FriPura filter

A health risk assessment of elements leaching into cooking oil

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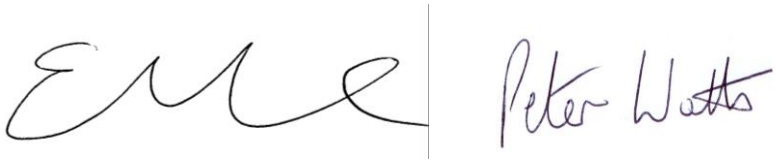

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Executive Summary

FriPura wishes to market a ceramic filter that can be added to retail outlet cooking oil (one filter per every 10 L of cooking oil) to extend its lifespan. Bibra was initially provided with six reports from Staffordshire Scientific Services (SSS) which analysed samples of "fresh" oil (before the addition of a filter), and "used" oil (after contact with the FriPura filter) for 14 elements that might be extracted. These reports provided a realistic simulation of leaching from the FriPura filter, but were not adequately informative about levels of leaching lead and chromium, from a health-assessment perspective. To clarify exposures to these two elements more precisely, bibra was subsequently provided with a summary report from Intertek testing of a filter ("practically identical" in composition to that which FriPura hopes to market) in sunflower oil for 10 days, and a summary report on a 12-day acetic acid extraction of a FriPura filter by West Yorkshire Analytical Services (WYAS). Bibra was asked whether ingestion of any of the 14 elements, at the estimated intakes, might pose any significant health risk to the consumers of foods (fish and chips) fried in the filter-treated oil.

Based on the SSS report, analysed concentrations of calcium, copper, iron, phosphorus and sulphur in oil were lower following the use of the filter, so these elements were excluded from further health risk assessment. For the remaining nine chemicals, bibra assessed the potential health risks associated with their daily consumption associated with one meal of fish and chips, fried in treated oil. Notably, for some of these elements, levels in both "fresh" and "used" oil were below the limit of quantification (LOQ, 0.2 mg/kg). In these cases, although there was no actual evidence of exposure from the Fripura filter, a worst-case (health-precautionary) assumption was made that levels in "used" oil were at LOQ, and levels in "fresh" oil were zero. The Intertek and WYAS reports were used to refine predicted exposures to lead and chromium. In the risk assessment of lead, children were considered to be a particularly susceptible subpopulation, so a child-specific health risk assessment was carried out, assuming that a child consumes fish and chips three times a week.

Based mainly on expert group assessments and HCVs, it was concluded with high confidence that none of the assessed elements (cadmium, chromium, lead, manganese, molybdenum, nickel, potassium, silicon and zinc) would pose any significant risks to the health of consumers under the specified use conditions, even when worst-case assumptions were made about exposure. Overall then, there was no evidence of leaching of elements from the filter in amounts that would raise significant health concerns for regular consumers of foods fried in oil containing the filter.

Background

FriPura manufactures a ceramic filter for use in retail outlet cooking oil, designed to extend the oil's lifespan. Bibra was informed that one filter will be used in 10 L of oil. Staffordshire Scientific Services (SSS) analysed samples of "fresh" oil (before the addition of a filter), and "used" oil (after contact with the FriPura filter) for a number of inorganic elements. Any elements leaching from the filter into the cooking oil could transfer to fried foods (in the absorbed oil) and be consumed.

Bibra was supplied with six analytical reports detailing the results of these SSS studies on three samples of "fresh" oil, and three samples of "used" oil. Bibra was asked to assess whether the leachable chemicals might pose any significant health risks to individuals consuming these elements along with fried foods (in this case, fish and chips). Later, bibra was also supplied with reports from Intertek and West Yorkshire Analytical Services (WYAS), and these were used to help clarify potential exposures to lead and chromium.

Expertise

Bibra was founded (as the British Industrial Biological Research Association) in 1961 to provide independent, high-quality research, information and advice on chemical toxicology to industry and governmental departments. Its risk assessors have a >50-year record of objectivity and scientific excellence. All of the senior scientists in the current team are accredited and listed in the EUROTOX and UK British Toxicology Society/Society of Biology Registers, and are thus bound by their specific codes of conduct. Peter Watts, the bibra Director of Toxicology, and a co-author of the current report, is a graduate chemist and has 36 years' experience in reviewing and critically evaluating toxicological data and other scientific information on a wide range of chemicals.

Analytical results

Bibra was provided with reports detailing the results of analyses of "fresh" (SSS, 2013a,b, 2014a) and "used" oil (SSS, 2013c, 2014b,c). Bibra was asked to take the average concentration from three samples of "fresh" oil as the baseline (control) figure. As a health-precautionary step, the highest concentration found in three samples of "used" oil was selected for comparison (i.e. a worst case approach).

Table 1. Concentrations of elements in "fresh" and "used" oil

Element	CAS RN[1]	Concentration in "fresh" oil (mg/kg)	Concentration in "used" oil (mg/kg)
Cadmium	7440-43-9	0*	0.2*
Calcium	7440-70-2	3.57	1.1
Chromium	7440-47-3	0*	0.2*
Copper	7440-50-8	0.33	0.2*
Iron	7439-89-6	0.5	0.2*
Lead	7439-92-1	0*	0.2*
Manganese	7439-96-5	0*	0.2*

[1] Chemical Abstracts Service Registry Number

Molybdenum	7439-98-7	0*	0.2*
Nickel	7440-02-0	0*	0.2*
Phosphorous	7723-14-0	24.83	13.91
Potassium	7440-09-7	0.27	0.7
Silicon	7440-21-3	0.43	12.4
Sulphur	7704-34-9	1.43	0.4
Zinc	7440-66-6	0.07	0.2*

* below the limit of quantification (LOQ) of 0.2 mg/kg. As an additional health-precautionary step, concentrations below LOQ were taken as 0 mg/kg in "fresh" oil and 0.2 mg/kg in "used" oil.

These analytical results indicate that concentrations of calcium, copper, iron, phosphorus and sulphur in cooking oil are apparently reduced by the filter. These elements were therefore excluded from further health risk evaluation. With concentrations below LOQ in both "fresh" and "used" oil samples, there is also no evidence of increased exposure to cadmium, chromium, lead, manganese or nickel. Nevertheless, as a health-precautionary step, these were subjected to a health risk assessment on the assumption that <LOQ in "fresh" oil represents a genuine zero result but they could be present at up to LOQ in the "used" samples.

Bibra was subsequently provided with two further summary analytical reports that helped to clarify levels of exposure to lead and chromium from the filter.

In the study relevant to chromium, WYAS immersed a 225-g ceramic block in 3% acetic acid at 20°C for 12 days (WYAS, 2014). The acetic acid was analysed, and 0.2 mg of chromium was detected. If 0.2 mg of chromium is released from the FriPura filter into 10 L of oil, the resulting concentration will be about 0.02 mg/kg, 10-fold lower than the figure derived by applying worst-case assumptions to the LOQ of the SSS analysis (where chromium was not detected). Release into (non-aqueous) oil is expected to be lower than that observed for (aqueous) acetic acid, so this is considered health-precautionary.

For lead, bibra was provided with a report from Intertek (Intertek, 2012) on a filter "practically identical" in composition to that which FriPura hopes to market. The filter was placed in 500 ml of sunflower oil at 60°C for 10 days (8 hours/day). Although temperatures greater than 60°C are anticipated for FriPura filters during use, bibra does not consider that this lower temperature would have significantly reduced the levels of non-organic elements leaching into oil. In three ceramic samples, lead in oil was below LOQ (0.01 mg/kg) at the end of incubation. As 500 ml of oil was used, concentrations in 10 L would not exceed 0.5 µg/kg.

Toxicity data searches

Toxicity data searches on the nine assessed elements (i.e. excluding calcium, copper, iron, phosphorus and sulphur) were based on the CAS RNs listed in **table 1.** As the elements are well-studied toxicologically, it was considered sufficient to limit searches essentially to the unique (and REACH guidance-approved) bibra TRACE database (see Appendix for details). The health risk assessments relied heavily on expert group reviews and opinions on the chemicals of interest, and searches of the more recent primary literature (post-review date) were carried out to ensure that no critical data were missed.

Exposure estimates

As a reasonable worst case, bibra was asked to assume that 70-kg adults may consume one meal of deep-fried fish and chips per day. Average portion sizes of 170 g fish and 285 g chips were assumed, as indicated by the National Federation of Fish Friers (NFFF, undated). Oil absorption (as % of final portion weight) was assumed to be 15% for battered fish and 10% for fresh French fries (Kochhar, 1997).

It was estimated that a 70-kg individual could, in these assumed circumstances (one meal/day), ingest about 54 g/day of cooking oil.

In the risk assessment of lead, it was assumed that a child could eat up to two thirds (by weight) of an adult portion, up to three times a week, providing an average of about 15.5 g/day of cooking oil. A default body weight of 20 kg was assumed for exposed children[2].

Table 2. Potential daily exposures from elements in 0.054 kg of cooking oil (or 0.0155 kg for a child)

Element	Concentration in "used" oil due to filter (mg/kg)	Potential exposure (µg/kg bw/day)
Cadmium	0.2	0.15
Chromium	0.02	0.015
Lead	0.0005	0.00039 (20-kg child and 70-kg adult)
Manganese	0.2	0.15
Molybdenum	0.2	0.15
Nickel	0.2	0.15
Potassium	0.43	0.33
Silicon	12.0	9.3
Zinc	0.13	0.10

Health risk assessments

Cadmium

Cadmium was potentially present in "used" oil at up to 0.2 mg/kg, and it was assumed that an individual could be orally exposed to cadmium at up to 0.15 µg/kg bw/day from this source.

In humans and other mammals, the principal targets of toxicity following long-term exposure to cadmium are the kidney and bone (ICH, 2013; JECFA, 2011). Cadmium causes lung cancer in workers exposed by inhalation; in 2009, the International Agency for Research on Cancer confirmed that it is "carcinogenic to humans" (Group 1) (IARC, 2012). Limited cancer studies have provided no convincing evidence that oral exposure to cadmium is carcinogenic (IARC, 2012; JECFA, 2011). Cadmium can be genotoxic, but does not directly bind to DNA; mechanisms of genotoxicity are believed to be indirect (production of reactive oxygen species and inhibition of DNA repair) (JECFA, 2011) and could thus demonstrate a threshold. Indeed, the Scientific Committee on Occupational Exposure Limits (SCOEL)

[2] The UK Environment Agency recommends this as a default value for children aged 6-7 years (UK EA, 2009).

of the European Commission considers cadmium (and its inorganic compounds) a category C carcinogen (genotoxic carcinogens for which a practical threshold is supported and a health-based occupational exposure limit (OEL) is proposed) (SCOEL, 2010).

For the general population, the diet is the main source of cadmium exposure, supplying, on average, about 2-13 µg/kg bw/month for adults and children, although higher exposures (of about 22 µg/kg bw/month) are expected for vegetarians (JECFA, 2011). In 2010, the Joint FAO/WHO Expert Group on Food Additives derived a provisional tolerable monthly intake (PTMI) of 25 µg/kg bw, based on a meta-analysis of selected studies evaluating the dose-response relationship between urinary cadmium and β2 microglobulin (a measure of cadmium kidney toxicity). A monthly value was considered appropriate due to cadmium's "exceptionally long half-life"; variation in daily ingestion in the food is expected to have "a small or even a negligible effect on overall exposure" (JECFA, 2011).

Previously, the European Food Safety Authority set a provisional tolerable weekly intake (PTWI) of 2.5 µg/kg bw, using a similar methodology (EFSA, 2009). EFSA has since analysed the differences between its derivation and JECFA's, and considers its own PTWI "appropriate" (EFSA, 2011). As absorption from drinking water was expected to be twice as efficient as from food, the US Environmental Protection Agency derived separate chronic oral reference doses[3] (RfDs) for non-cancer effects of 0.5 and 1 µg/kg bw/day for cadmium in the drinking water and food, respectively, again based on kidney toxicity. The US EPA limited its carcinogenicity evaluation to inhaled cadmium [which might suggest a lack of concern over oral carcinogenicity] (US EPA, 1992, 1994).

Since these evaluations, the US Agency for Toxic Substances and Disease Registry set a chronic oral minimal risk level (MRL) for non-cancer endpoints of 0.1 µg/kg bw/day, again considering epidemiological data and toxicokinetics. The critical level of urinary cadmium was about an order of magnitude less than that proposed by JECFA (ATSDR, 2012a). ATSDR's MRL was the basis of an oral permitted daily exposure (PDE) in pharmaceuticals of 5 µg [based on 0.1 µg/kg bw and a 50-kg body weight], recently derived by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH, 2013).

A REACH dossier on cadmium has been submitted by industry to the European Chemicals Agency. A long-term derived no-effect level (DNEL[4]) of 1 µg/kg bw/day is recommended for systemic effects to the general population exposed orally, the driving factor being repeated dose toxicity. No oral derived minimal-effect level (DMEL) was calculated, indicating a lack of concern for non-threshold carcinogenicity by the oral route (ECHA, undated a).

The assessed exposure from "used" oil (0.15 µg/kg bw/day) is about 5 times lower than the averaged daily dose derived from JECFA's PTMI (0.83 µg/kg bw/day), 2 times lower than that derived from EFSA's PTWI (0.36 µg/kg bw/day), 3-7 times lower than the US EPA's chronic RfDs, and 7 times lower than industry's chronic oral DNEL. Based on comparison with the health criteria values (HCVs) from these key, prestigious experts, the assessed dose would be deemed tolerable. The assessed dose is a little higher than the ATSDR MRL and the ICH PDE (0.1 µg/kg bw/day). However, given that levels of cadmium were <LOQ in both "used" and "fresh" oil (i.e. there was no actual analytical evidence of cadmium exposure) and the fact that daily consumption of fish and chips cooked in oil containing the filter is highly improbable, it seems unlikely that the use of the filter could supply cadmium at doses that would have any significant impact on human health.

[3] The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

[4] The DNEL is the level of exposure to the substance above which humans should not be exposed. At exposures below the DNEL, health risk is believed to be controlled adequately.

Chromium

Based on the WYAS report, chromium concentrations in used oil would not exceed 0.02 mg/kg. It was assumed that an individual could be orally exposed to chromium at up to 0.015 µg/kg bw/day as a result of the FriPura filter. The oxidation state of the chromium present was not specified in the analytical reports provided to bibra.

Chromium exists in various oxidation states, the most abundant environmental form being chromium(III), an essential element involved in glucose metabolism in humans.

The US EPA has derived a chronic oral RfD of 1.5 mg/kg bw/day for insoluble chromium(III) salts, based on a chronic feeding study in rats given chromium(III) oxide, which saw no adverse effects at the highest tested dose (about 1500 mg/kg bw/day) (US EPA, 1998a). Later, the UK Expert Committee on Vitamins and Minerals (EVM) derived a tolerable daily intake (TDI) of 0.15 mg/kg bw/day for chromium(III) from a no-observed-adverse-effect level (NOAEL) of 15 mg/kg bw/day (as chromium) in a subchronic study on rats given chromium chloride (EVM, 2003). More recently, ATSDR evaluated chromium(III), but no oral MRLs were derived as data on the levels of exposure causing toxicity were considered inadequate. ATSDR noted that several laboratory animal studies involving chronic oral exposure to chromium(III) compounds saw no adverse effects, "even at very high daily doses" (ATSDR, 2012b). Meanwhile, ICH's oral PDE of 11 mg [0.16 mg/kg bw for a 70-kg adult] was generated by applying appropriate modifying factors to a NOAEL of 10.7 mg/kg bw/day (as chromium), seen in a chronic NTP[5] study on rats treated orally with chromium(III) picolinate, the critical effect being equivocal evidence of benign testicular tumours in males (ICH, 2013).

A greater degree of toxicity is expected from chromium(VI), the key endpoint being genotoxic carcinogenicity (ICH, 2013). In a draft report from the US EPA, it was assumed that tumours seen in the gastrointestinal tract of rodents subject to chronic oral treatment resulted from a DNA-reactive mode of action, without a threshold. The EPA estimated that chronic oral exposure to chromium(VI) at 1 mg/kg bw/day represents an extra lifetime cancer risk of 50%. Accounting for the potentially greater sensitivity of children, an average dose of 0.1 µg/kg bw/day for an entire lifetime was expected to be associated with an extra cancer risk of 8×10^{-5} (US EPA, 2010). For non-cancer effects, the EPA derived a chronic oral RfD of 3 µg/kg bw/day, based on a 1-year drinking water study in rats, where no adverse effects were seen at the highest tested dose (2.5 mg/kg bw/day) (US EPA, 1998b). ATSDR's chronic non-cancer MRL was 0.9 µg/kg bw/day, based on non-neoplastic lesions in the duodenum of mice treated chronically in the drinking water (ATSDR, 2012b).

Whether DNA-reactive events are key or not in the development of the gastrointestinal tract tumours in rodents remains unclear. In a recent publication, WHO experts were only able to conclude that "there is significant uncertainty associated with the carcinogenic risk to humans of chromium(VI) compounds via oral exposure" (IPCS, 2013). In a detailed publication, other experts have recently stated that the weight of evidence supports a cytotoxic (threshold) mode-of-action (MOA) with key events being absorption of chromium(VI) from the intestinal lumen, toxicity to intestinal villi, crypt regenerative hyperplasia and clonal expansion of mutations within the crypt stem cells, resulting in late onset tumorigenesis. It was concluded that the data argue against a mutagenic MOA for chromium(VI)-induced intestinal tumors (Thompson et al., 2013).

[5] US National Toxicology Program

The World Health Organization has set a provisional drinking water guideline of 50 µg/L for chromium (total chromium III and VI) (WHO, 2011). For an adult weighing 70 kg and drinking 2 L/day of water containing chromium at this guideline limit, the chromium dose would be about 1.4 µg/kg bw/day.

The REACH dossiers on chromium metal (valency state 0) and chromium(III) contain only DNELs relating to inhaled chromium (ECHA, undated b,c). The REACH dossier on chromium(VI) oxide proposes only a long-term inhalation derived minimal-effect level (DMEL) for workers (of 0.01 mg/m^3), indicating concern over non-threshold toxicity (ECHA, undated d).

The assessed chromium exposure is 0.015 µg/kg bw/day. If this is chromium(III), then the exposure is clearly toxicologically insignificant, because it is 100,000 times lower than the US EPA's oral RfD, and about 10,000 times lower than ICH's oral PDE and EVM's TDI.

If the extracted chromium is chromium(VI), the current US EPA position implies that the assessed exposure could represent an excess cancer risk of up to about 1.2 per 100,000 persons exposed daily for a lifetime, practically the same value as the 1 in 100,000 risk that is generally considered tolerable. It should also be remembered that levels leaching into the acetic acid used by WYAS are likely to be higher than those leaching into oil (a non-aqueous medium), and that the daily consumption of fish and chips cooked in oil containing the filter is highly improbable.

Overall, it seems highly unlikely that the use of the filter could supply chromium at doses that would have any significant impact on human health.

Lead

Based on the Intertek report, lead concentrations in "used" oil would not exceed 0.5 µg/kg. This concentration could give rise to a maximum dose of 0.39 ng/kg bw/day, both for 70-kg adults exposed daily, and for 20-kg children aged 6-7 years exposed three times a week.

Lead has no known useful biological function in humans. Exposure has been associated with neurological, cardiovascular, immune, renal, reproductive, and developmental toxicity. The foetus and the young child are generally more susceptible than adults, and adverse neurological effects are considered the most sensitive and relevant endpoint for humans exposed orally. Epidemiological studies have shown that blood lead levels below 5 µg/dL may be associated with neurobehavioral deficits in children (ICH, 2013). Normal blood concentrations have been reported to be up to 40 µg/dL, although concentrations in children are generally much lower (BloodBook, 2013).

ICH set a PDE of 5 µg for lead in pharmaceuticals; this is expected to give rise to blood concentrations of 1-2 µg/dL in children up to 7 years of age (assuming 100% bioavailability and no other sources of exposure) (ICH, 2013). Although the PDE was clearly intended for children (who are most susceptible), ICH did not set a separate value for adults. For a 20-kg child and a 70-kg adult, the PDE equates to 0.25 and 0.07 µg/kg bw/day, respectively.

A provisional guideline of 10 µg/L has been set by WHO for lead in drinking water. This was previously based on a JECFA PTWI. JECFA withdrew its PTWI due to concerns over non-threshold toxicity. In the absence of a new PTWI, WHO maintained its guideline value, but designated it as "provisional" on the basis of treatment performance and analytical achievability (WHO, 2011). Assuming a daily water intake of 2 L for adults, this provisional guideline value equates to 20 µg/day [0.3 µg/kg bw/day].

EFSA and JECFA both considered that, as no threshold for the key adverse effects of lead could be identified, human health risk assessments should adopt a margin of exposure (MoE) approach. EFSA

generated BMDL values[6] of 1.2, 1.5 and 3.6 µg/dL respectively for blood lead's effects on the nervous system of children (decreased IQ), on the kidney, and on the blood pressure of adults. Toxicokinetic modelling indicated that children exposed orally to 0.5 µg/kg bw/day would have a blood lead level of 1.2 µg/dL, a level that EFSA concluded could cause a 1-point decrease in a child's IQ (EFSA, 2010a).

Lead and numerous lead compounds are the subjects of REACH dossiers, but these dossiers do not contain DNEL proposals (ECHA, undated e), probably because ECHA had selected lead for listing as a restricted substance. ECHA's Committee for Risk Assessment (RAC) proposes restrictions to limit lead intake to up to 0.05 µg/kg bw/day. Such a dose is not expected to increase blood levels in children by more than 1.2 µg/dL, with an associated IQ reduction of no more than 0.1 points (ECHA, 2013).

The ICH PDE of 5 µg infers that doses of about 0.25 µg/kg bw/day in a 20-kg child would be tolerable, a dose level that is higher than that being assessed here for both adults and children. Similarly, daily consumption by children of about 900 ml of water (EFSA, 2010b) containing lead at the WHO limit would provide some 9 µg/day (0.45 µg/kg bw/day) which is also higher than the dose level being assessed here. The most conservative proposal has been made by ECHA's RAC, suggesting that lead intake should be limited to 0.05 µg/kg bw/day, again with the focus on the IQ of children. It is reassuring that the exposure assessed here for children (up to 0.39 ng/kg bw/day) is 640 times lower than ICH's PDE, more than 1000 times lower than the exposure expected at WHO's drinking water limit, and about 130 times lower than RAC's proposed limit. It thus appears highly unlikely that lead from the FriPura filter could cause significant adverse health effects in children. Adults are less susceptible to lead toxicity than children, so clearly an intake of 0.39 ng/kg bw/day is not of concern, particularly as the daily consumption of fish and chips cooked in oil containing the filter is in itself highly improbable.

Manganese

Manganese was potentially present in "used" oil at up to 0.2 mg/kg. It was assumed that an individual could be exposed orally to up to 0.15 µg/kg bw/day from the FriPura filter.

Manganese is an essential component of certain metalloenzymes involved in carbohydrate, amino acid and lipid metabolism (EFSA, 2013a).

Although some studies have reported neurological effects in humans exposed for extended periods to manganese in the drinking water, findings were not repeated in other studies, and significant potential confounding factors were noted. Rodent studies were considered to be of limited predictive value by expert groups. WHO derived a health-based value of 400 µg/L in water from dietary surveys showing that intake at 11 mg/day [0.16 mg/kg bw/day] is without observed adverse effects. This health-based value is well above concentrations of manganese normally seen in drinking water, and was withdrawn on the basis that it is higher than the concentration affecting taste (100 µg/L) (WHO, 2011). The US EPA derived a chronic oral RfD for manganese of 0.14 mg/kg bw/day, as the human database on dietary manganese available at the time indicated that an intake of 10 mg/day was "appropriate" (US EPA, 1996).

EFSA has proposed an adequate intake (AI) of 3 mg/day for adults [0.04 mg/kg bw/day], including pregnant and lactating women (EFSA, 2013a). The UK EVM has suggested that total intakes of 12.2 mg/day for the general population and 8.7 mg/day for older people [0.17 and 0.12 mg/kg bw/day] should be without adverse effect (EVM, 2003).

[6] The respective benchmark responses were a 1% change in full-scale IQ score (a 1-point decrease in IQ), a 10% change in the prevalence of chronic kidney disease, and a 1% change in systolic blood pressure (corresponding to an increase of 1.2 mm Hg from the baseline value of 120 mm Hg in a normotensive adult).

No PDEs have been established by ICH for manganese "due to its inherent low toxicity" (ICH, 2013).

REACH dossiers have been submitted on manganese and various manganese compounds. The manganese dossier does not propose a chronic oral DNEL for systemic effects to the general population (ECHA, undated f), but a value of 4.3 mg/kg bw/day is recommended for manganese diacetate (ECHA, undated g).

The potential intake from "used" oil (up to 0.15 µg/kg bw/day) is about 1000 times lower than the US EPA's chronic oral RfD, and more than 250 times lower than EFSA's dietary AI. Clearly, manganese in "used" oil is not of concern with regards to consumer health. As levels of manganese were <LOQ in both "used" and "fresh" oil, there was in any case no actual analytical evidence of manganese exposure from the filter.

Molybdenum

Molybdenum was potentially present in "used" oil at up to 0.2 mg/kg. It was assumed that an individual could be exposed orally to molybdenum at up to 0.15 µg/kg bw/day from the FriPura filter.

Molybdenum is an essential component of certain enzymes. Deficiency has not been observed in otherwise healthy humans. EFSA established an AI of 65 µg/day [0.93 µg/kg bw/day], based on molybdenum intakes at the lower end of mean dietary intake estimates from various studies (58 to 157 µg/day [0.83-2.2 µg/kg bw/day]). This value was considered applicable to pregnant and lactating women (EFSA, 2013b).

Data were insufficient for EVM to derive a safe UL for molybdenum. Limited data suggested intakes of more than 1 mg/day [14 µg/kg bw/day] may be associated with gout-like symptoms (joint pain and increased serum uric acid). UK dietary intakes (estimated then to be up to 230 µg/day [3.3 µg/kg bw/day]) were not expected to present any risk to health (EVM, 2003).

ICH established an oral PDE of 180 µg/day for molybdenum [2.6 µg/kg bw/day for a 70-kg adult], derived from a NOAEL of 0.9 mg/kg bw/day (as molybdenum) from a reproductive and developmental toxicity study on female rats given sodium molybdate in the drinking water. The critical toxic effects were on the oestrous cycle, gestational weight gain, and the foetus, at 1.8 mg/kg bw/day and higher (ICH, 2013).

The US EPA has derived a chronic oral RfD of 5 µg/kg bw/day, based on a lowest-observed-adverse-effect level (LOAEL) of 0.14 mg/kg bw/day in a 6-year-to-lifetime human dietary study. Exposure was associated with increased levels of serum uric acid (US EPA, 1993).

WHO has derived a health-based guidance value of 0.07 mg/L for molybdenum in drinking water, from a 2-year human study that saw no adverse effects on clinical chemistry at a drinking water concentration of 0.2 mg/L. Assuming a water intake of 2 L/day, this is equivalent to about 2 µg/kg bw/day molybdenum (WHO, 2011).

A chronic oral DNEL of 3.4 mg/kg bw/day is recommended for the general population in a REACH dossier submitted by industry (ECHA, undated h). Unfortunately, the derivation of this value could not be assessed independently as insufficient information was given in the dossier.

The assessed intake from "used" oil of up to 0.15 µg/kg bw/day is 6 times lower than EFSA's AI, more than 17 times lower than the oral PDE and more than 30 times lower than the US EPA's RfD.

Molybdenum in "used" oil seems highly unlikely to be associated with any adverse health effects in consumers of fried food. As levels of molybdenum were <LOQ in both "used" and "fresh" oil, there was in any case no actual analytical evidence of molybdenum exposure from the filter.

Nickel

Nickel was potentially present in "used" oil at up to 0.2 mg/kg. It was assumed that an individual could be exposed orally to nickel at up to 0.15 µg/kg bw/day from the FriPura filter.

Nickel is not an essential nutrient for humans, but deficiency can cause adverse effects in other animals (ICH, 2013). Ingestion of nickel in food and, to a lesser extent, the drinking water is the primary route of exposure for non-smokers (IARC, 2012). Dietary intakes are roughly between 100 and 200 µg/day [1.4-2.9 µg/kg bw/day] (Danish EPA, 2013; IARC, 2012). It is thought that nickel is genotoxic, but not mutagenic. There is no evidence that ingested nickel causes cancer, but certain nickel salts have increased tumour incidences in inhalation studies on rodents, and nickel is classified as "carcinogenic to humans" (Group 1) by IARC (IARC, 2012; ICH, 2013). Large oral doses of nickel can cause stomach pain, depression of body weight, and adverse effects on the kidneys and blood. Sensitisation can develop in humans following prolonged skin contact (ICH, 2013).

Sensitisation was considered the most sensitive endpoint by ICH in its derivation of an oral PDE for nickel in pharmaceuticals. Human data indicate that an oral challenge with 12 µg/kg bw can induce dermatitis in people sensitised to nickel. The oral PDE was established at 600 µg [8.6 µg/kg bw for a 70-kg adult] (ICH, 2013).

The UK EVM considered that ingestion of 4.3 µg/kg bw/day would not be associated with adverse effects in non-sensitized individuals (EVM, 2003), but EFSA has since concluded that data are inadequate to estimate a tolerable upper intake level (EFSA, 2005).

A TDI of 12 µg/kg bw has been derived by WHO. Again, this was based on the oral provocation of individuals sensitised to nickel. From this value, a drinking water guideline of 70 µg/L was established (WHO, 2011). In the US, a chronic oral RfD for non-cancer effects of 20 µg/kg bw/day was derived from a NOAEL of 5 mg/kg bw/day seen in a 2-year dietary study in rats. This level was not expected to cause individuals to become sensitised to nickel, although it might provoke reactions in individuals already sensitised (US EPA, 1991). Most recently, the Danish EPA derived a TDI of 5.5 µg/kg bw from a NOAEL of 1.1 mg/kg bw/day. The critical effect was foetal mortality seen in a reliable 2-generation study on nickel sulphate. Based on this value, a health-based limit of 20 µg/L was proposed for soluble inorganic nickel compounds in the drinking water (Danish EPA, 2013).

In the REACH dossier on nickel, submitted by industry, an oral long-term DNEL of 20 µg/kg bw/day is proposed for systemic effects to the general population, based on "developmental toxicity/teratogenicity". A short-term oral DNEL of 12 µg/kg bw/day is also proposed for systemic effects to the general population, skin sensitisation being the most sensitive endpoint in this case (ECHA, undated i).

The assessed intake of up to 0.15 µg/kg bw/day is nearly 40 times lower than the Danish EPA's recent TDI, 57 times lower than the ICH PDE, and 80 times lower than the WHO TDI, providing good evidence that exposure to nickel from "used" oil will not be associated with any adverse effects in consumers. As levels of nickel were <LOQ in both "used" and "fresh" oil, there was in any case no actual analytical evidence of nickel exposure from the filter.

Potassium

Potassium was present in "used" oil at up to 0.7 mg/kg, of which 0.43 mg/kg was estimated to have come from the filter. It was assumed that an individual could be exposed orally to potassium at up to 0.33 µg/kg bw/day from the FriPura filter.

Potassium is an essential element in humans, and is considered to have a very low order of toxicity following ingestion. Many potassium salts have been accepted for use as direct additives to food, usually without a toxicity-based limit (JECFA, 1986). Normal concentrations in blood and serum range from 140-210 mg/L (BloodBook, 2013).

WHO notes that potassium is "seldom, if ever, found in drinking water at levels that could be a concern for healthy humans", and that the recommended daily requirement is greater than 3000 mg [42.9 mg/kg bw/day]. As such, a health-based guideline for drinking water has not been derived (WHO, 2011). The UK EVM did not derive a safe UL for potassium, due to insufficient data, but concluded that "supplemental doses of up to 3700 mg potassium/day appear to be without overt adverse effects … but may be associated with gastrointestinal lesions diagnosed by endoscopy" (EVM, 2003).

REACH dossiers have been submitted by industry on numerous potassium compounds. For potassium chloride, a long-term oral systemic DNEL of 91 mg/kg bw/day is proposed for the general population (ECHA, undated j).

Potassium in "used" oil is clearly not a health concern, given that the assessed filter-related exposure of up to 0.33 µg/kg bw/day is 130,000 times lower than the recommended daily requirement.

Silicon

Silicon was present in "used" oil at up to 12.4 mg/kg, of which 12.0 was estimated to be sourced from the filter. It was assumed that an individual could be exposed orally to silicon at 9.3 µg/kg bw/day from the FriPura filter.

Simple silicon compounds are considered to exhibit a very low level of toxicity when given orally (presumably their low solubility and bioavailability is a major factor). JECFA considers that silicon dioxide and certain silicates can be used as food additives, without the need for a toxicity-based upper limit (JECFA, 1974, 2013). It has not been established whether silicon is essential for humans, or if it has a functional role (EFSA, 2004). Reported normal serum concentrations of silicon are between 17 and 350 µg/L (Peters et al., 1995; Teuber et al., 1995).

EFSA concluded in 2004 that a UL could not be established for silicon due to a lack of suitable dose-response data. Typical dietary intakes (of 20-50 mg/day [0.29-0.71 mg/kg bw/day]) were considered unlikely to cause adverse effects (EFSA, 2004).

The UK EVM has set a safe UL of 760 mg/day [10.9 mg/kg bw/day] for adults consuming silicon in food and water over a lifetime (EVM, 2003).

REACH dossiers on silicon (ECHA, undated k) and various silicon compounds have been submitted by industry. The only oral DNEL identified for the general population was for silicon carbide – a value of 13 mg/kg bw/day for short-term exposure (ECHA, undated l). Uncertainty over the relevance of this compound to silicon toxicology meant that this figure was not used in the current assessment.

The assessed exposure (up to 9.3 µg/kg bw/day) resulting from the use of the FriPura filter is at least 30 times lower than typical dietary intakes, and more than 1000 times lower than EVM's safe UL. Intake from "used" oil is clearly not a health concern.

Zinc

Zinc was potentially present in "used" oil at up to 0.2 mg/kg. It was assumed that an individual could be exposed orally to zinc at up to 0.1 µg/kg bw/day as a result of the FriPura filter.

Zinc is an essential element in humans. Normal blood concentrations reportedly range from 1000 to 7320 µg/L (ATSDR, 2005; BloodBook, 2013).

Upon ingestion, concentrations of 0.91 mg/ml, and acute doses of about 2-10 mg/kg bw are emetic to humans. It is not clear whether the effects are driven mainly by dose or concentration (ATSDR, 2005; JECFA, 1982).

JECFA set a provisional maximum tolerable daily intake (PMTDI) of 1 mg/kg bw (JECFA, 1982, 2013), while the UK EVM does not expect daily oral intakes of 42 mg [0.6 mg/kg bw/day] to produce systemic toxicity in the general population (EVM, 2003). SCF derived a tolerable UL of 25 mg/day [0.36 mg/kg bw/day], the critical effect being decreased copper status in humans (SCF, 2003).

The US EPA's chronic oral RfD for non-cancer effects is 0.3 mg/kg bw/day, based on a LOAEL of 0.91 mg/kg bw/day for blood effects (decreased erythrocyte Cu, Zn-superoxide dismutase (ESOD) activity) in healthy volunteers (US EPA, 2005).

Higher doses are used therapeutically; individuals with stomach ulcers may, for example, be given 200 mg of zinc sulphate per day [3.5 mg zinc/kg bw/day] (MedlinePlus, 2013). Such doses have been administered for periods of several months, without reported adverse effects (JECFA, 1982).

Industry has submitted REACH dossiers for zinc and numerous zinc compounds. The zinc dossier includes a long-term oral DNEL for systemic effects in the general population of 0.83 mg/kg bw/day (ECHA, undated m).

The assessed exposure (up to 0.1 µg/kg bw/day) to zinc resulting from the use of a FriPura filter is 10,000 times lower than JECFA's PMTDI, 3600 times lower than the SCF UL, and 3000 times lower than EPA's chronic RfD and clearly not of concern with regards to human health. As levels of zinc were <LOQ in the "used" oil, and in two of the three samples of "fresh" oil, there was in any case no actual analytical evidence of zinc exposure from the filter.

Conclusion

The FriPura filter did not increase detected levels of calcium, copper, iron, phosphorus or sulphur in cooking oil. Thus, these elements were not considered relevant for the health risk assessment. There was also no evidence of increased exposure to cadmium, chromium, lead, manganese, nickel or zinc (concentrations were below LOQ in the "used" oil samples). Nevertheless, these were assessed on the assumption that they were absent in "fresh" oil and present at LOQ in the used samples (with the exception of zinc, which was found above LOQ in one of three "fresh" oil samples analysed). Potassium and silicon levels were higher in the used oil samples, so were also assessed.

Based mainly on expert group assessments and HCVs, it was concluded with high confidence that none of the assessed elements (cadmium, chromium, lead, manganese, molybdenum, nickel, potassium, silicon and zinc) would pose any significant risks to the health of consumers, even when worst-case assumptions were made about exposure.

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Appendix: The TRACE database and databank

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TRACE includes information from peer-reviewed toxicology and nutrition journals as well as secondary sources and websites. In addition to primary literature on the health effects of chemicals, TRACE covers official publications and evaluations issued by authoritative groups including:

- WHO/IPCS reports and evaluations (including CICADs and EHCs, and IARC, JECFA and JMPR monographs), and the WHO Air Quality and Drinking-Water Quality Guidelines
- OECD SIDS dossiers/SIARS
- IUCLID data sets
- EU Risk Assessment Reports
- EU expert committee opinions (including EU scientific committees, and EFSA scientific panels) and other reports from EU agencies and institutes etc (including ECHA, ECVAM, EMEA and CPS&Q)
- ECETOC, HERA, Council of Europe and other pan-European programmes
- UK government agency (including Defra, EA, FSA, DoH, HSE, HPA, PSD and VMD) and advisory committee (eg COT, COM, COC, ACNFP, SACN, ACP, ACAF, VPC, VRC and ACRE) reports and evaluations
- Opinions from other UK organisations such as the Royal Society
- US agency reports and evaluations (EPA, ATSDR, FDA, NTP, OSHA, NCEA, CFSAN, CERHR, NIEHS, CDC, OEHHA and ACGIH)
- Health Canada evaluations
- BUA, DFG, BG Chemie and BfR reports and monographs
- Gezondheidsraad opinions, including those from its various committees such as DECOS
- RIVM reports
- Danish EPA reviews
- Reports and other information provided by Swedish governmental organisations, including the National Food Administration and the Swedish Chemicals Agency
- Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals
- Australian agency reviews including NICNAS Priority Existing Chemical Assessments, APMVA reports and (jointly with New Zealand) FSANZ assessments
- Japanese Chemical Industry Ecology-Toxicology & Information Center reports
- CIR, RIFM and other specialist industry groups
- Bibra Toxicity Profiles