Presentation #25. Laurence Castle

Safety assessment of ‘waxes, paraffinic, refined, derived from petroleum-based or synthetic hydrocarbon feedstock, low viscosity’ for use in food contact materials

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FCM No. 93 evaluated by the EFSA AFC Panel in 2006

- Currently listed in Reg. 10/20112 with an SML of 0.05 mg/kg food and ‘Not to be used for articles in contact with fatty foods for which simulant D is laid down’

Specifications

- Average molecular weight not less than 350 Da.
- Viscosity at 100°C not less than 2.5 cSt (2.5 9 106 m2/s).
- Content of hydrocarbons with carbon number less than 25, not more than 40% (w/w).

SML of 0.05 mg/kg food and ‘Not to be used for fatty foods’

Stems from the tiered approach to data requirements for FCM (plastics), coming from the SCF guidelines:-

high migration (5–60 mg/kg food)
-> an extensive data set is needed

migration between 0.05 and 5 mg/kg food
-> a reduced data set may suffice

low migration (i.e. < 0.05 mg/kg food)
-> only a limited data set is needed.

The applicant requested to extend the use to all food contact types, including fatty foods, for long-term storage at room temperature or below. Typical concentrations in the final articles are 1% to 3% w/w.

Waxes FCM No.93 as an example of:-

- Dealing with variability (non-defined mixture, a UVCB).
- The migrate has a composition different to the additive used.
- Whole mixture approach and component based approach to evaluating mixtures.
- Fractionation/pre-concentration prior to gentox tests.
- Use of the TTC.
- Having human data on accumulation to indicate which animal model is the more relevant.
- Recommending specifications to remove/reduce certain contaminants and components in the additive.

Waxes FCM No.93

According to the applicant, this group of paraffin waxes is also used as

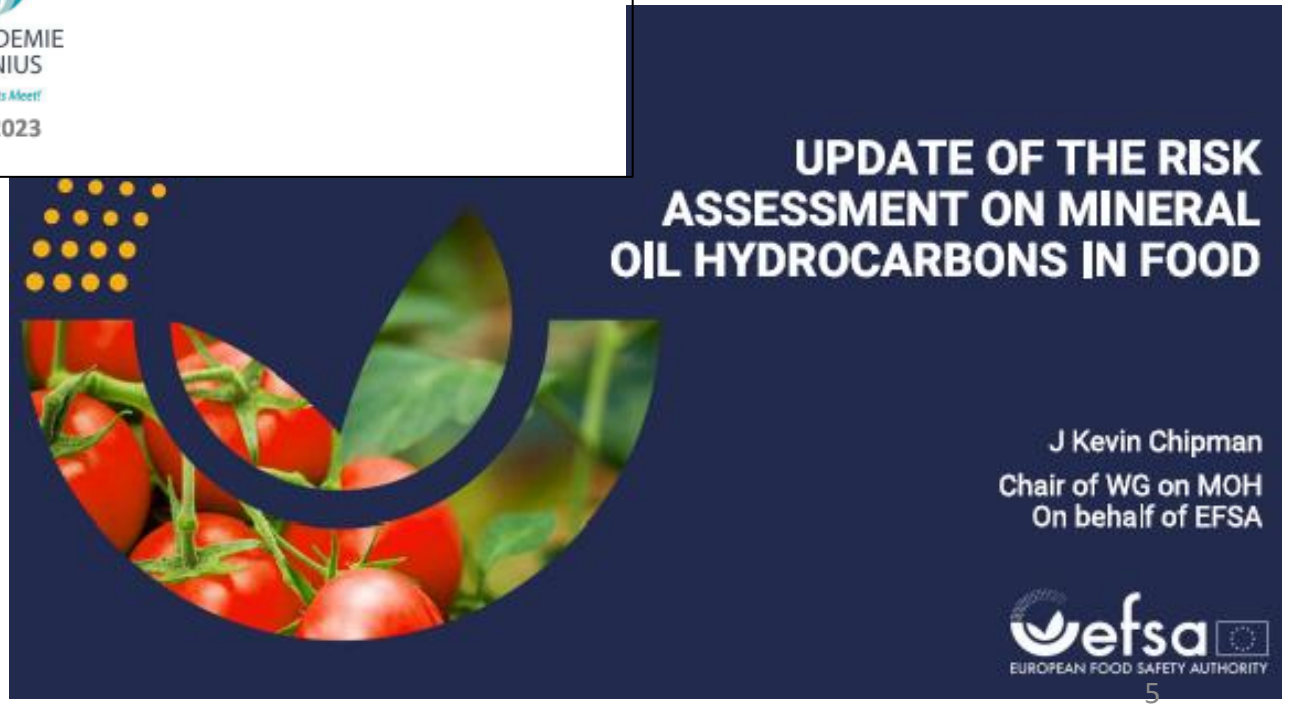
- a component in paper production
- wax coatings on paper
- in hot-melt adhesives
- in PVC intended to come into contact with drinking water
- wax coatings on cheese

FCM No. 93 waxes are non-defined mixtures (ECHA = UVCB) produced from **petroleum-based feedstock** or from polymerised **synthetic feedstock** of bio-mass or natural gas (Fischer–Tropsch).

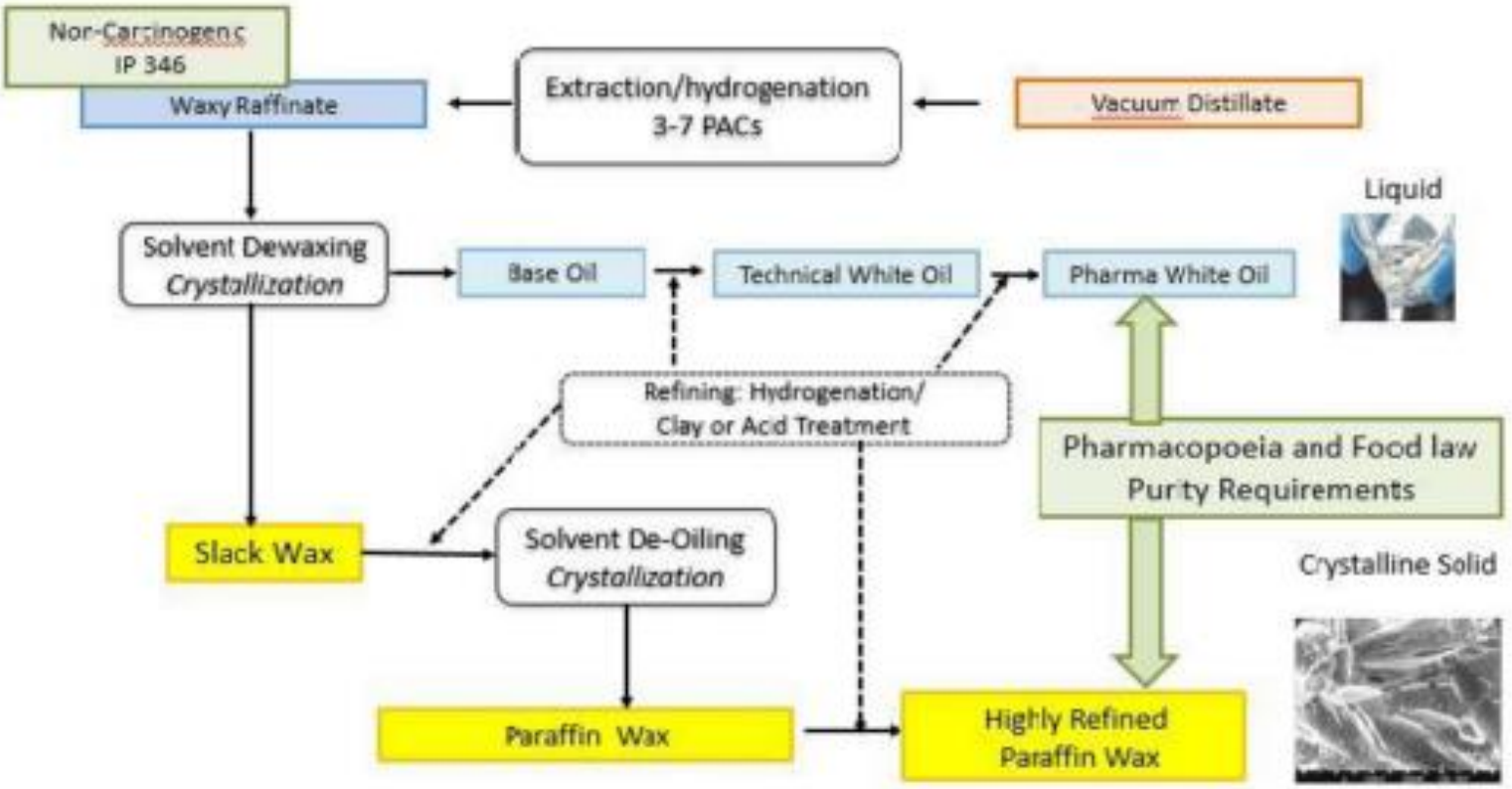
Acknowledgement of Presentations made at Fresenius FCM conference 5-6.10.2023

Some information in the dossier was confidential (blacked-out in the published Opinion).

The FCM assessment was running in parallel with the EFSA CONTAM Panel update on the RA of mineral oil hydrocarbons in food.

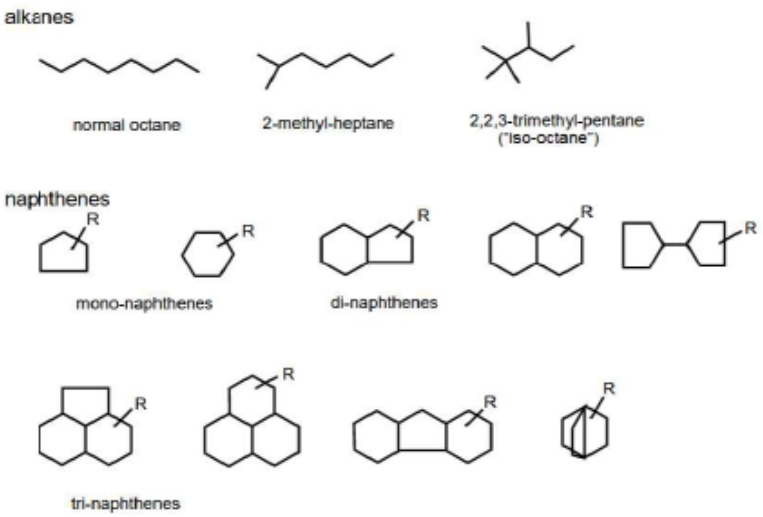


Manufacturing of FCM 93 Hydrocarbon Waxes

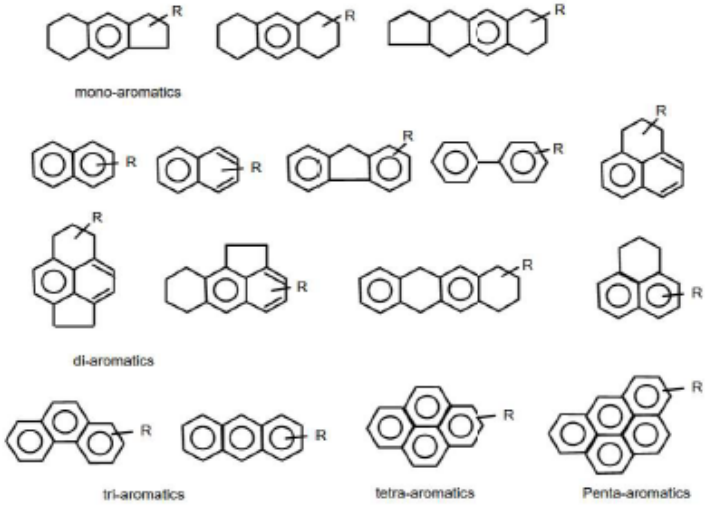


Taken from: Dirk Danneels (EWF) and Martin Lommatzsch (Lab Lommatsch & Sager). Hydrocarbon waxes: From migration testing to tissue analysis, a comprehensive GCxGC supported food contact dossier. Presented at: Residues of food contact materials in food. 12th International Akademie Fresenius Conference, 5-6 October 2023, in Cologne (D) and via LiveStream.

MOSH



MOAH



Taken from: James Kevin Chipman (Birmingham University, UK). EFSA assessment of mineral oil hydrocarbons in food. Presented at: Residues of food contact materials in food. 12th International Akademie Fresenius Conference, 5-6 October 2023, in Cologne (D) and via LiveStream.

Waxes FCM No.93

When made from **mineral oil** the manufacturing process includes a number of isolation and purification steps.

Waxes obtained from **polymerised synthetic feedstock** (Fischer–Tropsch) are almost exclusively n-alkanes (e.g. 93%) with some iso- and no cyclics and are virtually free of MOAH.

As a result, FCM No. 93 waxes are

- predominantly (> 60%, mostly > 80%) n-alkanes;
- little branched isoalkanes with side-branches limited in number and length and located towards one end of the alkyl chain;
- cyclohexanes and cyclopentanes with predominantly straight chain alkyl groups (naphthenes);
- a small fraction of MOAH, almost exclusively alkylated and with a single aromatic ring.

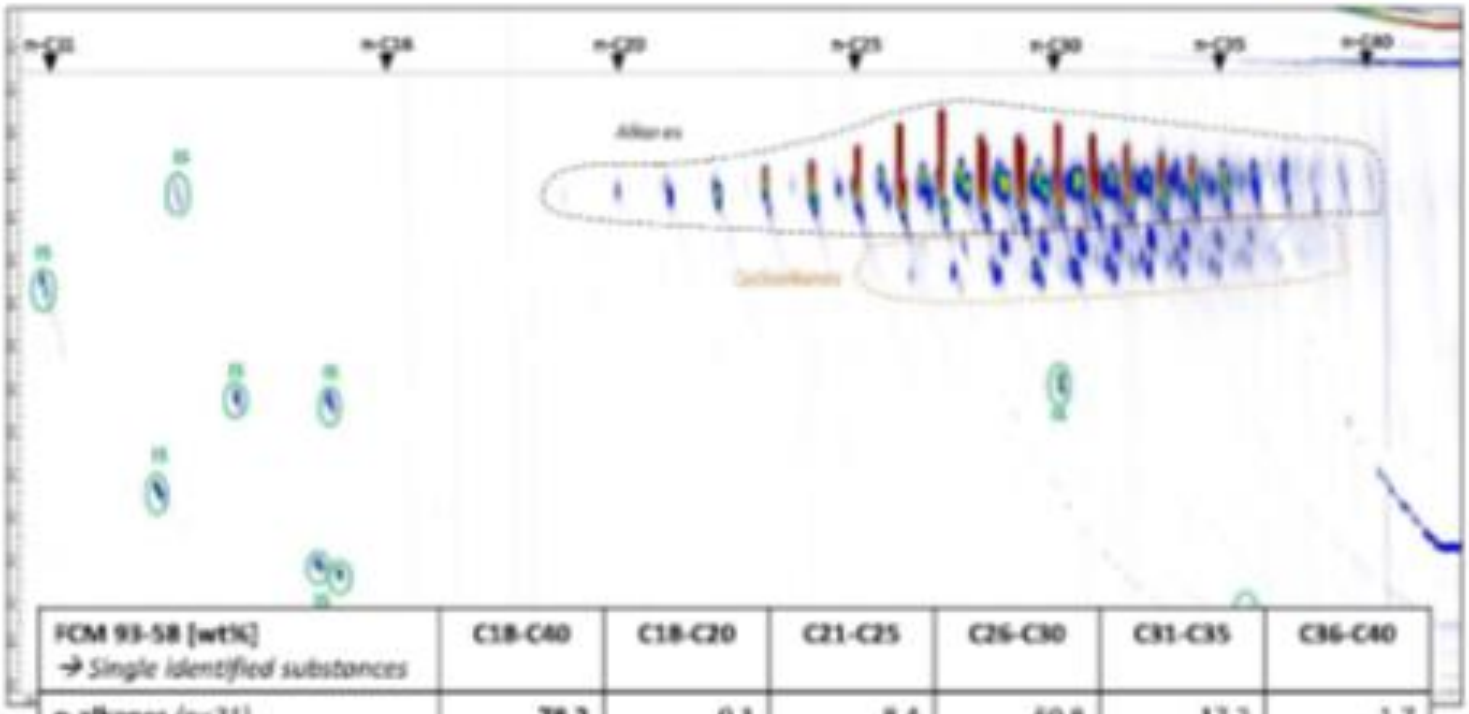
The applicant submitted detailed hydrocarbon compositions of seven waxes. How to deal with this variability in composition?

Dealing with variability in composition of FCM No.93 waxes

Requested migration data (levels and detailed composition of the migrate) on a wax with the lowest average carbon number and Mp, as a suitable worse-case with regard to migration.

Based on comprehensive analytical characterisation of that migrate, requested tox testing on a material representing as closely as possible the migrate i.e. low in n-alkanes and high in iso- and cyclics-.

GC x GC FCM 93-58



FCM 93-58 [wt%] → *Single identified substances*	C18-C40	C18-C20	C21-C25	C26-C30	C31-C35	C36-C40
n-alkanes *(n=21)*	**78.2**	0.1	8.4	50.8	17.2	1.7
iso-alkanes *(n=34)*	**12.3**	<0.1	0.2	6.6	4.9	0.5
monocyclo-alkanes *(n=47)*	**6.2**	<0.1	0.1	3.3	2.7	0.2
Total *(n=102)*	96.7	0.1	8.7	60.7	24.8	2.4

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Migration tests

The wax was added at 1% into low-density polyethylene (LDPE).

LDPE was selected as the worse-case polymer for its high diffusivity.

Fatty food simulants were **Miglyol** 812 and olive oil

Test conditions up to 12 days at 60°C and up to **64 days at 40°C**.

The migration of MOSH was 142 mg/kg, comprising:-

- n-alkanes 97 mg/kg
- isoalkanes 36 mg/kg
- naphthenes 8.4 mg/kg

The composition of the migrate is different to the wax, with higher proportion of iso- and cycloalkanes migrating.

Specific migration into the food simulants water, 3% acetic acid and 10% ethanol was ≤5ug/kg, as expected due to solubility limitations.

Migration tests - MOAH

n-alkanes	97 mg/kg
isoalkanes	36 mg/kg
naphthenes	8.4 mg/kg
SUM of MOSH	142 mg/kg

- The applicant did not provide results on the migration of MOAH.
- The Panel calculated it *pro-rata* to the migration of wax.
- The MOAH in 22 wax samples tested was up to 3.9% w/w.
- ➢ The resulting MOAH migration would be 0.19 and 2.3 mg/kg food for a migration of wax at 5 mg/kg food and 60 mg/kg food, respectively.

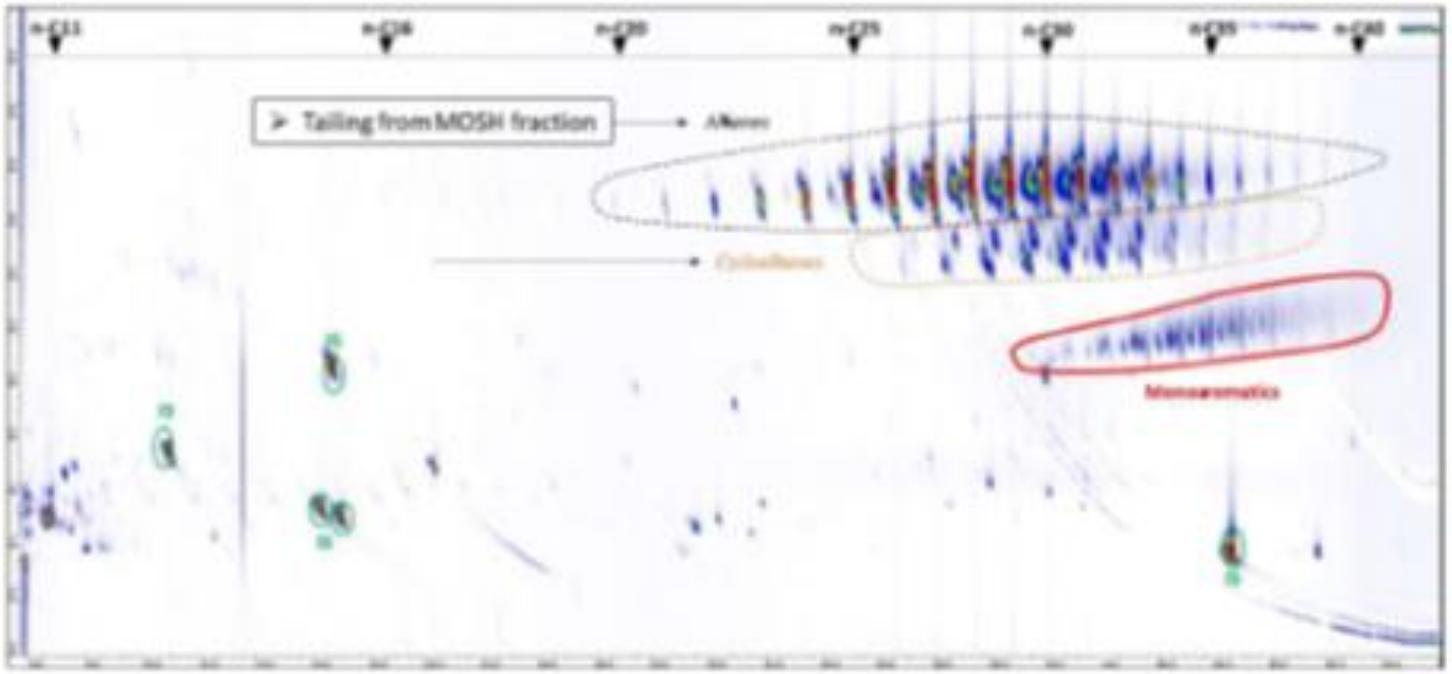
PAH & MOAH with 2-, 3- or more rings

- The resulting MOAH migration would be 0.19 and 2.3 mg/kg food for a migration of wax at 5 mg/kg food and 60 mg/kg food, respectively.

The sum of the PAH16 content (middle-bound, setting non-detects to half the LoD) for the five samples tested, was in the range of 0.1 to 2.7 ug/kg wax.

The applicant provided only limited data regarding the content of MOAH with two or more conjugated aromatic ring by GCxGC analysis of the wax EWF FCM 93 58 used in the sub-chronic toxicity study.

GC x GC FCM 93 (MOAH fraction)



GCxGC analysis of MOAH fraction obtained after enrichment via HPLC

- 25x Fractionations required because of the very low MOAH concentration in FCM 93-58

Taken from: Dirk Danneels (EWF) and Martin Lommatzsch (Lab Lommatsch & Sager). Hydrocarbon waxes: From migration testing to tissue analysis, a comprehensive GCxGC supported food contact dossier. Presented at: Residues of food contact materials in food. 12th International Akademie Fresenius Conference, 5-6 October 2023, in Cologne (D) and via LiveStream.

MOAH content and migration

The (non-genotoxic) Phenanthrene (not included in PAH16) was by far the predominant PAH, at up to 21 ug/kg wax.

This value was used by the Panel to estimate the potential content of alkylated 3-ring MOAH.

For a batching oil (a cruder mineral oil fraction than FCM No. 93 waxes) the non-alkylated 3-ring MOAH fraction (phenanthrene and anthracene) corresponded to 1.8% w/w of the total 3-ring MOAH content (Grob et al., 1991).

- From this, a total concentration of 3-ring MOAH of 1.17 mg/kg in the wax was estimated by the Panel.

Genotoxic potential

The genotoxic potential of the wax was assessed by the EFSA AFC Panel 2006 with the three in vitro tests required at that time.

The wax selected was considered representative for the low-molecular weight paraffin waxes used in food contact applications.

The wax (a solid) was extracted with DMSO to obtain any soluble component that could potentially induce a mutagenic response.

The actual concentrations were not determined but the highest technically applicable volumes of extracts were tested.

Genotoxic potential

The DMSO extracts tested negative:-

for gene mutations (with- and w/o S9)

- bacteria (four strains of Salmonella Typhimurium and one strain of Escherichia coli
- mammalian cells (mouse lymphoma L5178Y cells)

for clastogenicity

- Chinese Hamster Ovary cells

A micronucleus assay, required by the more recent (2008) Note for Guidance to cover aneuploidy, was not available. However, the results of the in vitro chromosomal aberration assay do not suggest an aneugenic potential.

Based on the available data, the CEP Panel, in agreement with the previous opinion of the AFC Panel (EFSA, 2006), concluded that there is no evidence for a genotoxic potential of the tested DMSO extracts.

- WMA (with fractionation /pre-concentration) plus CPA for PAH and >2-ring MOAHs

Sub-chronic toxicity

13-Week oral toxicity study in Sprague–Dawley rats followed by a 6-week recovery period including toxicokinetics

Based on comprehensive analytical characterisation of the test material, the CEP Panel considered that EWF FCM 93 58 used in the repeated dose 90-day subchronic toxicity study in Sprague–Dawley rats is representative of the migrate of FCM No. 93 waxes.

A lack of toxicological relevant effects allowed the identification of the NOAEL at the highest dose tested, 9 g/kg bw per day.

Potential for accumulation

(the same) 13-Week oral toxicity study in Sprague–Dawley rats followed by a 6-week recovery period including toxicokinetics

Accumulation of wax in SD rats reached a steady-state after 30 days (the first measurement point) which is much faster than for F344 rats.

The profile of hydrocarbons in many tissue (esp liver and MLN) is more similar between SD rats and humans. The F344 rat strain has a particular sensitivity to n-alkanes (and possibly other wax components) and therefore the effects observed in this rat strain are considered non-relevant for humans.

n-Alkanes and other wax components were almost completely eliminated from the liver and spleen of SD rats after the 6-week recovery period (5.7% residual).

Additionally, data from literature demonstrate that accumulation in humans is limited.

PAHs and MOAH with 3 or more rings

For a wax migrating at 5 mg/kg food in fatty food, a *pro rata* migration of the sum of the 16 genotoxic PAH would be up to 0.00059 ug/kg food. So no concern.

No evidence of 3-ring or higher MOAH in the analysis of the waxes. Some calculations were made based on concentration of phenanthrene.

Based on the highest measured MOAH content found in all the 27 waxes (3.9% w/w) and for a migration of 5 mg/kg food, the *pro rata* migration of 3-ring MOAH would be 0.26 ug/kg. The migration from FCM No. 93 waxes is expected to be much lower. The relevant TTC is 0.15 ug/person/day. So any concern is allayed.

CONCLUSION ON FCM No. 93 WAX

The CEP Panel concluded that the provided information on chronic toxicity and carcinogenicity was inadequate to reach conclusions on these endpoints.

Following the tiered approach, the CEP Panel concluded that FCM No.93 does not raise safety concern if its migration does not exceed 5 mg/kg.

It was recommended that specifications should include an obligatory hydrogenation step in the manufacturing process.

It was noted that migration is expected to exceed 5 mg/kg food under some of the intended uses proposed by the applicant.

Timeline EFSA Q-2018-00558

13-7-2018	Dossier Received
18-6-2019	Dossier Valid (EFSA has 6 months)
17-9-2019	STC ADR letter (data within 6 months)
11-6-2020	Add data submitted
21-7-2020	STC ADR letter (data within 12 months)
31-9-2022	Add data submitted
7-12-2022	Opinion Adopted
1-2-2023	Opinion Published

*** QUESTIONS / COMMENTS / OBSERVATIONS ? ***

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