted] did not prove the hydrolysis of the [redacted]. Therefore, the data provided does not allow to perform the read-across from [redacted] and the [redacted] of OLA8, which would enable to waive toxicological data (such as the 90-day rat study) required for migration above 0.05 mg/kg food.

The migration was demonstrated to be below 0.05 mg/kg food only when the substance was used at up to 15% in PLA in contact with 3% acetic acid for 10 days at 40°C. In 10% ethanol, simulating other requested conditions of contact (as well as in fatty food simulants), the migration was above 0.05 mg/kg food. Migration of OLA8 (present at 5% w/w) from PLA containing starch during 10 days at 40°C exceeded the 0.05 mg/kg in both 10% ethanol and 3% acetic acid. Moreover, some of the testing conditions of the migration (film thickness, % of starch) were inconsistently reported.

In addition, neither additional data nor information requested on intended uses that could comply with the 0.05 mg/kg food have been provided. Lastly, no appropriate toxicological data were provided to support the migration above 0.05 mg/kg food. Therefore, the Panel concluded to restrict both the migration and the intended uses.

4. Conclusions

Based on the above-mentioned data, the CEP Panel concluded that the substance poly(2-hydroxypropanoic acid), n-octyl/n-decyl esters is not of safety concern for the consumer if it is used as an additive up to 15% w/w in the manufacture of PLA food contact materials and articles provided that:

- the migration does not exceed 0.05 mg/kg food;
- materials and articles do not contain starch (and other additives with similar function); and
- they are intended to be in contact for up to 10 days at 40°C with foods simulated by simulant B (as defined in the Regulation (EU) 10/2011).

5. Documentation as provided to EFSA

1) Initial dossier on OLA8 – Oligomeric lactic acid. March 2021. Submitted on behalf of Condensia Química S.A.
2) Additional data. May 2022. Submitted on behalf of Condensia Química S.A.
3) Additional data. March 2023. Submitted on behalf of Condensia Química S.A.

[11] Technical dossier/ADD DATA_MARCH 2023/Appendix B/Section 8.2.4 and Annex XIV.

References

EFSA (European Food Safety Authority), 2009. Guidance of the Scientific Committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: general principles. EFSA Journal 2009;7 (5):1051, 22 pp. https://doi.org/10.2903/j.efsa.2009.1051

EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2008. Note for guidance for the preparation of an application for the safety assessment of a substance to be used in plastic food contact materials. EFSA Journal 2008;6(7):21r, 41 pp. https://doi.org/10.2903/j.efsa.2008.21r

European Commission, 2001. Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out82_en.pdf

OECD, 1997. Test No. 471: Bacterial Reverse Mutation Test, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris. https://doi.org/10.1787/9789264071247-en

OECD, 2016. Test No. 473: In Vitro Mammalian Chromosomal Aberration Test, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris. https://doi.org/10.1787/9789264264649-en

Abbreviations

CEF Panel	EFSA Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CEP Panel	EFSA Scientific Panel on Food Contact Materials, Enzymes and Processing Aids
FCM	food contact materials
OECD	Organisation for Economic Co-operation and Development
PLA	polylactic acid
Po/w	octanol/water partition coefficient
SCF	Scientific Committee on Food
SML	specific migration limit
TGA	thermogravimetric analysis
w/w	weight by weight