Risk Characterisation - Statement on the risk assessment of cow’s milk in children aged 1 to 5 years, in the context of plant-based drinks evaluations

In this guide

123. EFSA calculated the contributions of individual food categories in the collected surveys using the mean LB occurrence value in their 2020 risk assessment. It was reported that ‘milk and dairy products’ were the most substantial contributor to AFM1 exposure for all age groups. However, it should be noted that there was a high percentage of non-detects (up to 90% or more) and the median LB was 0. For the group other children (≥ 36 months to < 10 years old), liquid milk was found to account for up to 89% of exposure to AFM1. Liquid

milk also contributed up to 49% of total exposure for infants < 12 months old and up to 74% of total exposure for toddlers (≥ 12 months to < 3 years old). In addition to this, in situations of high exposure, liquid milk could contribute up to 89% of total exposure to AFM1. Liquid milk is therefore a significant contributor to AFM1 exposure levels. However, exposure to AFM1 from milk at these levels will usually be limited to a short period in life.

124. Analysing the information within EFSA’s 2020 risk assessment ‘milk and dairy products’ contributed <1% of total AFB1 exposure in all surveys. This suggests that there is unlikely to be any health concern from AFB1 exposure from milk to children aged 6 months to 5 years of age.

125. EFSA also concluded that liquid milk was an important source of exposure of AFM1 + AFT (the sum of AFB1, AFB2, AFG1 and AFG2) for infants, toddlers and children. However, this is driven by high AFM1 contributions.

126. In 2020 EFSA utilised both an animal derived BMDL10 and human epidemiological data to perform two risk characterisations; the animal derived BMDL10 approach and the subsequent total dietary exposure assessment are discussed below, as this is easier to communicate and was in line with the conclusions drawn from the human data.

127. In (EFSA, 2020a), for AFM1 a 0.1 potency factor was applied to account for the fact that in a study on Fischer rats, AFM1 was found to induce liver cancer with a potency of 0.1 of that of AFB1. This produced a value of 4.0 μg/kg bw per day for use in an MOE approach to assess AFM1 (EFSA, 2020a). For mean total dietary AFM1 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 total 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 occur only for a short period in a child’s life. For total AFT + AFM1 dietary exposure, all age groups and exposure levels exhibited MOEs below 10,000 suggesting there is a potential health concern from the total diet. MOEs for AFM1 exposure for total dietary exposure are presented below in Tables 9 through to 12. MOEs for AFT + AFM1 for total dietary exposure are presented below in Tables 13 through to 16.

Table 9. MOEs at the lower bound of the minimum, median and maximum mean exposure levels in the total diet 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 10. MOEs at the upper bound of the minimum, median and maximum at mean exposure levels to AFM1 in the total diet 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 11. MOEs at the lower bound of the minimum, median and maximum at 95th percentile exposure levels to AFM1 in the total diet 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 12. MOEs at the upper bound of the minimum, median and maximum at 95th percentile exposure levels to AFM1 in the total diet 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 13. MOEs at the lower bound of the minimum, median and maximum at mean exposure levels to AFT + AFM1 in the total diet 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 14. MOEs at the upper bound of the minimum, median and maximum at mean exposure levels to AFT + AFM1 in the total diet 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 15. MOEs at the lower bound of the minimum, median and maximum at 95th percentile exposure levels to AFT + AFM1 in the total diet 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 16. MOEs at the upper bound of the minimum, median and maximum at 95th percentile exposure levels to AFT + AFM1 in the total diet from (EFSA, 2020a).

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

128. In light of EFSA’s latest risk assessment it is unlikely that AFB1 in liquid milk presents a risk to children aged 6 months to 5 years of age. Cow’s milk was, however, found to contribute significantly (up to 89%) to total dietary 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 estimated mean exposure levels, a risk to human health cannot be excluded for infants and children aged 6 months to 5 years.

129. From the above information, the COT concluded that a risk to health from aflatoxin M1 from consumption of cow's milk by children aged 6 months to 5 years of age cannot be excluded. A risk to health also cannot be excluded for

total aflatoxins within milk, however the low MOEs present are largely driven by levels of AFM1 within cow’s milk. Other aflatoxins did reduce the MOE further. It was noted that there was a high percentage on non-detects in the milk and dairy samples, which would affect the way in which exposure is best calculated.

Per- and polyfluoroalkyl substances (PFAS)

130. 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. Thet are also used, or have been used, in firefighting foams. 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.’

131. The 2 main classes of PFAS are perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkane sulfonic acids (PFSAs). In 2020 EFSA undertook a risk assessment of the potential effects on human health related to the presence of perfluoroalkyl substances in food, focussing on four 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).

132. Further information on establishment of HBGVs and on risk characterisation have been provided in Annex A. Within EFSA’s 2020 dietary exposure evaluation no samples tested positive for the four PFAS compounds above the analytical method reporting levels.

133. In an article by Hill, Becanova and Lohmann, (2021), 13 milk samples were taken from US cattle in areas of concern. These were farms which reported biosolid amendments on cropland or were located within proximity to aqueous film forming foam (AFFF) contaminated soils. No perfluoroalkyl acids (PFAAs) were detected, with the authors concluding that uptake of PFAAs into dairy milk within the U.S. is low.

134. Kowalczyk et al., (2013) in their study of absorption, distribution, metabolism and excretion (ADME) of PFAS contaminated feed in dairy cows

concluded that the kinetics of PFOA were similar to PFBS and differed from PFHxS and PFOS. Low levels of PFBS were detected in milk, plasma and trace amounts were detected in the kidneys and liver. Coupled with a high urinary excretion the authors concluded that PFBS does not accumulate in dairy cows.

135. 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 the levels of PFAS in cow’s milk are not of health concern to infants and children aged 6 months to 5 years.

Brominated flame retardants (BFRs)

136. 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.

137. 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.

138. The use of many of the BFRs is 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)

139. HBCDDs are non-aromatic, brominated cyclic alkanes used primarily as additive flame retardants 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 vary depending on product application.

140. 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).

141. 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. This produces a value of 8. For MOEs above this level there is adequate reassurance that there is no health concern.)

142. In light of the (EFSA, 2021b) and (COT, 2015c) conclusions (see Annex A) the COT concluded that the levels of 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

143. (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, televisions, textiles and plastic foams, and were able to migrate from 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.

144. EFSA concluded that 'the risk to the European population from exposure to PBBs through the diet is of no concern.' Levels in milk were 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.

145. 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 on their use (COT, 2015a). Within the literature (discussed in Annex A), minimal levels of PBBs have been reported in milk.

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

PBDEs

147. 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.

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

149. A review of the literature for occurrence of PBDEs in milk did not show a concern for health as concentrations were low (discussed in Annex A).

150. 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 (COT, 2015b). An addendum to this statement was produced in 2017 that further concluded that '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, 2017a).

151. Reviewing the EFSA (2011b) and COT (2015b; 2017a) conclusions in addition to the evidence from the literature that cow's milk contains only very low levels, the COT concluded that the levels of PBDEs in cow's milk do not pose a risk to health for infants and children aged 6 months to 5 years.

Tetrabromobisphenol A (TBBPA)

152. 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.

153. (EFSA, 2011b) and the COT (2019c) concluded that there was no risk to health from TBBPA. EFSA found that dietary exposures resulted in large MOEs, with cow's milk not containing any TBBPA above reporting levels. The work by COT in 2019 resulted in MOEs greater than those reported in EFSA's 2011 evaluation. The COT concluded that with respect to cow's milk exposure, the MOEs were adequately protective. This is further discussed in Annex A.

154. In light of the EFSA (2011b) and COT (2019c) conclusions and evidence from the literature (further discussed in Annex A) that levels in cow's milk were very low, so that the MOEs were not of concern, the COT concluded that levels of TBBPA in cow's milk do not pose a risk to health for infants and children aged 6 months to 5 years.

Microplastics

155. 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.

156. Due to their widespread presence in the environment, microplastics also occur in food (e.g. seafoods, salt, honey, vegetables) and drinks (e.g. bottled water, milk, soft drinks, tea, beer) (Jin et al., 2021; 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.

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

158. (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 levels of microplastics in different food types and the difficulty of performing an accurate exposure assessment. However, whilst risks from microplastics

cannot be quantified currently, microplastic contamination in milk is likely to be lower than in other foodstuffs.

159. The current view of the COT from the above information and that included in Annex A, is that exposure to microplastics from the consumption of cow’s milk does not represent a risk to health for children aged 6 months to 5 years of age.