TOX/2022/04

Committee on Toxicity of Chemicals in Food, Consumer products and the Environment

First draft statement on the risk assessment of cow's milk in children aged 1 to 5 years, in the context of plant-based drinks evaluations

1.   This draft statement consists of a chemical risk assessment of contaminants and chemicals within milk which were reviewed as part of the work being conducted by the SACN/COT joint working group on plant based drinks. This will allow a comparison to be made between milk and the chemical risk assessment performed for plant based drinks performed in 2021 (COT, 2021a) This will facilitate the use of milk as a comparator against plant based drinks. It contains the risk characterisation and where applicable exposure assessments for a range of chemicals at the levels identified within cows' milk for children aged 6 months to 5 years.

2.   The majority of chemicals did not present any risk to health to children aged 6 months to 5 years at the levels of exposure identified within cows' milk.

3.   Iodine was identified as being of low concern. This is in line with previous COT statements in 2000 and 2017 as being due to the close proximity of recommended dietary levels and HBGVs, uncertainty in HBGV calculation and the small nature of the HBGV exceedance.

4.   Aflatoxin M_1 was identified as being of low concern. There is a low concern for total aflatoxins within milk, however, this is driven by levels of AFM_1 within cows' milk.

5.   The draft statement is attached as Annex 1 to this paper. In order to ensure the statement is not excessively long, detailed supporting information for chemicals deemed to be no risk is attached as Annex A to the main statement.

Questions for the Committee

6.   The Committee are asked to consider:

   a)   Does the Committee have any comments on the general structure and content of this statement and its Annex?

b)   Does the Committee concur with the conclusions presented within this statement?

c)   Does the Committee have any other comments on this statement or its Annex?

Secretariat

February 2022.

Annex 1 to TOX/2022/04

Committee on Toxicity of Chemicals in Food, Consumer products and the Environment

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Background

1.   Plant-based drinks have become increasingly popular in the United Kingdom (UK) both for individuals with an allergy to cows' milk or lactose intolerance and those who wish to avoid dairy products for other ethical or cultural reasons.

2.   Current UK Government advice regarding the use of plant-based drinks for infants and young children is that unsweetened calcium-fortified plant-based drinks, such as soya, oat and almond drinks, can be given to children from the age of 12 months as part of a healthy balanced diet; rice drinks should not be given due to the levels of arsenic in these products (NHS, 2018). As Members are aware, the Committee reviewed three of the drinks, with a statement being published last year at the request of the Department of Health and Social Care (DHSC) (COT, 2021a). The Scientific Advisory Committee on Nutrition (SACN) have also been considering the nutritional aspects of plant based drinks and in order to bring together the nutritional and chemical risk assessments of these drinks, a joint working group of SACN and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) has been established.

3.   DHSC is in the process of conducting an Equalities Analysis covering both the Nursery Milk Scheme and the Healthy Start Scheme which considers equalities issues posed by the current legislation as it pertains both to plant-based drinks, and also to animal milks other than cow's milk. DHSC is keen to ensure that this Equalities Analysis reflects the most up-to-date advice on safety and toxicity issues from COT, and on nutritional issues from the SACN. However, this process is currently on hold whilst the joint Working Group considers plant-based drinks.

4.   The Committee was asked to consider the potential for adverse effects arising from the consumption of plant drinks by young children (aged 6 months- 5 years) who were following a plant-based diet. The drinks considered were soya, oat and

almond; rice drinks were not reviewed since there is existing advice that these should not be given to young children due to their arsenic content. The three drinks were selected as they were the most popular alternatives to dairy at the time of review. The statement setting out the views and conclusions of the Committee was published in January 2021 (COT, 2021a).

5.   The Committee agreed during their meeting in July 2021 that the main comparator for plant-based drinks should be cow's milk and that a discussion paper should be produced looking at the potential chemical risks in the consumption of this over the identical population group of interest, children aged 6 months to 5 years

6.   Most of the fresh cow's milk available in the UK is UK derived, thus the risks and relevant chemical exposures for this paper are European Union (EU) or UK focused and it is assumed that EU farming practices are similar to the UK.

7.   This statement follows two discussion papers presented over the course of 2021 (TOX/2021/53 and TOX/2021/58) which presented exposure assessments and subsequent risk characterisation for a large range of chemical compounds that could potentially contaminate milk. The compounds discussed were:

Part 1 (TOX/2021/53):

    I.   Veterinary medicines

    II.   Pesticides

    III.   Nitrate and Nitrite

    IV.   Bisphenol A (BPA)

    V.   Phthalates

    VI.   Dioxins and Dioxin-Like Polychlorinated Biphenyls (DL-PCBs)

    VII.   Non-Dioxin-Like Polychlorinated Biphenyls (NDL-PCBs)

    VIII.   Polycyclic Aromatic Hydrocarbons (PAHs)

    IX.   IX. Isoflavones: Genistein (GEN), Daidzein (DAI), Equol (EQU, metabolite of DAI), Formononetin (FOR) and Biochanin A (BIO)

Part 2 (TOX/2021/58):

    X.   Heavy metals: Lead (Pb), Arsenic (As), Mercury (Hg) and Cadmium (Cd)

XI.   Iodine

XII.   Perchlorate and Chlorate

XIII.   Mycotoxins: Aflatoxins (AFB1 and AFM1) and others including Deoxynivalenol (DON)

XIV.   Hormones – Oestrogens, Insulin-Like Growth Factor 1 (IGF-1)

XV.   Per- and polyfluoroalkyl substances (PFAS)

XVI.   Brominated Flame Retardants (BFRs)

XVII.   Microplastics

8.   The Committee considered compounds to be of minimal risk within cows' milk where evidence suggested that there was no exceedance of health based guidance values from exposure through consumption of cow's milk. In these cases supplementary information, including the discussion of health-based guidance values (HBGVs), detailed exposure assessments and, where relevant, risk characterisation are included in Annex A to this statement.

9.   It is acknowledged from scrutiny of the historical EU RASFF (Rapid Alert System for Food and Feed) data and FSA's alert tools that occasional incidents of contamination of cow's milk have occurred; this has involved chemicals such as mineral oils (Montgomery, Haughey and Elliott, 2020), other plant toxins from feed contamination, other agricultural contaminants (e.g. urease inhibitors) (Byrne *et al.*, 2020) and other industrial contaminants (e.g. Parabens). As 'one-off' incidents these are acknowledged but not discussed or evaluated in this statement as the overall risks are negligible.

10.   Members discussed comparing the levels of particular contaminants within selected plant-based drinks and cow's milk. Due to the independent nature of the cow's milk assessment, compounds present in cows' milk may not be present at significant levels in plant-based drinks and vice versa. Where compounds are shared between drink types, comparisons have been made.

Consumption data

11.   The National Diet and Nutrition Survey (NDNS) rolling programme and Diet and Nutrition Survey of Infants and Young Children (DNSIYC) data were used to undertake any chronic exposure assessments in this statement, required for

assessing the safety of milk from a chemical contaminant perspective, in young children aged 6 months to 5 years (Department of Health, 2011; Bates *et al.*, 2014; Roberts *et al.*, 2018). The data presented in Table 1 includes consumption data for cow's milk consumed as a drink and when used in recipes. Consumption data for children aged 6 – 12 months are derived from milk used in recipes only, as cow's milk is not recommended by the NHS as a main drink for infants in this age range (NHS, 2018). Table 2 presents consumption data for milk as a drink only. As these values are only slightly lower, all exposure assessments have been undertaken using the highest consumption estimates from Table 1 only.

Table 1. Estimated chronic consumption of cow's milk in consumers (as a drink and with recipes)

Age (months)	Number of Consumers	(g/kg bw/day) Mean	(g/kg bw/day) 97.5th percentile
6 – <12	1257	13	48
12 – <18	1275	32	75
18 – <24	157	29	79
24 – <48	351	23	59
48 – <60	618	17	46

Table 2. Estimated chronic consumption of cow's milk in consumers (as a drink without recipes)

Age (months)	Number of Consumers	(g/kg bw/day) Mean	(g/kg bw/day) 97.5th percentile
12 – <18	1148	30	71
18 – <24	147	28	73
24 – <48	337	21	54
48 – <60	585	15	42

Chemicals assessed

Veterinary medicines

12.   Veterinary medicines, for example antibiotics, are used in animal husbandry to alleviate suffering and disease. UK farmers should follow the Veterinary Medicines Directorate (VMD) recommended guidance on responsible use (VMD, 2014). These include accurate record keeping, purchasing from authorised sources, correct administration and observing relevant withdrawal periods (the length of time any subsequent animal products must not enter the food chain) after administration.

13.   Animal medicines, however, do enter the food chain on occasions when procedures are not followed correctly. Cow's milk is routinely monitored through ongoing surveys with the UK National Reference Laboratory (NRL).

14.   Between 2015 and the end of 2020, 21,574 analyses of cow's milk samples were undertaken as part of the VMD survey covering, anthelmintics, avermectins, cephalosporins, chloramphenicol, dapsone, florfenicol, Non-Steroidal Anti-inflammatory drugs (NSAIDS), and other antimicrobials (as a screening method) (VMD, 2015, 2016, 2017, 2018, 2019, 2020). From the analysis over this 6-year period only 0.12% (24) returned a positive result. Positive results were considered instances where medicines were above the maximum residue limit (MRL) for milk. From these only two residues, penicillin G and triclabendazole both in 2017, resulted in a subsequent risk assessment concluding the milk samples represented a potential food safety risk to the consumer, and this was before taking any dilution effect into account, e.g. from bulk tanks at dairies.

15.   Based on the last 6 years UK statutory survey the COT concluded that it appears that the risk of veterinary medicine exposure after isolated incidents from drinking cow's milk is negligible.

Pesticides

16.   Pesticides primarily enter the dairy food chain via consumption of contaminated feed or water by cattle. They are routinely monitored through ongoing statutory surveillance with the UK National Reference Laboratory.

17.   Between 2015 and the end of 2020, 1,723 cow's milk samples were analysed and reported by The Expert Committee on Pesticide Residues in Food (PRiF), 2015, 2016, 2017, 2018, 2019, 2020). From all the samples analysed over this 6-year period only 1 returned a positive result above the Maximum Residue Limit (MRL). This residue, in 2019, was a persistent quaternary ammonium compound at 0.3 mg/kg, likely a contaminant from a cleaning product.

18.   Based on the last 6 UK statutory survey results the COT concluded that the risk of pesticide exposure from drinking cow's milk is negligible.

Nitrate and nitrite

19.   Nitrate and nitrite are naturally occurring chemicals that form part of the nitrogen cycle. They act as oxidising agents that can cause methemoglobinemia in animals and humans after high consumption. They occur naturally in vegetables but are also used widely as meat preservatives, in agricultural waste streams e.g. from fertiliser use, and as chemical contaminants from industrial processes and materials.

20.   Nitrates are widely consumed by animals and humans, although nitrite is regulated as an undesirable substance in animal feed (EU 574/ 2011). In animals the largest potential exposure of nitrite is from the in-vivo transformation of nitrate to nitrite. Feed and contaminated water can have high levels of nitrate and represent the main contributor to nitrite exposure for food-producing animals (Cockburn *et al.*, 2013).

21.   An exposure assessment has been undertaken for nitrate within Annex A using UK consumption data (Table 1 above). This is presented alongside a discussion of EFSA's 2009 opinion on nitrite. Nitrate exposure was found to be below 1% of the ADI. EFSA's 2009 opinion concluded that nitrite is present at extremely low levels in fresh animal products and therefore not of human health concern (EFSA, 2009).

22.   In light of the very low percentages of the recommended ADI for nitrate that would occur through consumption of cow's milk in young children, along with the EFSA (2009) opinion's conclusion, the COT concluded that nitrite and nitrate contamination pose a minimal risk in the daily consumption of cow's milk.

Bisphenol A

23.   Bisphenol A (BPA) is a compound used as a monomer in the production of many plastics and resins, particularly polycarbonate materials employed in the manufacture of food contact materials and food storage containers such as cans. It is known to potentially migrate from plastic containers, or resins from coatings, into food and drinks. It is also widely used in the production of non-food related products such as surface coatings, resin-based paints, flame retardants and medical devices. For cow's milk, potential BPA contamination may come from the mechanical milking apparatus and subsequent storage vessels in the dairy chain such as cooling tanks.

24.   BPA is an endocrine disrupter in that it potentially interferes with the regulation of hormones in the endocrine system. It is therefore assumed to have toxic effects on metabolism, growth, sexual development, stress response, insulin

production, gender behaviour, reproduction, and foetal development (Cirillo *et al.*, 2015). It is also considered a contributing factor in the onset of metabolic disorders, including diabetes and obesity, and immune dysfunction (Bansal, Henao-Mejia and Simmons, 2018).

25.   EFSA's 2015 opinion on BPA, discussed in Annex A, advises a reduced temporary tolerable daily intake (t-TDI) and concluded that BPA poses no health concern for consumers at any age group (EFSA, 2015b).

26.   In 2019, COT was asked to review the risk of toxicity of chemicals in the diets of infants and young children aged 0-5 years, in support of a review by SACN of Government recommendations on complementary and young child feeding (COT, 2019c, 2020) and BPA was considered as part of that. For BPA, COT's current position is that they are awaiting EFSA's new updated scientific opinion (currently ongoing) to conclude if a new COT evaluation is required. However, based on the 2015 opinion, the COT do not currently consider that BPA within cows' milk presents a risk to health for children aged 6 months to 5 years of age.

Phthalates

27.   Phthalates are esters of the aromatic dicarboxylic acid phthalic acid that have a long history of use as additives to plastics to improve their flexibility but also have wide applicability across industry, for example in pharmaceutical coatings, paints, cosmetics and food contact materials.

28.   Phthalates do not form covalent bonds with the material into which they are incorporated, therefore can readily migrate into food from packaging materials. The extensive and historic use of phthalates has led to their being widely distributed in the environment and the food chain. The general population is exposed to phthalates via food (including migration from food contact materials) and drinking water, but also through inhalation and dermal exposure (Heudorf, Mersch-Sundermann and Angerer, 2007).

29.   In 2005, EFSA performed risk assessments on a small range of the most widely used phthalates, namely, di-butylphthalate (DBP), butyl-benzyl-phthalate (BBP), bis(2- ethylhexyl)phthalate (DEHP), di-isononylphthalate (DINP) and diisodecylphthalate (DIDP) and derived TDIs for them (EFSA, 2005b, 2005c, 2005d, 2005e, 2005f)

30.   In Annex A, EFSA's 2005 and 2019 risk assessments of phthalates are discussed. In 2019 the group phthalates (DEHP+ DBP+ BBP+ DINP expressed as DEHP equivalents) contributed up to 14% of the recommended group TDI whilst for

95th percentile consumers a maximum of 23% (EFSA, 2019). For DIDP both mean and 95th percentile consumers were exposed to well below the TDI.

31.   In May 2011, COT produced a statement COT, (2011) on dietary exposure to the phthalates DBP, BBP, DEHP, DINP, DIDP and diethyl phthalate (DEP) using data from the UK Total Diet Study (TDS), and concluded that the levels of phthalates that were found in samples from the 2007 TDS did not indicate a risk to human health from dietary exposure, either when the compounds were assessed alone or in combination.

32.   In the recent COT review of EFSA's public consultation on the EFSA Opinion "Draft update of the risk assessment of dibutylphthalate (DBP), butyl-benzyl-phthalate (BBP), bis(2-ethylhexyl)phthalate (DEHP), di-isonylphthalate (DINP) and diisodecylphthalate (DIDP) for use in food contact materials", the COT were content that for DBP, BBP, DEHP and DINP the exposures estimated by EFSA did not indicate a health concern using the group TDI (COT, 2019b).

33.   From this information the COT concluded that phthalates within cows' milk do not present a risk to health for children aged 6 months to 5 years of age.

Dioxins and Dioxin-Like polychlorinated biphenyls (DL-PCBs)

34.   Formed as by-products of a number of industrial processes, polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are two groups of tricyclic planar compounds that are formed by combustion of organochlorine compounds or of non-chlorine compounds in the presence of chlorine. Of these, 75 PCDD and 135 PCDF "congeners" are known, with structures varying in the number of chlorine atoms and their positions in the rings. Only 17 of these are relatively persistent in animals and humans and therefore considered relevant (EFSA, 2018).

35.   HBGVs have been generated by multiple authorities and these are discussed within Annex A.

36.   An exposure assessment has been undertaken for cow's milk using consumption data from Table 1 and is presented within Annex A using occurrence levels from EFSA's 2018 opinion paper (EFSA, 2018), compared against the recommended TDI of 2 pg WHO-TEQ/kg bw per day from COT in 2001 (COT, 2001). Utilising the upper bound (UB) mean occurrence levels led to exceedances of the TDI in two age groups. Factors including the worst-case assumption of a 3.5% fat content of milk and using the upper bound of the mean occurrence concentrations suggest that realistic exposure will be below the levels estimated in this exposure assessment.

37.   At the 95th percentile occurrence value, exceedances of the TDI occurred for both mean and high level consumers, however, this scenario is considered to be highly conservative and unrealistic.

38.   The COT concluded that dioxins within cows' milk do not present a risk to health for children aged 6 months to 5 years of age.

Non-dioxin-like PCBs

39.   Some PCBs do not share the same toxic endpoints as the dioxins and have different effects, for example oestrogenic and anti-oestrogenic effects, and are therefore regarded as a separate group of persistent organic chemicals that are present in the environment and food.

40.   Dietary exposure assessments by EFSA, (2005a) and JECFA, (2016) are discussed within Annex A, these surveys suggest that dietary exposure is within safe levels for young children,

41.   The COT concluded, based on the above evidence, that there was no risk to health from NDL-PCBs within cows' milk for children aged 6 months to 5 years of age.

Polycyclic Aromatic Hydrocarbons (PAHs)

42.   PAHs (polycyclic aromatic hydrocarbons) are organic compounds characterised by the presence of 2 or more fused aromatic rings, many of which are known carcinogens. Although naphthalene, with 2 fused rings, would technically be part of this group of compounds it is usually not regarded as a member. PAHs are common products of combustion and are widely distributed in the environment as the result of vehicle exhaust and industrial processes and in the diet in cooked food and cooking by-products such as oils vaporised from frying pans and smoke from barbecues. Production of PAHs by cooking is greater when fat expressed from the food drips directly onto the heating element or hot coals.

43.   An exposure assessment for benzo[a]pyrene (BaP) and a separate assessment for PAH4 (sum of BaP, benz[a]anthracene (BaA), benzo[b]fluoranthene (BbF) and chrysene (ChR), was undertaken. These are presented within Annex A utilising consumption data in Table 1 and the UK TDS from 2012 (Fernandes *et al.*, 2012).

44.   The subsequent MOEs presented are all above 10,000 for both average and high-level consumers across all age ranges of young children. These high MOE's indicate there is a very low safety risk of the PAH4 from drinking cow's milk.

45.   In the recent COT review with SACN on the risk of toxicity of chemicals in the diets of infants and young children, the COT concluded the intakes of PAHs (BaP and PAH4) from human breast milk and food are of low concern for health in children aged 12 to 60 months (COT, 2020).

Isoflavones

46.   Phytoestrogens are chemicals of plant origin that have been shown to influence biological processes mainly through their structural similarities to oestrogens, and their ability to bind to oestrogen receptors (ERs).They can therefore potentially cause unfavourable effects such as disruptions in sexual behaviour and brain sexual differentiation, changes in hormone levels, and increases in breast cancer risk (Xiao, 2008; Socas-Rodríguez *et al.*, 2015). The largest group of phytoestrogens are flavonoids, which can be further divided into three subclasses, coumestans, prenylated flavonoids and isoflavones.

47.   Isoflavones can be found in many plants, including barley, sunflower, clover, lentils, alfalfa sprout, broccoli and cauliflower. However, the richest sources of isoflavones in the human diet are foods and dietary supplements made from soya bean and soya protein (McCarver *et al.*, 2011). Soya isoflavones in foods occur mainly as carbohydrate conjugates (glycosides), the major group being the glucose conjugates (glucosides), e.g. genistein (GEN) and daidzein (DAI). The other most commonly considered isoflavones include formononetin (FOR), biochanin A (BIO) and a metabolite of DAI, equol (EQU).

48.   The phenolic and hydroxyl moieties (and the distance between them) are key structural similarities between isoflavones and17β-oestradiol which allow them to bind to ERs. Numerous studies have indicated that GEN is the isoflavone with the greatest oestrogenic activity (McCarver et al., 2011).

49.   Animal studies performed before 2003 indicated that intake of isoflavones in early life can produce oestrogenic effects, affect thyroid function, alter protein concentrations and structures in the brain, and alter some parameters of immune function, as well as sexual development in older animals. Although some animal studies indicated possible risks to humans, overall, the results of animal studies were inconsistent. The COT 2003 report noted that human data were limited, and that most of the relevant scientific information was derived from experimental studies in animals, mainly rodents. The extrapolation of such studies to humans was difficult because of inter-species differences in ADME (absorption, distribution, metabolism,

and excretion), sexual development and reproductive function, and the use of relatively high doses or non-oral routes of administration.

50.   *In vitro* experiments reviewed in the 2003 COT report (COT, 2003) showed that phytoestrogens could modulate the levels of sex hormone binding globulin (SHBG), inhibit enzymes involved in oestrogen biosynthesis and metabolism to modulate concentrations of endogenous oestrogens, and inhibit thyroid peroxidase activity to reduce the concentrations of thyroid hormones. GEN was found to interact with topoisomerase II and protein kinases (enzymes involved in cellular proliferation and differentiation) and to inhibit human T-cell proliferation and interleukin-2 production.

51.   The 2003 COT report concludes that it is not possible to propose HBGVs for infants (COT, 2003). Reasons for this include the difficulty in extrapolation from animals to humans because of differences in toxicokinetics, uncertainty about differences between adults and infants (particularly those arising from development of the gut microflora), and the lack of dose-response data and the possibility of bias and chance effects in the available human studies. In a more recent 2013 COT report COT, (2013a) assessing literature since 2003, the same conclusions were drawn, in that it is not possible to propose HBGVs due to limitations in the available data.

52.   Other health authorities have proposed HBGVs such as the Nordic Council in 2020 (Nordic Council of Ministers, 2020). For children they proposed 'a rounded value of 0.07 mg/kg bw per day of GEN. This corresponds to 2.1 mg genistein per day for a person weighing 30 kg.' This value was derived from the Li *et al.*, (2014) rat study taking the LOAEL of 20 mg/kg bw and applying a further uncertainty factor of 3 on top of the factors of 10 for inter species differences and intraspecies variation.

53.   Isoflavones are known to be transferred to cow's milk after digestion of plant-based feed stuffs (Bláhová *et al.*, 2016). Occurrence in the milk is dependent on the feed. Milk phytoestrogen concentration is strongly influenced by silage plant composition. Feed with either deliberate addition of, or inadvertently contaminated with red clover for example will have greatly increased concentrations of isoflavones (Höjer *et al.*, 2012).

Risk characterisation

54.   To obtain published concentrations for Isoflavones in cow's milk a literature search was undertaken using the keywords Isoflavone AND Cow AND Milk AND Risk in both PubMed and Science Direct. A large number of results with very varied isoflavone concentrations were returned from European countries. The UK data only are summarised below (Table 3) from (Nørskov *et al.*, 2019).

Table 3. Summary of mean isoflavone concentrations (all µg/kg) GEN, EQU, FOR and DAI from differing cow's milk types in the UK and a comparison with mean soya milk concentrations (µg/kg)

Milk Type	Number of samples	GEN	EQU	FOR	DAI	Sum
Conventional	48	0.83	63.6	0.08	0.95	67.7
Organic	48	2.32	411	1.10	2.69	417
Free range	24	0.85	66.4	0.09	0.96	70.4
Low fat soya*	1	875	-	-	567	1,442

*From 2019 COT report (COT, 2019a), isoflavone content of soya-based foods and beverages is highly variable and these figures are a guide only

55.   As noted above, COT have not established a HBGV for isoflavones for young children and the significance of the concentrations summarised in Table 3 is uncertain. However, isoflavone concentrations from cow's milk are considerably lower than those from soya alternatives, suggesting that any associated risk will also be lower.

Lead

56.   Lead is a well-known heavy metal and pollutant which can cause multiple negative health effects in humans, its impact on the health of infants was evaluated by the COT, (2013) in their statement on the potential risks from lead in the infant diet and their addendum (COT, 2016a).

57.   EFSA's 2012 opinion on lead and the COT's 2013 and 2016 statements on lead exposure in the diets of infants and children have been discussed (Annex A). Whilst some exceedances of the benchmark dose lower confidence limit (BMDL)$_{01}$ were observed in EFSA's total dietary exposure estimate, the contribution of cows' milks to total lead exposure did not exceed 5% and therefore lead within cows' milk is not a concern (EFSA, 2012b). COT's statement found diet contributed little to lead exposure with other sources of exposure being the most significant (COT, 2013b, 2016a).

58.   Based on the information provided in EFSA (2012b) and the evaluation by the COT in 2013 and 2016 the COT concludes that it is unlikely that lead in cow's milk would pose a risk to infants and children from the ages of 6 months to 5 years.

Arsenic

59.   Inorganic arsenic is the focus of this evaluation as it with the previous COT statement (COT, 2016b).

60.   The COT's 2016 statement and EFSA's 2021 evaluation have been discussed in Annex A. The COT's 2016 risk assessment suggest that at mean levels of consumption, for infants aged 4 months to 5 years the MOE's were below 10, therefore a risk to health may exist from dietary exposure. However, in EFSA's recent 2021 evaluation cow's milk was shown to contain minimal amounts of iAs (EFSA, 2021a).

61.   The COT concluded from the above information that inorganic arsenic in cows' milk does not present a risk to health to children aged 6 months to 5 years of age.

Mercury

62.   Mercury is a metal released from both anthropogenic and natural sources. It is found as elemental mercury (Hg^0), inorganic mercury (mercurous and mercuric cations (Hg^+ and Hg^{2+} respectively) and organic mercury. Methylmercury is the most abundant organic mercury compound in the food chain (COT, 2018c).

63.   The toxicity of mercury varies depending on whether the mercury is in an organic or inorganic form. The focus of this paper is inorganic mercury as in EFSA's 2012 report it was assumed the majority of mercury within milk was inorganic in nature (EFSA, 2012c).

64.   The COT's 2018 statement on methylmercury in the diets of infants and children and EFSA's 2012 opinion have been discussed in Annex A. EFSA did not consider total dietary exposure to inorganic mercury to be a risk for the European population. For all age groups, excepting toddlers, the TWI for inorganic mercury was not exceeded. Cows' milk contributed a maximum of 15% to this total exposure. The COT in 2018 found no exceedances of the inorganic mercury TWI using either TDS or infant metals survey data for the assessment.

65.   From the above information the COT concluded that the risk of harm to infants and children aged 6 months – 5 years from exposure to inorganic mercury in cows' milk is low.

Cadmium

66.   Cadmium (Cd) is a soft, silver-white or blue-white metal existing in various mineral forms and is present throughout the environment. It is used in many processes such as electroplating, alloy production, paints and pigments and is found in a wide range of industrial and consumer products. Environmental cadmium

concentrations are reflective of natural sources such as volcanic activity as well as anthropogenic sources for example non-ferrous metal smelting.

67.   Exposure assessments performed by (EFSA, 2012a) and the COT have been discussed, this can be found within Annex A. Whilst exceedances of the TWI were observed in both (COT, 2018b) and EFSA, (2012a) exposure assessments the relative contribution of cow's milk in both of these assessments was low.

68.   The COT concluded from the above information that cadmium in cow's milk presents a low risk to the health of infants and children aged between 6 months and 5 years.

Iodine

69.   Iodine is an essential micronutrient necessary to produce thyroid hormones. The COT released a statement (COT, 2017) discussing in depth the potential risks of excess iodine in the diets of infants and children aged 0-5 years. Milk is a considerable source of iodine in the diet, this may be due to fortification of animal feed with iodine compounds and teat dipping with sterilising compounds prior to milking.

70.   Iodine excess is well tolerated by healthy individuals. For some it may cause hypothyroidism, hyperthyroidism, goitre and/or thyroid autoimmunity. Individuals with prior exposure to iodine deficiency or pre-existing thyroid disease may be more vulnerable to iodine excess induced thyroid disorders (Farebrother, Zimmermann and Andersson, 2019).

71.   In 1989 the Joint Expert Committee on Food Additives (JECFA) established a provisional Maximum Tolerable Daily Intake (PMTDI) for iodine of 17 µg/kg bw/day from all sources, based on the same longer term studies in adults used by the European Scientific Committee on Food (SCF) in 2002 in support of their TUL, recorded in EFSA, (2006). No safety factors were used as these studies encompassed a relatively large number of subjects (JECFA, 1989).

72.   The COT (2017) stated "Excess iodine has considerably varied effects between individuals. The adult thyroid gland secretes about 80 µg thyroxine per day which requires a dietary intake of between 100 and 150 µg/day of iodine. Humans have a number of mechanisms by which they can counter an excess of iodine. These include the sodium-iodide symporter which blocks the transport of iodine into the thyroid cells and the Wolff-Chaikoff effect, more details of which can be found in the review by Bürgi, (2010). Most people can tolerate a chronic excess of iodine of up to 2 g of iodine per day but there will be some individuals who experience effects at much lower levels, close to the upper recommended limit for intake (Bürgi, 2010)."

73.   In the COT's 2017 statement on the risks of excess iodine exposure to infants and young children they assessed three HBGVs, This assessment is paraphrased below.

74.   The Expert Group on Vitamins and Minerals (EVM) looked in detail at the metabolism of iodine and the effects of excess iodine in 2003 (EVM, 2003). The EVM concluded that there were insufficient data to set a Safe Upper Level (SUL) for iodine. For guidance purposes, they indicated that a level of 0.5 mg/day of supplemental iodine in addition to the background intake of 0.43 mg/day would be unlikely to cause adverse effects in adults based on slight alterations in serum thyroid hormone levels at supplemental doses of 0 - 2 mg/day in a range of human studies. From this data the EVM proceeded to set a guidance level for iodine at 15 µg/kg bw/day for adults. This value is utilised in an exposure assessment in this paper due to its conservative nature.

75.   In 2002, the SCF published an opinion on the tolerable upper intake levels of vitamins and minerals, recorded in EFSA, (2006). For iodine, they set a tolerable upper level (TUL) of 600 µg/day for adults, reduced on a body surface area (body weight$^{0.75}$) basis for children to 200 µg/day for ages 1-3 years and 250 µg/day for ages 4-6 years. This TUL was based on dose-response studies of short duration in humans, which showed changes in serum thyroid hormone levels at dose levels of 1800 µg/day and was supported by longer term studies with approximately similar doses that did not show adverse effects, but lacked detailed iodine intake data. An uncertainty factor of 3 was used. These values were endorsed by EFSA (2006).

76.   In 2017 the COT calculated new HBGVs based on the EFSA (2006) endorsed values in their statement assessing the risks of excess iodine in the diet. This used differing mean bodyweights for separate age groups based on different mean bodyweights. These HBGVs are displayed in Table 4.

Table 4: Table displaying the HBGVs generated using EFSA endorsed values and mean bodyweight for age found in (COT, 2017).

Age group	0-<12 months	12-<15 months	15-<18 months	18-<24 months	24-<60 months
HBGV	No tolerable upper limit (TUL) specified	18.9 µg/kg bw/day TUL	17.9 µg/kg bw/day TUL	16.7 µg/kg bw/day TUL	15.5 µg/kg bw/day TUL

	for this age group				

Exposure Assessment and risk characterisation

77.   The 2016 infant metals survey provided comprehensive occurrence information for iodine in UK milk. Iodine was found to be present at a mean level of 271 μg/kg (FSA, 2016).

78.   In addition to the infant metal survey, occurrence levels were found through an interrogation of the PubMed database using the terms "iodine AND cows AND milk" and " Iodine AND excess AND milk" with search results limited to 2001-2021.

79.   A review article by Reijden et al., collated iodine occurrence data from 30 European and 1 United States (US) study including 2 from the UK in 2012 and 2016 (Reijden, Zimmermann and Galetti, 2017). The 2012 UK study presented a median iodine level in conventional milk at 250 μg/kg from 80 samples whilst the 2016 study presented a mean value of 458 μg/kg from 24 samples (Bath, Button and Rayman, 2012; Payling *et al.*, 2015).

80.   Bath *et al* (2017) also documented iodine at median levels of 438 μg/kg in conventional (non-organic) milk. Sample numbers were restricted to 5 samples, taken at a single time in winter, due to the seasonal variation in iodine levels this may have increased levels of iodine in samples as winter milk is often recorded as having higher iodine levels (Bath et al., 2017; Reijden, Zimmermann and Galetti, 2017).

81.   A study by O'Kane et al. investigating seasonal variation in iodine and selenium concentration in milk found mean (± SD) (standard deviation) iodine levels were 475.9 (± 63.5) μg/kg in pasteurised Northern Irish milk (O'Kane *et al.*, 2018). This mean was obtained from the analysis of 36 samples. 95th percentile or maximum occurrence data were not presented in this study. The highest recorded mean concentration was 543.3 (± 53.7) μg/kg from 9 samples of milk collected in spring.

82.   The highest found UK mean iodine concentration was found in O'Kane et al. (475.9 μg/kg). Using the consumption rates in Table 1 and the EVM, (2003) guidance value of 15 μg/kg bw /day, an exposure assessment was undertaken which is presented in Table 5.

Table 5. Exposure assessment from cows' milk consumption using mean iodine occurrence in O'Kane et al. (2018), consumption data from the NDNS (Table 1) and the EVM 2003 guidance value (EVM, 2003).

Age (months)	Estimated exposure mean µg/kg bw/day	Estimated exposure 97.5th percentile µg/kg bw/day	Mean % guidance value	97.5th percentile % guidance value
6 – <12	6.19	22.8	41.2	152
12 – <18	15.2	35.7	102	238
18 – <24	13.8	37.6	92.0	251
24 – <48	10.9	28.1	73.0	187
48 – <60	8.09	21.9	54.0	146

83.   Average consumers in the age group 12 - < 18 months slightly exceed the guidance value of 15 µg/kg bw/day set by the EVM in 2003. High consumer exposures exceed the guidance value for all age groups.

84.   In the COT's 2000 paper, a survey of UK cows' milk from 1998-9 was discussed which identified the overall mean iodine concentration in cow's milk to be 311 µg/kg with a lowered mean concentration in summer (200 µg/kg). These values were used to generate exposure data and their safety assessed against guidance values calculated from the JECFA PMTDI of 0.017 mg/kg bw/day (17 µg/kg bw day) which was available at the time. At mean levels of consumption of the total diet, exceedance of the guidance values was observed for the age group 1½ - 2½ years at 221 µg/day. For the age groups 2½ - 3½, and 3½ - 4 years iodine exposure approached the guidance level at 215 and 204 µg/day respectively. For high level consumers, exceedances for the 3 age groups 1 ½ - 2 ½, 2 ½ - 3 ½, and 3 ½ - 4 ½ years at 362, 379 and 330 µg/day respectively were observed. For milk consumption alone, exceedances of the guidance values calculated from the previously adopted PTWI were present in high level consumers (97.5th percentile) for the groups aged 1 ½ - 2 ½, 2 ½ - 3 ½ years. The COT concluded that iodine in cows' milk was unlikely to pose a risk to health even in children who are high level consumers (COT, 2000).

85.   The COT's 2000 conclusion was reaffirmed in the COT 2017 paper on the risk of excess iodine in the diets of infants and young children arguing:

'These HBGVs are based on limited data. In all cases the relevant studies on which the HBGV was established did not allow an accurate estimation of dietary intakes. The response to high iodine intakes can be highly variable between individuals and will depend on iodine status. Individuals with a low

iodine status who are suddenly exposed to high iodine levels are more likely to experience adverse effects than those with an adequate iodine status.

For many of the parameters of thyroid function normally assessed, it is difficult to distinguish between adverse effects and normal homeostatic changes due to iodine. Further, the RNI and the guidance levels/tolerable daily intakes are of a similar order of magnitude. These two factors, together with the fact that the relevant available studies are all in adult populations, make it difficult to identify a safe upper level which is applicable for all infants and children.'

86.   In the COT paper of 2000 on iodine in cow's milk, exceedances were identified for 97.5th percentile consumers. This was mirrored in the exposure assessment produced in this paper with high level consumers of milk exceeding the TDI. For mean level consumers however, iodine exposure approached the 2003 EVM's 15 µg/kg bw/day TDI for the group 12- <18 months. COT's 2000 and 2017 statements stated that iodine levels in cow's milk were seen to pose no toxicological concern due to the close proximity of the exposures to HBGVs and reasons discussed above. With similar results in this exposure assessment the COT concluded that the risk to health from iodine in cows' milk is likely to be low.

Perchlorate

87.   Perchlorate (ClO4 -) has both natural and anthropogenic sources. Previous biomonitoring studies have suggested it is most likely to be a ubiquitous compound. It is present in the environment due to Chilean fertilisers and industrial emissions such as ammonium perchlorate in solid rocket fuel propellants and formation of perchlorate from degradation of chlorine-based cleaning products. Within the EU likely sources include Chilean nitrate (fertiliser) leading to accumulation in plants. Plant protection products and water disinfection could slightly increase exposure (EFSA, 2014).

88.   Perchlorate acts on the thyroid, inhibiting iodine uptake via the sodium-iodide symporter protein. This leads to depletion in levels of thyroid hormones leading to hypothyroid effects in individuals with a moderate iodine deficiency; this was discussed in a discussion paper in 2018 by the COT (COT, 2018a).

89.   An exposure assessment is presented within Annex A using occurrence data for liquid milk from EFSA's 2017 exposure assessment and NDNS consumption data. For mean occurrence at the UB concentration, there were no exceedances of the TDI of 0.3 µg/kg bw/day (from EFSA, 2014) at mean levels of consumption for any age group. For the age range 12-<48 months there were exceedances of the TDI. Using the 95th percentile UB occurrence value there was an exceedance at

mean consumption levels for the age group 12-<18 months and for all assessed age groups at high level (97.5th percentile) consumers. This, however, is an extremely conservative assessment due to the use of upper bound occurrence values in addition to high consumption levels (97.5th percentile).

90.   The COT (2019c) discussed EFSA's assessments (EFSA, 2014, 2017) in 2019. The COT concluded that in both long and short term exposure scenarios for all age groups, there was potential concern, particularly in the case of individuals with mild to moderate iodine deficiency.

91.   Based on the exposure assessment presented in Annex A which showed that the TDI was unlikely to be exceeded in a realistic scenario, and, their previous conclusions, the COT concluded that perchlorate levels in cows' milk do not represent a significant health risk to children aged 6 months to 5 years. However, milk is a significant contributor to total perchlorate exposure levels.

Chlorate

92.   Chlorate is formed as a by-product of chlorine, chlorine dioxide or hypochlorite usage in disinfecting drinking water, water for plant production and food surface contacts. Chlorine washing of animal derived products is illegal within the EU however plant derived foods can be washed.

93.   The EFSA CONTAM panel concluded in their 2015 opinion that the majority of chlorate enters the food chain by washing of food and food contact surfaces. Chlorate is likely to enter milk by cleaned surfaces and sterilised containers (EFSA, 2015a).

94.   COT's previous statement on the infant diet (2019c) which included chlorate, discussed EFSA's 2015 opinion and stated that chlorate levels in the total diet were of potential concern for high consumers particularly for individuals with iodine deficiency.

95.   In EFSA's 2015 scientific opinion on the risks of chlorate, the mean occurrence of chlorate in liquid milk was calculated at 10 -17 µg/kg (LB-UB) from 38 samples. There was no higher or maximum occurrence value provided. The COT considered that this number of samples was low.

96.   An exposure assessment was performed using the mean UB occurrence of chlorate in liquid milk from EFSA (2015a) and is presented in Annex A. No exceedances of the TDI of 3 µg/kg bw day were observed for any age group for both mean and higher level (95th percentile) consumers.

97.	From this information the COT concluded that chlorate in cow's milk is unlikely to pose a risk to health to infants and children aged 6 months – 5 years.

Insulin-like Growth Factor (IGF-1)

98.	IGF-1 is a hormone naturally present in both cow's milk and humans. Through treatment with bovine somatotropin (BST), IGF-1 levels in cows can be artificially increased to improve milk production through treatment of cows with bovine somatotropin (BST). BST treatment of cows is illegal within the UK and EU, however milk from BST treated cows can be legally imported. IGF-1 in the diet has been discussed in the scientific literature due to concern over its potential links to cancer.

99.	The COC stated in 2018 (COC, 2018) there was no expected increase to cancer risk from IGF-1 in the diet. In addition to this using data from DEFRA (DEFRA, 2021), liquid drinking milk from BST treated cows is unlikely to enter circulation into the UK in significant amounts. These details are discussed further in Annex A

100.	From this information above the COT concluded that it is unlikely that IGF-1 within cows' milk poses a risk to health for children aged 6 months to 5 years of age.

Naturally occurring oestrogens in cow's milk

101.	Exogenous endocrine active chemicals have been suggested by researchers as potential sources for a range of developing health issues. This has arisen due to a mimicry between them and the hormones naturally produced by individuals and the potential effects this may cause due to effects on the hypothalamic-pituitary-gonadal axis (HPG axis). This has raised concerns about endogenous oestrogens and their consumption.

102.	Opinions from the Veterinary Products Committee (Veterinary Products Committee, (2006), JECFA (WHO, 2000) and the European Scientific Committee (SCVPH, 2002) have been discussed within annex A. There are varied regulatory opinions on the genotoxicity of 17β-oestradiol. The COT considers that any genotoxic effect is likely due to an indirect mechanism.

103.	An exposure assessment has been performed and is presented within Annex A. This compares exposure to the JECFA (2000) ADI of 0.05 µg/kg bw/day, based on hormonal effects for 17β-oestradiol. No exceedance of the ADI was seen in any population group.

104.	From the above information discussed further in Annex A, the COT concluded that a risk to health to children aged 6 months to 5 years is unlikely; however, due to

uncertainty regarding 17β-oestradiol's genotoxicity, a risk to health cannot be fully excluded.

Mycotoxins

105.   Mycotoxins are a highly toxic group of fungi derived compounds. Cow's milk can be contaminated with multiple mycotoxins. A large wealth of information exists regarding occurrence of the aflatoxin M1 in milk. Regarding other mycotoxins, contamination studies have shown variation in the transfer of fumonisins, zearalenone, ochratoxin and trichothecenes from feed to dairy cows and then subsequently into milk. The scientific literature contains far less information on these other mycotoxins and their occurrence in milk.

Aflatoxins

106.   Aflatoxins can enter cow's milk through feed contaminated with fungi such as *Aspergillus flavus* and *Aspergillus parasiticus*. The aflatoxin AFB_1 is a common aflatoxin in feed. This is converted within the bovine liver via cytochrome P450 hydroxylation to form the major metabolite AFM_1. AFM_1 is the most commonly reported and researched mycotoxin within milk, however, AFB1 has also been detected (Scaglioni *et al.*, 2014; Becker-Algeri *et al.*, 2016). Other aflatoxins include aflatoxins B_2, G_1, G_2 and M_2 (AFB_2, AFG_1, AFG_2 and AFM_2) and these have also been detected in milk, however, far less information is available on these compounds (EFSA, 2020a).

107.   Chronic aflatoxin exposure can lead to immunotoxic effects due to impaired DNA duplication in bone marrow resulting in low leukocyte levels and immunodeficiency, as well as carcinogenic and mutagenic effects. Non-specific cell multiplication inhibition can also affect other cell types with effects particularly apparent within the gastrointestinal tract. The liver is the primary target for aflatoxin exposure. This results in bile duct proliferation, hepatic lesions, centrilobular necrosis and fatty acid infiltration. This often results in liver cancer (Ráduly *et al.*, 2020)

108.   Aflatoxins have been reviewed by the SCF in 1996, and EFSA in 1996, 2007 and 2020. They have also been evaluated by JECFA in 1998, 2001 and AFM_1 was also reviewed in 2018. EFSA's most recent risk assessment produced by the CONTAM panel concluded that the chronic endpoint of liver carcinogenicity in rats was the most relevant endpoint (EFSA, 2020a). They considered the Wogan et al, study of 1974 to be the most satisfactory for dose response modelling (Wogan, Paglialunga and Newberne, 1974). This value was also used in the COT's 2021 statement on plant-based drinks (see below).

109.   The COT's (2021a) overarching statement on consumption of plant-based drinks in children aged 6 months to 5 years of age describes the Wogan, et al.

(1974) study as follows: "Groups of male Fisher rats were administered diets containing 0, 1, 5, 15, 50, or 100 µg/kg diet of AFB_1 (purity >95%) until clinical deterioration of animals was observed, at which time all survivors in that treatment group were killed. EFSA converted the dietary concentrations of AFB_1 into daily intakes assuming that an average adult male rat consumed 40 g diet per kg body using weight per day. EFSA also adjusted the daily intake to 104 weeks in order to compensate for the shorter study duration in some of the AFB_1 groups. In the modelling of the results from the Wogan et al. (1974) study the highest dose was omitted because this dose resulted in a 100% tumour incidence. Using model averaging, the $BMDL_{10}$ for AFB_1 was 0.4 µg/kg bw per day.

Risk characterisation

110.   EFSA calculated the contributions of individual food categories in the collected surveys using the LB mean occurrence value in their 2020 risk assessment. It was reported that 'milk and dairy products' were the most substantial contributor to AFM_1 exposure for all age groups. For the other children (≥ 36 months to < 10 years old), liquid milk was found to account for up to 89% of exposure to AFM_1. Liquid milk also contributed up to 49% of total exposure for infants < 12 months old and up to 74% of total exposure for toddlers (≥ 36 months to < 10 years old). In addition to this, in situations of high exposure liquid milk could contribute up to 89% of total exposure to AFM_1. Liquid milk is therefore a significant contributor to AFM_1 exposure levels.

111.   Analysing the information within EFSA's 2020 risk assessment 'milk and dairy products contributed <1% of total AFB_1 exposure in all surveys. This suggests that the risk of harm from AFB_1 exposure from milk is low.

112.   EFSA also concluded that liquid milk was an important source of exposure of AFM_1 + AFT (the sum of AFB_1, AFB_2, AFG_1 and AFG_2) for infants, toddlers and children. However, this is driven by high AFM_1 contributions.

113.   In 2020 EFSA utilised both an animal derived $BMDL_{10}$ and human epidemiological data to perform 2 risk characterisations.

114.   In (EFSA, 2020a), for AFM_1 a 0.1 potency factor was applied to account for the fact that in a study on Fischer rats AFM_1 was found to induce liver cancer at a rate of 0.1 of that of AFB_1. This produced a value of 4.0 µg/kg bw/day for the assessment of AFM_1 using a MOE approach (EFSA, 2020a). For mean dietary AFM_1 exposure, MOE values were below 10,000 for infants (< 12 months old) in median and maximum exposure groups, all exposure groups for toddlers (≥ 12 months to < 36 months old) and median UB exposure values and maximum exposure for other children (≥ 36 months to < 10 years old). For the 95th percentile of dietary exposure

all populations within relevant groups ('infants', 'toddlers' and 'other children') exhibited MOE values below 10,000. EFSA commented that this is a health concern however it was noted that high levels of milk exposure may only occur for a short period in a child's life. For AFT +AFM$_1$ all age groups and exposure levels exhibited MOEs below 10,000 suggesting there is a health concern. MOEs for AFM$_1$ exposure are presented below in Tables 6 through to 9. MOEs for AFT + AFM$_1$ are presented below in Tables 10 through to 13.

Table 6. MOEs at the lower bound of the minimum, median and maximum mean exposure levels to AFM1 from (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	28571	7018	2564
Toddlers	8889	5882	2817
Other Children	22222	11429	5128

Table 7. MOEs at the upper bound of the minimum, median and maximum at mean exposure levels to AFM1 from EFSA (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	19048	4938	2020
Toddlers	6250	3810	2210
Other Children	14286	7692	4000

Table 8. MOEs at the lower bound of the minimum, median and maximum at 95th percentile exposure levels to AFM1 from (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	6061	2703	642
Toddlers	3810	2721	1053
Other Children	9302	5000	1852

Table 9. MOEs at the upper bound of the minimum, median and maximum at 95th percentile exposure levels to AFM1 from (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	4082	1942	508
Toddlers	2685	1835	825
Other Children	6452	3175	1465

Table 10. MOEs at the lower bound of the minimum, median and maximum at mean exposure levels to AFT + AFM_1 from (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	2222	952	396
Toddlers	541	325	195
Other children	460	328	208

Table 11. MOEs at the upper bound of the minimum, median and maximum at mean exposure levels to AFT + AFM_1 from (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	455	155	40
Toddlers	79	44	32
Other children	75	46	32

Table 12. MOEs at the lower bound of the minimum, median and maximum at 95th percentile exposure levels to AFT + AFM_1 from EFSA (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	615	345	122
Toddlers	310	172	90
Other children	235	174	91

Table 13. MOEs at the upper bound of the minimum, median and maximum at 95th percentile exposure levels to AFT + AFM_1 from (EFSA, 2020a).

Age group	Minimum MOE	Median MOE	Maximum MOE
Infants	99	54	14
Toddlers	48	26	15
Other children	53	25	17

115.   In light of EFSA's latest risk assessment it is unlikely that AFB1 in liquid milk presents a risk to human health. Cow's milk was, however, found to be a significant contributor (up to 89%) to exposure of AFM1 and AFM1 + AFT in 'infants', 'toddlers' and 'other children'. As total dietary exposures to AFM1 and AFM1 + AFT produced MOEs below 10,000 in these populations at a mean exposure level, a risk to human health cannot be excluded for infants and children aged 6 months to 5 years.

116.   In the overarching statement on plant-based drinks it was noted that the margins of exposure for estimated exposure to aflatoxins from almond drink or from the general diet in children 6 months to < 10 years were in general below 10,000, the indicative value for low concern from exposure to a genotoxic carcinogen. However, the exposure estimates were very uncertain, and while exposure would have been overestimated, it was not possible to determine by how much (COT, 2021a).

117.   From the above information, the COT concluded that Aflatoxin M_1 was identified as being of low concern for children aged 6 months to 5 years of age. There is also a low concern for total aflatoxins within milk however the low MOEs present are largely driven by levels of AFM_1 within cow's milk. Other aflatoxins did reduce the MOE further.

Per- and polyfluoroalkyl substances (PFAS)

118.   PFAS are a range of synthetic compounds that contain multiple fluorine atoms. They possess excellent surfactant properties and are widely used in consumer products such as paints, polishes and stain repellents. The Organisation for Economic Co-operation and Development (The Organisation for Economic Co-operation and Development OECD, (2021) define PFAS as:

> 'fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (without any H/Cl/Br/I atom attached to it), i.e. with a few noted exceptions, any chemical with at least a perfluorinated (–CF3) or a perfluorinated (–CF2–) is a PFAS.'

119.   The 2 main classes of PFAS are perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkane sulfonic acids (PFSAs). In 2020 EFSA undertook a risk assessment related to human health related to the presence of perfluoroalkyl substances in food focussing on 4 of the PFAS. These were two PFCAs: Perfluorooctanoic acid (PFOA), Perfluorononanoic acid (PFNA) and two PFSAs: Perfluorohexane sulfonic acid (PFHxS) and Perfluorooctane sulfonic acid (PFOS) (EFSA, 2020b).

120.   Further information on HBGV derivation and a risk characterisation have been discussed within Annex A. Within EFSA's 2020 dietary exposure evaluation no

positive samples for the 4 PFAS compounds were detected above the analytical method reporting levels.

121.   Considering the lack of reported quantifiable amounts of PFHxS, PFOS, PFOA and PFNA in all liquid milk sample data presented by EFSA (2020c) plus the conclusions from(Kowalczyk *et al.*, (2013) and Hill, Becanova and Lohmann, (2021), the COT concluded that PFAS exposures via cow's milk are unlikely to be of current health concern to infants and children aged 6 months to 5 years.

Brominated flame retardants (BFRs)

122.   Brominated flame-retardants (BFRs) are structurally diverse chemicals used in plastics, textiles and other materials to enhance their flame-retardant properties. There are 5 main classes of BFRs:

    i)   Hexabromocyclododecanes (HBCDDs), example uses include thermal insulation

    ii)   Polybrominated biphenyls (PBBs), example uses include in consumer appliances, textiles and plastic foams

    iii)   Polybrominated diphenyl ethers (PBDEs), example uses include in electronic circuitry, casings and textiles

    iv)   Tetrabromobisphenol A (TBBPA) and other phenols, example uses include in electronic circuitry and within thermoplastics in TV sets

    v)   Other brominated flame retardants.

123.   Some BFRs, including polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) are mixed into polymers rather than being chemically bound to them and can leach out of the products/materials in which they are used and into the environment.

124.   The use of many of the BFRs are restricted or prohibited within the EU, nevertheless due to their persistent nature they are widely distributed in the environment such as within water systems, air and soil. BFRs can therefore readily enter the food chain primarily through animal products such as milk and meat.

Hexabromocyclododecanes (HBCDDs)

125.   HBCDDs are non-aromatic, brominated cyclic alkanes used primarily as additive flame retardant in materials such as styrene resins. The commercial product consists of three diastereoisomers α, β and γ-HBCD. Although technical HBCD typically consists primarily of γ-HBCD, the relative proportions of the isomers varies depending on product application.

126.   A discussion of the MOE approach taken by EFSA, COT's 2015 opinion on this work in addition to additional work by EFSA is presented within Annex A (EFSA, 2011a, 2021b; COT, 2015c)

127.   Regarding risk characterisation, in EFSA's 2021 assessment the mean LB concentration of HBCDDs within milk was < 0.01 µg/kg. The COT concluded that the MOEs by dietary intake of breast milk, infant formula, commercial infant food, fish oil and food in general are at least 400 and not a cause for concern for any age group, as they are considerably greater than 8 (A factor of 2.5 to cover inter-species differences and a factor of 3.2 to cover uncertainties in the elimination half-life in humans were multiplied. MOEs. This produces a value of 8. For MOEs above this level there is adequate reassurance that there is no health concern.)

128.   In light of the (EFSA, 2021b) and (COT, 2015c) conclusions (see Annex A) the COT concluded that HBCDDs in cow's milk do not pose a health risk to infants and children aged 6 months to 5 years.

Polybrominated biphenyls (PBB)s

129.   (PBBs) are brominated hydrocarbons formerly used as additive flame retardants. As such these substances were added, rather than chemically bound to plastics used in a variety of consumer products, such as computer monitors, television, textiles and plastic foams, and were able to leave the plastic and enter the environment. They are structurally similar compounds in which 2-10 bromine atoms are attached to the biphenyl molecular structure. In total, as with the structurally similar Polychlorinated Biphenyls (PCBs), 209 different PBB congeners are possible.

130.   EFSA concluded that 'the risk to the European population from exposure to PBBs through the diet is of no concern.' Levels in milk were obtained for BB-52 and BB-101 at the levels of 0.55 to 6.83 ng/kg fat (LB and UB) and 0.64 to 6.92 pg/g fat (LB and UB) for BB-52 and BB-101 respectively (EFSA, 2010). This is discussed further in Annex A.

131.   In 2015 the COT concluded that a reliable estimation of infants' exposures to PBBs was not possible due to limitations within data sources such as the number of congeners covered and a lack of UK data. In spite of this they considered it a low priority due to the restriction of their use (COT, 2015a). Within the literature (discussed in Annex A), minimal levels of PBBs have been reported in milk .

132.   In light of the EFSA, (2010) conclusion, the COT 2015 statement and evidence from the literature the COT concluded that PBBs in cow's milk do not pose a health risk to infants and children aged 6 months to 5 years.

PBDEs

133.   PBDEs are produced by direct bromination of diphenyl ether. There are 209 individual PBDE congeners, each of which is identifiable by a unique congener number. Three commercial PBDE flame-retardants, pentabromodiphenyl ether (pentaBDE), octabromodiphenyl ether (octaBDE) and decabromodiphenyl ether (decaBDE) have been available in the UK. The commercial PBDEs are not pure products but a mixture of various diphenyl ethers with varying degrees of bromination.

134.   EFSA's 2011 exposure assessment (discussed further in Annex A) determined that the only safety concern was for young children aged 1- < 3. Milk contributed a low percentage to this total dietary exposure.

135.   A review of the literature for occurrence of PBDEs in milk did not show a concern for health (discussed in Annex A).

136.   The COT concluded in 2015 that there was a 'possible concern with respect to exposure of infants to BDE-99 and (to a lesser extent) BDE-153 from food, other than commercial infant food. The current analysis indicated that exposure of young children aged 1-5 years to these congeners from such food was unlikely to be a health concern' (COT, 2015b).

137.   In light of the EFSA (2011b) and COT (2015b) conclusions and the evidence from the literature that cow's milk does not contain levels of concern, the COT concluded that PBDEs in cow's milk does not pose a health risk to infants and children aged 6 months to 5 years.

Tetrabromobisphenol A (TBBPA)

138.   Worldwide, TBBPA is the most widely used BFR and approximately 90% of TBBPA, manufactured by bromination of bisphenol A, is used as a reactive intermediate in the manufacture of epoxy and polycarbonate resins. In this case it is covalently bound to the polymer and is unlikely to escape into the environment. The remaining 10% is used as an additive flame retardant, where it does not react chemically with the other components of the polymer and may therefore leach out of the matrix into the environment.

139.   (EFSA, 2011b) and the COT (2019d) concluded that there was no risk to health from TBBPA. This is further discussed in Annex A.

140.   In light of the EFSA (2011b) and COT (2019d) conclusions and evidence from the literature (further discussed in Annex A) that cow's milk does not contain levels of concern, the COT concluded that TBBPA in cow's milk does not pose a health risk to infants and children aged 6 months to 5 years.

Microplastics

141.   Plastic pollution has been widely recognised as a global environmental problem (Villarrubia-Gómez, Cornell and Fabres, 2018). The adverse effects of plastic litter have been widely documented for marine animals (e.g. entanglement, ingestion and lacerations); however, the potential risks from exposure to smaller plastic particles i.e. micro- and nanoplastics in humans are yet to be fully understood.

142.   Due to their widespread presence in the environment, microplastics also occur in food (e.g. seafoods, beer, salt and honey, tea, vegetables) and drinks (e.g. bottled water, milk, soft drinks) (Toussaint *et al.*, 2019). The occurrence of microplastics in milk will likely be due to contamination from dairy machinery and / or packaging rather than the cow itself.

143.   The ECHA in 2019 listed their four major concerns posed by the presence of microplastics in the environment, listed in Annex A (ECHA, 2019).

144.   (COT, 2021b) stated that a full risk assessment on the potential toxic effect(s) of microplastics could not be carried out. This was due to the lack of toxicokinetic and toxicity data in general, the paucity of currently available data for microplastics in different food types and the difficulty of performing an accurate exposure assessment.

145.   The COT concluded from the above information and that included in Annex A that microplastics in milk currently do not represent a risk to health for children aged 6 months to 5 years of age. They also noted that microplastic contamination in milk is likely to be lower than other foodstuffs.

Summary

To aid in the risk assessment of the chemicals described in this statement three summary tables are provided (Tables 14, 15 and 16) providing a summary of the conclusions and where appropriate to this paper, the HBGV for each substance and highest age range estimated exposure via the diet, based on the mean consumption data.

Conclusions

146. The COT reviewed an extensive of chemical compounds that could be present as contaminants in cow's milk to allow comparison with plant based dairy alternatives.

147. As can be seen in the summary tables, the vast majority of these potential contaminants present no risk of adverse health effects at the levels currently observed within cow's milk.

148. Based on the high levels found in cow's milk, iodine, AFM1 specifically and total aflatoxins due to high AFM_1 levels, represent a low risk to health.

Table 14. Summary of risk assessment conclusions for selected compounds and their occurrence levels within cows' milk based on previous authority opinions.

Compound (s)	HBGV, (endpoint)	Effect (s)	Authority	Conclusion: Health risk from cow's milk
Nitrite	n/a	Methemoglobinemia	EFSA	No health concern
Bisphenol A	4 µg (Increase in mouse kidney weight	Endocrine disrupter affecting metabolism, growth, sexual development, stress response, insulin production, gender behaviour, reproduction, and foetal development	EFSA	No health concern
DBP, BBP, DEHP, DINP (Summed as DEHP equivalents)	0.05 mg (reproductive effects in rats)	Reproductive effects, hepatic effects	EFSA / COT	No health concern
DEP	5 mg (increased liver and prostate weights, decreased epididymal sperm concentration of the F1 generation in mice)	Organ weight changes	WHO / COT	No health concern
NDL-PCBs	n/a	Neurological, endocrine, immunological and carcinogenic effects	JECFA	No health concern
Isoflavones GEN, EQU, FOR, DAI	0.07 mg (GEN only)	Endocrine disrupter (oestrogenic effects) effecting	Nordic Council	No health concern

		thyroid and immune function and sexual development		
Lead	None, $BMDL_{01}$ of 0.5 µg/kg bw/day ((development of intellectual function)	Multiple toxic effects	EFSA/COT	No health concern
Inorganic Arsenic	None. $BMDL_{0.5}$ of 3 µg/kg bw/day JECFA / COT (lung cancer)	Multiple toxic effects including carcinogenicity	EFSA/COT	No health concern
Inorganic Mercury	TWI – 4 µg/kg bw/week (kidney weight change in rats)	Multiple toxic effects including renal, haematological, hepatic and gastrointestinal effects.	EFSA / COT	No health concern
Cadmium	TWI – 2.5 µg/kg bw/week (urinary β-2-microglobulin (B2M) as a marker for kidney damage)	Multiple toxic effects including renal toxicity, hepatotoxicity, osteoporosis and osteomalacia.	EFSA / COT	No health concern
AFM_1	None. Guidance value of 4 µg/kg bw/day derived from a $BMDL_{10}$ based on tumour incidence for AFB1 in rats with a 0.1 potency factor applied	Multiple effects such as immunotoxicity, carcinogenicity and mutagenicity	EFSA / COT	Low - concern
AFB_1	None. $BMDL_{10}$ of 0.4 µg/kg bw/day based on tumour incidence in rats after AFB1 exposure.	Multiple effects such as immunotoxicity, carcinogenicity and mutagenicity	EFSA / COT	No health concern

Total aflatoxins	None. BMDL$_{10}$ of 0.4 µg/kg bw/day based on tumour incidence in rats after AFB1 exposure.	Multiple effects such as immunotoxicity, carcinogenicity and mutagenicity	EFSA / COT	Low concern, contributions driven by AFM1 milk occurrence.
PFAS (PFHxS, PFOS, PFOA and PFNA)	TWI of 4.4 µg/kg bw/day (reduced antibody levels against diptheria vaccine in 1-year old children)	increased relative liver weight, effects on the immune system	EFSA	No health concern
HBCDDs	None. From a LOAEL (neurodevelopmental effects in mice) maximum chronic intake of 2.35 µg/kg bw per day	Neurodevelopmental, immune system effects, reproductive system effects, liver effects and thyroid hormone homeostasis	EFSA	No health concern
PBBs	None. NOEL of 0.15 mg/kg bw (hepatic carcinogenicity)	Multiple effects (dioxin like) such as altered vitamin A homeostasis, chloracne and body weight changes	EFSA	No health concern
PBDEs	None. Range of BMDL$_{10}$s between 12 and 1,700 µg/kg bw (neurodevelopmental effects)	Neurodevelopmental, immune system effects, reproductive system effects, liver effects and thyroid hormone homeostasis	EFSA	No health concern
TBBPA	None. BMDL$_{10}$ of 16 mg/kg bw (thyroid hormone homeostasis)	Thyroid hormone regulation	EFSA	No health concern

Table 15. Summary table displaying a comparison of highest estimated mean exposures (occurrence and consumption) to potential chemical contaminants of cow's milk with their health-based guidance values, from exposure assessments presented in this paper and its annex.

Compound (s)	HBGV, (endpoint)	Authority	Highest Exposure (mean consumption), kg bw/day	% HBGV or MOE	Highest exposure age range (months)	Effect	Conclusion: Health risk from cow's milks
Nitrate	3.7 mg (growth retardation in dogs and rats)	EFSA	0.00416 mg	0.112	12 – <18	Methemoglobinemia	No health concern
Dioxins plus DL-PCBs	2 pg WHO-TEQ, (reproductive effects in rats)	EFSA	1.024 pg	51.2	12 – <18	Range of toxic effects including chloracne and reproductive effects	No health concern
Benzo[a]pyrene (BaP)	None, $BMDL_{10}$ of 70 µg (total tumour-bearing animals)	EFSA	0.00128 µg	54,688 (MOE)	12 – <18	Carcinogenic	No health concern
Sum of BaP, BbF,ChR and BaA (PAH4)	None, $BMDL_{10}$ of 340 µg (total tumour-bearing animals)	EFSA	0.0032 µg	106,250 (MOE)	12 – <18	Carcinogenic	No health concern
Iodine	Guidance level of 15 µg/kg bw/day (Alterations in serum thyroid hormone	COT	15.2 µg	102	12 – <18	Varied effects dependent on previous exposure to iodine.	Low health concern

	levels from human studies)						
Perchlorate	TDI of 0.3 µg/kg bw/day (inhibition of radiolabelled iodine uptake by the thyroid)	EFSA	0.179 µg	59.6	12 – <18	Inhibition of iodine uptake, depletion of thyroid hormones	No health concern
Chlorate	TDI of 3 µg/kg bw/day (Carried over from perchlorate with a 0.1 potency factor, inhibition of radiolabelled iodine uptake by the thyroid)	EFSA	0.544 µg	18.1%	12 – <18	Inhibition of iodine uptake, depletion of thyroid hormones	No health concern
Naturally occurring oestrogens within cows' milk	ADI – 0.05 µg/kg bw/day for 17β-oestradiol (NOEL based off of multiple hormone dependent parameters in postmenopausal women. To protect	JECFA	0.0875 µg	17.5%	12 – <18	Suggested effects in children include developmental effects in the urogenital, hormonal and central nervous systems and	No health concern. Levels of oestrogens are low compared to endogenous circulating

					mammary glands, 17β-oestradiol is a carcinogen with uncertainty regarding its status as a genotoxic carcinogen.	hormones in humans.
	sensitive population subgroups an uncertainty factor of 10 was applied.)					

Table 16. A summary of information for compounds within milk where a satisfactory standard risk assessment of the compounds within cows' milk could not be performed.

Compound (s)	Literature evaluation	Effect	Conclusion: Health risk from cow's milk
Veterinary Medicines	Incidents where veterinary medicines are found within UK milk are uncommon. isolated incidents.	Various effects	No health concern
Pesticides	Between 2015 and the enmd of 2020 only 1 cows' milk sample of 1,723 returned a positive result (above the maximum residue level). The risk of pesticides form cow's milk is minimal	Various effects	No health concern
IGF-1	IGF-1 supplementation is unlikely to generate a risk to consumer health. In addition milk from IGF-1 treated cow's is unlikely to enter the UK as fresh milk in significant quantities.	No substantiated carcinogenic effects	No health concern
Other mycotoxins	Milk is considered unlikely to contain significant amounts of other mycotoxins	Effects including	No health concern

		immunotoxicity, carcinogenicity and mutagenicity	
Microplastics	A lack of toxicokinetic and toxicity data in general, the paucity of currently available data for microplastics in different food types and difficulties in performing an accurate exposure assessment	Various, depending on type	n/a

This is a draft statement and does not reflect the views of the Committee.
It should not be cited.

Annex B to TOX/2022/04

Abbreviations and Technical Information

ADI	Acceptable Daily Intake
15-Ac-DON	15-Acetyldeoxynivalenol
3-Ac-DON	3-Acetyldeoxynivalenol
ADME	Absorption, Distribution, Metabolism and Excretion
AFB_1	*Aflatoxin* B1
AFB1	Aflatoxin B_1
AFB2	Aflatoxin B2
AFG1	Aflatoxin G1
AFM_1	*Aflatoxin M1*
AFM1	Aflatoxin M_1
AFM2	Aflatoxin M2
AFT	Sum of AFB1, AFB2, AFG1 and AFG2
AhR	Aryl Hydrocarbon Receptor
As	Arsenic
BaA	Benz[a]anthracene
BaP	Benzo[a]pyrene
BbF	Benzo[b]fluoranthene
BBP	Butyl-benzyl-phthalate
BFR	Brominated Flame Retardants
BIO	Biochanin A
BMDL	Benchmark Dose Lower Confidence Limit
BPA	Bisphenol A
Br	Bromine
BST	Bovine Somatotropin
bw	Body Weight
CAR	Constitutive androstane receptor
Cd	Cadmium
CEP	EFSA Panel on Food Contact Materials, Enzymes and Processing Aids
CF2	Perfluorinated Methylene Group
CF3	Perfluorinated Methyl Group
ChR	Chrysene
Cl	Chlorine
COC	The Committee on Carcinogenicity Food, Consumer Products and the Environment
CONTAM	EFSA Panel on Contaminants in the Food Chain
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
DAI	Daidzein
DBP	Di-butylphthalate
DecaBDE	Decabromodiphenyl ether
DEFRA	Department for Environment, Food and Rural Affairs
DEHP	Bis(2- ethylhexyl)phthalate
DHSC	Department of Health and Social Care

DIDP	Di-isodecylphthalate
DINP	Di-isononylphthalate
DL-PCBs	Dioxin-Like Polychlorinated Biphenyls
DL-PCBs	Dioxins and Dioxin-Like Polychlorinated
DNSIYC	Diet and Nutrition Survey of Infants and Young Children
DON	Deoxynivalenol
DON-3-glucoside	Deoxynivalenol-3-Glucoside
E1	Oestrone
E2	17β-Oestradiol
EC	European Commission
ECHA	European Chemical Agency
EFSA	European Food Safety Authority
EFSA	European Food Safety Authority
EHDI	Estimated Human Daily Intakes
EQU	Equol
EQU	Equol (metabolite of DAI)
ERs	Oestrogen Receptors
EU	European Union
EVM	Expert Group on Vitamins and Minerals
FAO	Food and Agriculture Organisation
FDA	Food and Drug Administration
FOR	Formononetin
FSA	Food Standards Agency
FSH	Follicle Stimulating Hormone
FTOHs	Fluorotelomer alcohols
GEN	Genistein
GH	Growth Hormone
GI	Gastrointestinal
H	Hydrogen
HBCD	Hexabromocyclodecane
HBGV	Health Based Guidance Value
HED	Human Equivalent Dose
Hg	Mercury
Hg^+	Mercurous cation
Hg^0	Elemental mercury
Hg^{2+}	Mercuric cation
HPG axis	Hypothalamic-Pituitary-Gonadal Axis
I	Iodine
IARC	International Agency for Research on Cancer
iAS	Inorganic Arsenic
ICES- 6	Indicator PCBS: 28, 52, 101, 138, 153 and 180
IGF-1	Insulin-like Growth Factor 1
IGFBP-3	Insulin Growth Promoting Factor Binding Protein 3
IQ	Intelligence quotient
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JECFA	Joint FAO/WHO Committee on Food Additives

LB	Lower Bound - Lower bound and upper bound approaches are utilised in order to assess left censored data (Occurrence values below the limits of detection or quantification). The lower bound refers to situations where a zero value has been assigned to occurrence values below the limit of detection or limit of quantification.
LH	Luteinising Hormone
LOD	Limit of Detection
MB	7. Middle Bound - The middle bound is and approach for assessing left censored data. Any values below the limit of detection (LOD) or limit of quantification (LOQ) are assigned the value LOD/2 or LOQ/2 respectively.
mg	Milligram
mm	Millimetre
MoBB	Margin of Body Burdens
MOE	Margin Of Exposure
MRL	Maximum Residue Limit
MT	Metallothionein
NDL-PCBs	Non-Dioxin-Like Polychlorinated Biphenyls
ng	Nanogram
NHS	National Health Service
NIS	Na^+/I^- symporter
nm	Nanometre
NOAELs	No-Observed-Adverse-Effect Levels
NOEL	No Observed Effect Level
NRL	National Reference Laboratory
NSAIDS	Non-Steroidal Anti-inflammatory drugs
OctaBDE	Octabromodiphenyl Ether
OECD	The Organisation for Economic Co-operation and Development
OTA	Ochratoxin A
PAHs	Polycyclic Aromatic Hydrocarbons
PAPs	Polyfluorinated Phosphate Esters
Pb	Lead
PBB-169	3,3',4,4',5,5'-hexaBB
PBBs	Polybrominated Biphenyls
PBDEs	Polybrominated Diphenyl Ethers
PCBs	Polychlorinated Biphenyls
PCDDs	Polychlorinated Dibenzodioxins
PCDFs	Polychlorinated Dibenzofurans
PE	Polyethene
PentaPBDE	Pentabromodiphenyl Ether
PFAAs	Perfluoroalkyl Acids
PFAS	Per- and polyfluoroalkyl substances
PFBS	Perfluorobutanesulfonic Acid
PFCAs	Perfluoroalkyl Carboxylic Acids
PFHxS	Perfluorohexane sulfonic acid

PFNA	Perfluorononanoic Acid
PFOA	Perfluorooctanoic Acid
PFOS	Perfluorooctane sulfonic acid
PFSAs	Perfluoroalkane Sulfonic Acids
pg	picograms
PHE	Public Health England
PMTDI	Provisional Maximum Tolerable Daily Intake
PP	Polypropene
PTMI	Provisional tolerable Monthly Intake
PTWI	Provisional Tolerable Weekly Intake
RASFF	Rapid Alert System for Food and Feed
SACN	Scientific Advisory Committee on Nutrition
SCF	Scientific Committee on Food
SCF	European Scientific Committee on Food
SCVPH	Scientific Committee on Veterinary measures relating to Public Health
SD	Standard Deviation
SUL	Safe Upper Level
TBBPA	Tribromobisphenol A
TCDD	2,3,7,8-Tetrachlorodibenzyl Dioxin
TDI	Tolerable Daily Intake
TDS	UK Total Diet Study
TEF	Toxicity Equivalency Factor
TEQ	Toxic Equivalent Value
TSH	Thyroid-Stimulating Hormone
TUL	Tolerable Upper Level
TWI	Tolerable Weekly Intake
UB	Upper Bound - Lower bound and upper bound approaches are utilised in order to assess left censored data (Occurrence values below the limits of detection or quantification). In the upper bound approach any occurrence levels below the limit of detection or limit of quantification (left censored data) are assigned the value of the limit of detection or the limit of quantification.
U-Cd	Urinary Cadmium
UK	United Kingdom
US	United States
US-EPA	United States Environmental Protection Agency
VMD	Veterinary Medicines Directorate
VPC	Veterinary Products Committee
WHO	World Health Organisation
β2M	β-2-microglobulin
µg	microgram

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