EFSA ASSESSMENT OF NIAS

FROM OPINION ON “RECENT DEVELOPMENTS...” (EFSA CEF PANEL 2016)

AND “WAX, RICE BRAN, OXIDISED” AND “WAX, RICE BRAN, OXIDISED, CALCIUM SALT” (EFSA FCM PANEL 2024)

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EUROPEAN FOOD SAFETY AUTHORITY

EFSA ASSESSMENT OF NIAS FROM OPINION ON "RECENT DEVELOPMENTS..." (EFSA CEF PANEL 2016) AND FROM "WAX, RICE BRAN, OXIDISED" AND "WAX, RICE BRAN, OXIDISED, CALCIUM SALT" (EFSA FCM PANEL 2024)

Abstract: The safety assessment of NIAS (non intentionally added substances) should take the same approach as used for authorised substances, since the same degree of safety should be warranted. This means following the generic process of (a) identification of the substances present in the material; (b) estimation of their migration level leading to an estimate of possible consumer exposure; (c) risk assessment which considers the potential exposure in context with any hazard (nature and potency) posed by the substances. The assessment of NIAS involves additional challenges, however. This presentation will focus predominantly on the recent (2024) evaluation of the NIAS, including the unidentified fraction, present in the title additives (rice bran waxes) that are themselves non defined mixtures.

NIAS (EFSA CEF PANEL, 2016) (SLIDE COURTESY OF EB)


SCIENTIFIC OPINION

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Recent developments in the risk assessment of chemicals in food and their potential impact on the safety assessment of substances used in food contact materials

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)

Section 8.8 "**Toxicological assessment of impurities, reaction and degradation products (other than oligomers)**"

- Some approaches have been proposed in the literature and/or are under further development (Rennen et al., 2011; Koster et al., 2014; ILSI, 2015).
- The same approach as used for authorised substances is applied as the same degree of safety should be warranted. Tiered approach to toxicity testing based on exposure applies to NIAS.
- For NIAS which migrate into foods, further considerations on **genotoxicity**.
  - Non-testing methods may be used (case-by-case basis). It includes grouping and 'read-across', computational methods ((Q)structure–activity relationships (SAR, QSAR)) and the TTC.
  - Considering the TTC approach, no genotoxicity data are needed for NIAS if exposure < 0.15 µg/person per day (provide sufficient protection against (genotoxic) carcinogenic and heritable effects, when it can be ruled out that the compounds are part of the exclusion category.
  - Testing on mixtures might help (EFSA SC, 2019). Sufficient sensitivity is needed for detecting substances constituting minor proportions. This may require fractionation, prior removal of bulk components which are then evaluated separately. Representativity of migrating species needed.

https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2016.4357

A RISK ASSESSMENT OF THE NIAS SHOULD HAVE THREE COMPONENTS:

(a) identification of the substances present in the material;

(b) estimation of their migration level leading to an estimate of possible consumer exposure;

(c) risk assessment which considers the potential exposure in context with any hazard (nature and potency) posed by the substances.

Safety assessment of the substances ‘wax, rice bran, oxidised’ and ‘wax, rice bran, oxidised, calcium salt’ for use in food contact materials.

EFSA FCM Panel, 2024.

EFSA carried out a public consultation on the non-confidential version of the application from 6 to 27 June 2024, for which no comments were received.

<u>Requested uses</u>

Additives, up to 0.3% w/w in PET, PA, TPU, PLA and PVC, acting as processing aids, lubricants, release agents or slip additives.

Requested for all types of food for long term storage at room temperature, including hot-fill.

Contact with infant formulae and human milk was not specified.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Production process

Starting material is crude rice bran wax (RBW) obtained by precipitation from rice bran oil that is sold for human consumption.

The applicant did not report the composition of crude RBW. Based on literature, crude RBW consists largely of linear wax esters with minor proportions of fatty alcohols, acids and hydrocarbons.

The crude RBW is oxidised. Details are confidential. The opinion mentions Cr(VI). The opinion mentions bleaching. The additive can be in the free acid form or the calcium salts.

Additive is stable up to 391 - 471°C so is expected to be thermally stable at the maximum processing temperature of the intended plastics.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Overall Composition

The additives are Non-Defined Mixtures.

The wax esters are C40–C64. Predominantly C46–C56 and predominantly saturated.

The fraction of branched acids and alcohols is expected to be negligible due to the composition of the rice bran oil and the precipitation process, which favours the incorporation of linear over branched species.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Comprehensive analysis?

Compositional analysis of the additives by GC-FID after silylation (MSTFA) and methylation (diazomethane).

The applicant quantified and identified the individual constituents by carbon number range and main functional groups (i.e. esters, carboxylic acids, alcohols, calcium salts).

Non-volatile fraction (high MW wax esters) was analysed by first hydrolysis and then silylation/methylation.

IAS. The products consist of wax esters (40 – 91%), carboxylic acids (4.6 - 56.4%), alcohols (0.4 - 4.7%) and calcium salts of carboxylic acids (13% - 46%).

NIAS. The organic substances detected but not identified were 0.7 to 2.9% w/w.

WAX, RICE BRAN, C[illegible], OXIDISED, CALCIUM SALT

Chemical class		
Wax esters (% w/w)		
Calcium salts of carboxylic acids (% w/w)		
Carboxylic acids (% w/w)	**Short chain** ($\leq C_{11}$)	Carboxylic
		Dicarboxylic
		Hydroxy carboxylic
		Total
	Medium chain (C_{12}–C_{18})	Carboxylic
		Dicarboxylic
		Hydroxy carboxylic
		Total
	Long chain ($\geq C_{19}$)	Carboxylic
		Dicarboxylic
		Hydroxy carboxylic
		Total
	Total carboxylic acids (% w/w)	
Alcohols (% w/w)		
Unknown organic compounds (% w/w)		
Total chromium (mg/kg)		
Chromium (VI) (µg/kg)		

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Unidentified fraction and impurities (= NIAS)

The applicant did not elaborate on the composition and the potential identity of the constituents of the unidentified fraction.

Based on the source material and the production process, the Panel assumed that the unidentified fraction consists of hydrocarbons and other minor natural compounds from the RBO such as squalene, partially hydrolysed triglycerides, sterols, sterenes and their oxidation products.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Migration of the various chemical classes – fat simulants

The solubility in water was reported as 2 to 21 mg/L but the overall solubility of a multi-component mixture has little meaning with various constituents of very different polarity.

Migration into 95% ethanol was reported but not considered to be representative. Test samples were PET and swelling expected.

The migration of the wax esters into isooctane was 257 – 297 µg/kg.

Regarding the other classes (carboxylic acids and alcohols), the migration of the sum of constituents of each class was below the LoD of 10 µg/kg.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Migration of the various chemical classes – aqueous simulants

For 10% ethanol and 4% acetic acid the migration of the individual constituents of each class was below the LoQ of 10 µg/kg, with LoQ defined as the lowest standard used in the calibration curve.

Based on the lowest standard for the wax ester surrogate (i.e. 10 µg/kg for the C56 ester) and on the raw data on calibration and migration analysis provided, the Panel estimated that the limit of detection (LoD) of the individual wax esters was in the region of 2 µg/kg.

Considering that the migration of wax esters into isooctane is essentially due to seven wax esters (C46–C58) and that a similar pattern is expected for the other simulants, the LoD was estimated to be around 12 µg/kg for the sum of the wax esters. Therefore, the migration of the sum of the wax esters in the aqueous food simulants was estimated to be below 12 µg/kg.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Migration of unidentified organic compounds

The migration of the sum of the unidentified organic compounds into isooctane was estimated by the Panel to be around 20 µg/kg, based on the composition of the additive and assuming a pro-rata migration to the wax ester class.

Similarly, the migration of the sum of the unidentified organic compounds into aqueous simulants was estimated by the Panel to be around 1 µg/kg, based pro-rata on the migration of the wax esters class below the LoD of ca. 12 µg/kg food.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Toxicity data

The applicant provided a battery of genotoxicity studies, 90-day oral toxicity studies, data to demonstrate the absence of potential for accumulation in humans and reproduction / developmental toxicity screening tests.

The Panel considered that the used Licocare RBW 106 and Licocare RBW 300 are acceptable choices as representative test items as the proportions of the various chemical classes reasonably cover the ranges of composition for the commercial products.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Discussion and conclusions on genotoxicity

Licocare RBW 106 and Licocare RBW 300 were negative in a battery of *in vitro* and *in vivo* genotoxicity studies, up to the limit of solubility.

The content of the individual unidentified organic compounds may be too low to elicit a response in experimental studies with the substances.

For fatty food simulants, the potential migration of the sum of the unidentified organic compounds was ca. 20 µg/kg food which could give exposure above the TTC for genotoxic carcinogens.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Discussion and conclusions on genotoxicity

For aqueous simulants, the potential migration of the sum of the unidentified organic compounds was ca. 1 µg/kg. The unidentified fraction consists of a large number of different individual compounds (up to 100 peaks in the GC-FID) and these compounds are expected to belong to various groups with similar structure or functionality.

Based on these considerations, the potential migration of unidentified compounds, either individually or as a group of chemically-related compounds, is expected to result in an exposure of consumers that would be below the TTC for genotoxic carcinogens.

By excluding contact with fatty foods, the migration potential of the unidentified constituents is expected to result in an exposure of the consumers that would be below the TTC for genotoxic carcinogens.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Other considerations

Only migration tests using PET were provided. The Panel concluded that the data provided also covered PLA and rigid PVC, but not PA, TPU and plasticised PVC because of higher diffusivity and/or swelling.

Due to the high lipophilic character, any migration into 20% ethanol is expected to be comparable to that into 10% ethanol and 4% acetic acid.

Any migration into solid foods would not be higher than into aqueous simulants.

Infant formula and human milk was not specified so these uses are excluded.

PET is used to pack water, which in turn is used to reconstitute infant formula. The known individual constituents migrate ca. 2 µg/kg or below and the individual unknowns are below the TTC for genotoxic carcinogens, so contact with water used to reconstitute infant formula is covered.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Conclusion of the Panel

The Panel concluded that the substances 'wax, rice bran, oxidised' and 'wax, rice bran, oxidised, calcium salt' are not of safety concern for the consumer if they are used :

as additives up to 0.3% w/w in PET, PLA and rigid PVC materials and article intended for contact with all food types except for fatty foods

for long-term storage at room temperature and below, including hot-fill and/or heating up to 100°C for up to 2 h.

WAX, RICE BRAN, OXIDISED' AND 'WAX, RICE BRAN, OXIDISED, CALCIUM SALT

Observations / reflections

The additive is non-defined mixture(s)

The source material is a food product.

Intentional transformations include oxidation, bleaching and alkali treatment to form salts.

The analysis of composition was certainly **not** state-of-the-art and a substantial fraction remained unidentified.

The nature of this faction could be inferred from the nature of the source material and the production process and chemical treatments used. So, should the source material and the production process be specified?

Excluding fatty contact keeps the migration low and exposure to unknown components below the relevant TTC.

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