TOX/2020/41

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Overarching paper on consumption of plant-based drinks in children aged 6 months to 5 years of age.

Introduction

1. The Department of Health and Social Care (DHSC), Public Health England (PHE) and the Food Standards Agency (FSA) are receiving an increasing number of enquiries regarding the use of plant-based drinks in the diets of infants and young children. Therefore, the COT are asked to consider the potential adverse health effects of soya, almond and oat drinks consumed in the diets of these age groups.

2. Currently the UK government advises that parents should only use infant formula as an alternative to breast milk in the first 12 months of a baby's life. It is also advised that whole cows' milk and unsweetened calcium-fortified milk alternatives, such as soya, almond and oat drinks can be given to children from the age of 1 as a part of a healthy, balanced diet (NHS, 2018).

3. The main challenge in the assessment of the safety of these drinks is the lack of information regarding dietary intakes for children following dairy-free or plant-based diets. A number of sources providing guidance for frequency and portion sizes for vegan children under 5 were deemed the most representative scenarios for the diet of children following dairy-free or plant-based diets. Members noted that although the exposure estimates made the best use of the available data, there was a high degree of uncertainty with regards to the actual exposures to these drinks in the diets of children following a plant-based diet as these recommendations were designed to ensure that dietary requirements were met, but consumption of the drinks and might differ in reality. It was agreed that the current approach, which assumed that consumption was exclusively of a single plant-based drink, was most appropriate as young children are likely to develop a preference for one drink. The need for consumption information for people following plant-based diets more generally was also highlighted by the Committee as the popularity of these diets is increasing and information on realistic dietary intakes would help inform future risk assessments on similar issues.

Soya

4. Soya drinks are a popular alternative to dairy products and their use is becoming more widespread. Soya products contain phytoestrogens (also known as isoflavones) which have been shown to produce some reproductive and developmental changes in animal studies. The safety of phytoestrogens was considered by the COT in 2003 and 2013 and, more recently, the Committee reviewed data published since the 2013 evaluation (COT 2019, 2020). The Committee concluded that the new animal studies did not add significantly to the overall database. As with previous evaluations, although there was some indication of possible adverse effects being reported in human studies, it was not possible to determine, on the basis of the available data, whether sensitivity to phytoestrogens varied among different age groups. Overall, the Committee concluded that that the intakes of phytoestrogens from consumption of soya drinks in children aged 6 months to 5 years of age was less than the previously estimated maximum in infants aged 0 to 6 months, 9.5 mg/kw bw per day, up to which level it was considered that soya-based infant formula could be used to ensure adequate nutrition, if circumstances dictated that this was necessary. The Committee agreed that, based on the information provided, exposure to phytoestrogens from other soya-based products in the diets of children aged 6 months to 5 years of age was lower, and hence there was no potential concern. It was, however, noted that when considered aggregately, the exposures were much closer to the level of 9.5 mg/kg bw per day. Members agreed that, in addition to potential toxicological concerns, consideration of nutritional issues would also be required to assess whether it was necessary to issue additional advice on the consumption of soya-based drinks in children aged 6 months to 5 years of age.

Oats

5. Oat drinks are an alternative to soya milk for children following plant based or dairy- free diets. Oats can be contaminated with mycotoxins, notably the trichothecene mycotoxins T-2 and HT-2, deoxynivalenol (DON), and Ochratoxin A (OTA). EFSA considered the safety of T-2 and HT-2 in 2017, where health-based guidance values were established for emetic effects following acute exposure, and for immune- and hepatotoxicity effects for chronic exposure. For OTA, EFSA (2020) established an MOE approach for neoplastic and non-neoplastic effects in the kidney, while a group TDI was established for the sum of DON, 3-Ac-DON, 15-Ac-DON and DON-3-glucoside based on reduced body weight gain in animals (EFSA, 2017b). The COT evaluated the available data and considered the estimated exposures to the above contaminants (COT, 2020). It was concluded that in terms of acute exposure to DON and the sum of HT-2 and T-2, consumption of a large quantity of oat drink was required to exceed their respective Acute Reference Doses (ARfD). Thus, acute exposure to DON, and HT-2 & T-2 from the consumption of oat drink was considered to be of low risk. Generally, all exposures for T-2, HT-2 and DON were below the respective Tolerable Daily Intakes (TDI), with the exception of minor exceedances observed (12-24 months for T-2 and HT-2 and in children > 12 months of age for DON). The assessment of aggregate exposures from oat drinks and the general diet was considered conservative and as the exceedances were only minor and transient in nature, it was concluded that there would be no chronic health effects in respect to T-2, HT-2 and DON.

6. In respect of OTA, the Committee were unable to conclude whether the exposure estimates indicated a potential health concern. Members agreed that although this exposure assessment was for young children, it needed to be extended to adults to establish whether there were potential health concerns for the general population. It was noted that there were many uncertainties in the cancer endpoint used for risk characterisation, and furthermore, it was unclear whether or not OTA was a genotoxic carcinogen, and thus which MOE threshold value would be applicable. The Committee noted that the MOE of 10,000 for substances that are directly genotoxic and carcinogenic may not be appropriate in this case because the evidence for a direct interaction of OTA with the DNA is inconclusive. Some age groups had MOEs lower than desirable for non-neoplastic effects while all age groups had MOEs lower than those considered of low concern for a genotoxic carcinogen. The uncertainty in the assessment was considered to be high, especially considering the lack of analytical information on the presence of these contaminants in oat drinks and the assumptions used in the exposure assessment and it was noted that it is likely that the risk was being overestimated.

Almonds

7. Almond drinks have a lower nutritional value than soya or oat drinks, however they are recommended as an alternative in cases where children refuse soya and oat drinks. The mycotoxin, aflatoxin B1 was identified as a common chemical contaminant in almonds which could be potentially transferred to almond drinks. Aflatoxin B1 is genotoxic and carcinogenic so its maximum levels set by the EU are established using the as low as reasonably achievable (ALARA) principle. The lack of analytical information on effect of processing of almonds during almond drink manufacture on the levels of aflatoxins, as well as the lack of information on the levels of this contaminant in almond drinks was considered the main limitation in assessing the risk to health. Overall and considering the above limitations it was concluded that the approach of estimating MOE based on the Maximum Residue Levels set by EFSA was highly uncertain and likely leading to an overestimation of risk and therefore not appropriate. The risk to health from exposure to AFB1 could not be determined.

8. Almonds also contain cyanogenic glycosides which, once macerated, may interact with the enzyme ß-glucosidase. This enzyme hydrolyses the cyanogenic glycosides and can yield hydrogen cyanide, benzaldehyde, glucose and ketone. The quantity of cyanogenic glycosides present in almond drinks is uncertain, but low levels of cyanide have been detected on analysis. Exposure to large amounts of the hydrogen cyanide component can lead to convulsions, loss of consciousness, dizziness, weakness, mental confusion and heart failure. Available information indicates that bitter almond varieties are not grown in commercial almond orchards and although the use of bitter almonds in almond milk drinks cannot be completely ruled out, bitter almonds would not be deliberately used in almond drinks as they would be unpalatable and impart a strong ‘marzipan’ flavour to the drink. However, contamination with bitter kernels or the presence of almond kernels or the presence of almond kernels could occur but there are no data on the level of cross-

contamination with bitter almonds if it does. Overall, Members agreed that there were no specific concerns for acute toxicity from cyanogenic compounds in almond drinks.

9. The Committee are asked to consider the information presented and address the questions posed in each Annex.

Annexes to this paper

- **Annex A: Draft Statement on the potential risks from soya drink consumption in children aged 6 months to 5 years of age.**

- **Annex B: Draft Statement on the potential risks from the consumption of oat drinks for children aged 6 months to 5 years of age**

- **Annex C: Follow up discussion paper on the potential risks from almond drink consumption in children aged 6 months to 5 years of age.**

Secretariat

August 2020

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

Annex A to TOX/2020/41

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft Statement on soya drink consumption in children aged 6 months to 5 years of age.

1. The first draft statement of soya drink consumption in children aged 6 months is attached for Members' comments. The conclusions are set out in paragraphs 16-20.

Questions for the Committee:

I. Do the Committee have any comments on the structure and content of the first draft statement?

Secretariat

September 2020

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Draft Statement on soya drink consumption in children aged 6 months to 5 years of age.

Background

1. Soya drinks are a popular alternative to dairy products and their use is becoming more widespread. In 2018, 95.6 million litres of soya drinks were sold in the UK amounting to sales of £135.6 million pounds. They are commonly consumed by all sectors of the population including those wishing to avoid dairy products and by individuals with an intolerance to lactose or another component of milk or, who follow a plant-based diet.

2. The Department of Health and Social Care (DHSC), Public Health England (PHE) and the FSA are receiving an increasing number of enquiries regarding the use of plant-based drinks in the diets of infants and young children. Therefore, the COT was asked to consider the potential health effects of soya drinks in the diets of these age groups since soya infant formula was only recommended where medically necessary.

3. Soya products contain phytoestrogens (also known as isoflavones) which have been shown to produce some reproduction and developmental changes in animal studies, although human epidemiological studies have not reported comparable effects[1,2].

4. Currently the UK government advises that parents should only use infant formula as an alternative to breast milk in the first 12 months of a baby's life as the main milk drink. It is also advised that whole cows' milk and unsweetened calcium-fortified milk alternatives, such as soya, almond and oat drinks can be given to children from the age of 1 as a part of a healthy, balanced diet. In addition, in 2013, the COT reviewed the potential risks from phytoestrogens in the infant diet and concluded that there is no substantive medical need for, nor health benefit arising from, the use of soya-based infant formula and it should only be used in exceptional circumstances to ensure adequate nutrition. Therefore, soya formula should only be introduced to the diet from the age of 6 months if it has been recommended or prescribed by a health visitor or GP. In recent evaluations of soya, the Committee noted that there was some uncertainty about the safety of soya-based formula and concluded that there was no scientific basis for a change in current advice.

[1] Report available at: https://cot.food.gov.uk/sites/default/files/cot/phytoreport0503.pdf
[2] Statement available at https://cot.food.gov.uk/sites/default/files/cot/cotstaphytos.pdf

Toxicity

5. As noted above, soya products contain phytoestrogens which have been shown to produce developmental and reproductive changes in animal studies, although the evidence for effects in humans from epidemiological studies is inconclusive.

6. The COT has considered the safety of phytoestrogens previously (2003, 2013). In 2013, the Committee concluded that, based on the evidence of some developmental and reproductive effects observed in animal studies along with evidence from human studies raising the possibility of subtle effects of uncertain clinical significance, there was some uncertainty about the safety of soya-based formula. Following the evaluation of more recent data (COT, 2019) the Committee concluded that the new animal studies did not add significantly to the overall database. As with previous evaluations, although there was some indication of possible adverse effects being reported in human studies, it was not possible to determine, on the basis of the available data, whether sensitivity to phytoestrogens varied among different age groups.

Exposure to phytoestrogens

7. The isoflavone content of a variety of soya-based foods (data adapted from Kuhnle et al, 2009; TOX/2020/33) was used to determine the occurrence of isoflavones in soya- based foods. These varied from 3994 µg/100g for soya sausages to 20850 µg/100g for soya mince.

8. Due to the limited information on the consumption of soya based foods by these age groups from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) and the National Diet and Nutrition Survey (NDNS), the chronic exposure estimates for isoflavones in children between 6 months and 5 years of age were calculated using several sources of including the British Nutrition Foundation (2019), the First Steps Nutrition Trust Eating Well: vegan infants and under 5s (2020), Vegan Society Food tips for vegan children (2017) and Public Health England's (PHE) published Example menus for Early Years Settings in England (EYS) (2017). The above sources provided guidance for frequency and portion sizes for children under 5 and, considering the lack of consumption information for the groups of interest they were deemed the most representative scenarios for the diet of children following dairy-free or plant-based diets. The latter group is important when considering aggregate exposures to isoflavones from soya in the diet as their diets may be likely to consist of multiple sources of soya-based products in order to meet the nutritional requirement usually provided by meat and dairy products.

9. In summary, the exposures were based on a number of assumptions (COT, 2020) that were considered representative of a worst-case scenario and would make allowance for foods such as soya cheese, for which the available information on consumption is limited. Based on the available information, tofu and soya meat

alternatives (including burgers and sausages) are used interchangeably to replace meat derived protein in children following a plant-based diet. As a worst-case scenario, the commodity with the highest concentration of isoflavones (soya mince) was selected for calculations.

10. The mean bodyweights used in calculations were based on data from the DNSIYC and the NDNS (DH, 2013; Bates et al, 2014; 2016; Roberts et al, 2018).

11. The exposures to isoflavones from soya products for children aged 6 months to 5 years are presented in Table 1. Soya drink is only recommended as a main milk drink after the age of 1 as part of a healthy, balanced diet (NHS, 2018). However, exposure from soya drinks used in cooking was considered from the age of 6 months and as a main milk drink from the ages of 1-5 years old.

Table 1: Exposure to isoflavones from soya products for children aged 6 months to 5 years.

Age (months)	Commodity	Exposure (µg/kg bw/d)
6-<12	Soya Based Formula	780 - 2000
6-<12	Soya Drink	1300
6-<12	Meat alternatives	625
6-<12	Soya Yoghurt	450
12-≤18	Soya Drink	1700 - 2800
12-≤18	Meat alternatives	1600
12-≤18	Soya Yoghurt	380
18-<24	Soya Drink	1500 - 2500
18-<24	Meat alternatives	1400
18-<24	Soya Yoghurt	342
24<48	Soya Drink	1200 – 2000
24<48	Meat alternatives	1400
24<48	Soya Yoghurt	270

48<60	Soya Drink	980 – 1600
48<60	Meat alternatives	2100
48<60	Soya Yoghurt	225

*Rounded to 2 SF

12. These exposures are indicative of the average diet of a child following a plant-based diet based on the dietary recommendations from the multiple sources described. However, lacking accurate consumption information, it is likely that these exposures would vary in practice, for example if a child consumes soya-based ice-cream as dessert on occasion.

13. Since isoflavones are present in other food commodities, aggregate isoflavone exposure from the diet was estimated. Table 2 presents isoflavone exposures from background diet, based on food consumption estimates taken from the DNSIYC (DH, 2013) for children up to 18 months of age and those between 18 months and 5 years from the NDNS (Bates et al, 2014; 2016; Roberts et al, 2018). Overall, the background diet does not significantly contribute to isoflavone intakes, considering exposure from soya products alone.

Table 2: Overall isoflavone exposure from background diet (µg/kg bw per day)

Age (months)	mean	maximum	97.5th percentile
6-<12	17	1400	67
12-≤18	26	600	73
18-<24	24	93	52
24-<48	26	480	66
48-<60	29	430	57

*Rounded to 2SF

14. For reference, the exposures to isoflavones from soya-based infant formula for infants aged 0-6 months are given in Table 3. This is based on information available from the Vegan Society[3] that: “If breastfeeding is not an option, infant formula is recommended. Soya-based infant formula can be fed to vegan infants when breastfeeding is not an option, but please speak to your health visitor or doctor before using it.”

Table 3: Estimated total isoflavone exposure (mg/kg bw/day) of infants fed exclusively soya-based infant formula.

Isoflavone level in mg aglycone equivalents/ L	Age in months (consumption)	Age in months (consumption)	Age in months (consumption)	Age in months (consumption)
	0-4 (800mL)	0-4 (1200 mL)	>4-6 (800 mL)	>4-6 (1200mL)

[3] https://www.vegansociety.com/resources/nutrition-and-health/life-stages/under-fives

Soya-based formula 18-46.7 mg/L	2.4-6.3	3.7-9.5	1.8-4.8	2.8-7.2

Conclusions

15. There is a large body of literature which demonstrates the adverse effects of soya phytoestrogens on reproductive endpoints in animal studies at levels varying from 1.6-500 mg/kg bw/day (COT, 2003), although many of these studies used administration via the intravenous or subcutaneous routes. It is generally accepted that soya-rich diets in animal models have a detrimental effect on reproductive systems which may be wholly or partly irreversible depending on the timing of exposure. It is also widely recognised that the levels of phytoestrogens found to cause these reproductive effects are similar to those consumed in a soya-rich western diet. What is not currently understood is the relative susceptibility of animals and humans to these effects. Many of the available studies consider total phytoestrogen consumption, therefore the pattern of any adverse effects produced may be affected by the composition of phytoestrogens in different foods.

16. Furthermore, based on the available information it was not possible to determine whether sensitivity to phytoestrogens varied among the age groups of concern; it was similarly not possible to determine whether the level of concern differed between age groups.

17. The background diet does not significantly contribute to isoflavone intakes, considering exposure from soya products alone. Estimates for isoflavone exposure from soya-based infant formula for infants aged 0-6 months were also presented and it can be concluded that soya formula contributes significantly to isoflavone exposure in these age groups. This is important to consider, given that advice from the Vegan Society for vegan infants is that "soya-based infant formula can be fed to vegan infants when breastfeeding is not an option, but please speak to your health visitor or doctor before using it.[4]"

18. The Committee agreed that the use of dietary information tailored to children who would be high consumers of these drinks was more appropriate than using consumption of animal-derived foods as a substitute for soya products. However, it was noted that there was a high degree of uncertainty with regards to the actual exposures to these drinks in the diets of children following a plant-based diet as these recommendations were designed to ensure that dietary requirements were met, but consumption of the drinks and other soya-based foods might differ in reality.

19. It was concluded that the intakes of phytoestrogens from consumption of soya drinks in children aged 6 months to 5 years of age was less than the previously estimated maximum in infants aged 0 to 6 months, 9.5 mg/kw bw per day, up to

[4] https://www.vegansociety.com/resources/nutrition-and-health/life-stages/under-fives

which level it was considered that soya-based infant formula could be used to ensure adequate nutrition, if circumstances dictated that this was necessary. The Committee agreed that exposure to phytoestrogens from other soya-based products in the diets of children aged 6 months to 5 years of age based on the information provided was lower, and hence there was no potential concern. It was, however, noted that when considered aggregately, the exposures were much closer to the level of 9.5 mg/kg bw per day. Members agreed that, in addition to potential toxicological concerns, consideration of nutritional issues would also be required to assess whether it was necessary to issue additional advice on the consumption of soya-based drinks in children aged 6 months to 5 years of age.

20. The need for consumption information for people following plant-based diets more generally was also highlighted by the Committee as the popularity of these diets is increasing and information on realistic dietary intakes would help inform future risk assessments on similar issues.

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

Glossary

COT – Committee on Toxicity

DHSC – Department of Health and Social Care

DNSIYC – Diet and Nutrition Survey of Infants and Young Children

EYS – Early Year Settings

NDNS– National Diet and Nutrition Survey

PHE – Public Health England

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

References

Bates, B.; Cox, L.; Nicholson, S.; Page, P.; Prentice, A.; Steer, T.; Swan, G. (2016) National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 – 2013/2014) Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/551352/NDNS_Y5_6_UK_Main_Text.pdf

Bates, B.; Lennox, A.; Prentice, A.; Bates, C.; Page, P.; Nicholson, S.; Swan, G. (2014) National Diet and Nutrition Survey Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012) Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/310995/NDNS_Y1_to_4_UK_report.pdf

BDA (2017) The Association of UK Dietitians: Soya and Health Fact Sheet. Available at https://www.bda.uk.com/foodfacts/soya2017.pdf (accessed 06/10/19)

British Nutrition Foundation (2019): Healthy eating for toddlers. Accessible at: https://www.nutrition.org.uk/healthyliving/resources/healthyeatingtoddlers.html

COT (2003) Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Report on Phytoestrogens and Health. Available at: https://cot.food.gov.uk/sites/default/files/cot/phytoreport0503.pdf

COT (2019): Discussion paper on soya drink consumption in children aged 6 months to 5 years of age. Available at: https://cot.food.gov.uk/sites/default/files/tox201971discussionpaperonsoyadrink.pdf

COT (2020): Overarching Discussion paper on consumption of plant-based drinks in children aged 6 months to 5 years of age. Available at: https://cot.food.gov.uk/sites/default/files/tox202033overarchingdiscussionpaper.pdf

DH (2013). Diet and Nutrition Survey of Infants and Young Children (DNSIYC), 2011. Available at: http://transparency.dh.gov.uk/2013/03/13/dnsiyc-2011/

First Steps Nutrition Trust (2018): *Good food choices and portion sizes for 1-4 years olds*, First Steps Nutrition Trust, Available online at: https://www.firststepsnutrition.org/

First Steps Nutrition Trust (2020): *Eating well: Vegan infants and under 5's*, First Steps Nutrition Trust, Available online at: https://www.firststepsnutrition.org/

Food Safety Authority of Ireland (2020) Scientific Recommendations for Food-Based Dietary Guidelines for 1 to 5 Year-Olds in Ireland. Available at: file:///C:/Users/901221/AppData/Local/Microsoft/Windows/INetCache/Content.Outlook/6TBU38T5/Ireland%20Sci%20Rec%20for%20Food%20based%20Dietary%20Guidelines%201-5%20(002).pdf

Kuhnle GGC, Dell'Aquila C, Aspinall,SM, Runswick SA, Mulligan AA, Sheila A. Bingham (2009) Phytoestrogen Content of Cereals and Cereal-Based Foods Consumed in the UK. Nutrition and Cancer, 61(3), 302–309

Linus Pauling Institute (2004) Micronutrient Information Centre: Soy Isoflavones. Last reviewed October 2016. This link leads to a website provided by the Linus Pauling Institute Oregon State University. The FSA is not affiliated or endorsed by the Linus Pauling Institute or Oregon State University: https://lpi.oregonstate.edu/mic/dietary-factors/phytochemicals/soy-isoflavones

PHE (2017): Example menus for early years settings in England. Available at: https://www.gov.uk/government/publications/example-menus-for-early-years-settings-in-england

Roberts, C.; Steer, T.; Maplethorpe, N.; Cox, L.; Meadows, S.; Page, P.; Nicholson, S.; Swan, G. (2018) National Diet and Nutrition Survey Results from Years 7 and 8 (combined) of the Rolling Programme (2014/2015 – 2015/2016) Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/699241/NDNS_results_years_7_and_8.pdf

Vegan Society (2017): A Nutrition Gide for vegans under five years old. Available at: https://www.vegansociety.com/sites/default/files/uploads/downloads/Under-fives%20PDF%202_0.pdf

Vegan Society(2016): Tips for vegan children:' Dietitian Heather Russell provides a kids' meal plan as well as fun ways to introduce the great fruit and vegetable adventure to young children', 18 November. Available at: https://www.vegansociety.com/whats-new/blog/food-tips-vegan-children#:~:text=Beans%2C%20chickpeas%2C%20lentils%2C%20tofu,are%20rich%20in%20vitamin%20C.

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

Annex B to TOX/2020/41

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft statement on oat drink consumption in children aged 6 months to 5 years of age.

1. The first draft statement on oat drink consumption in children aged 6 months is attached for Members' comments. The conclusions are laid out in paragraphs 49-57.

Questions for the Committee:

I. Do the Committee have any comments on the structure and content of the first draft statement?

Secretariat

September 2020

Annex B to TOX/2020/XX

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft statement on oat drink consumption in children aged 6 months to 5 years of age.

Background

1. The Department of Health and Social Care (DHSC), Public Health England (PHE) and the Food Standards Agency (FSA) are receiving an increasing number of enquiries regarding the use of plant-based drinks in the diets of infants and young children. Therefore, the COT has been asked to consider the potential health effects of oat drinks in the diets of these age groups.

2. Currently the UK government advises that parents should only use infant formula as an alternative to breast milk in the first 12 months of a baby's life as the main milk drink. It is also advised that whole cows' milk and unsweetened calcium-fortified milk alternatives, such as soya, almond, and oat drinks can be given to children from the age of one as a part of a healthy and balanced diet.

3. Oat drinks are proposed as an alternative to soya milk for children following plant based or dairy- free diets. The most likely potential adverse health effect arising from the consumption of oats was considered to be the possible exposure to mycotoxins. Oats can be contaminated with the trichothecene mycotoxins T-2 and HT-2, deoxynivalenol (DON), and Ochratoxin A (OTA) and the implications of exposure to these three mycotoxins are considered below.

Toxicity of HT-2 and T-2

Acute Reference Dose

4. In 2017, the EFSA Panel on Contaminants in the Food Chain (CONTAM) established an acute reference dose (ARfD) of 0.3 µg for T-2 and HT-2/kg bw, based on acute emetic events in mink (EFSA, 2017a; Wu *et al*., 2016). Using a $BMDL_{10}$ of 2.97 µg/kg bw for T-2 and HT-2 based on their emetic effects, and the application of an uncertainty factor of 10 for intraspecies differences, an ARfD of 0.3 (rounded from 0.297) µg T-2 and HT-2/kg bw was established. An interspecies uncertainty factor

was not included because humans were not considered to be more sensitive to this endpoint than mink.

Tolerable Daily Intake

5. For chronic exposure, the CONTAM Panel established a tolerable daily intake (TDI) for T-2 and HT-2 of 0.02 µg/kg body weight (bw) per day based on a new 90-day sub-chronic toxicity study in rats that confirmed that immune- and haematotoxicity are the critical effects of T-2 (EFSA, 2017a; Rahman *et al*., 2014). The Panel used decreases in leukocytes counts as the critical endpoint to derive a $BMDL_{10}$ of 3.3 µg T-2/kg bw. Based on rapid metabolism of T-2 to HT-2 and structural similarities, this value was used as a reference point for establishing a TDI for both T-2 and HT-2. An uncertainty factor of 200 was used (x 10 for interspecies differences, x 10 for intraspecies variation, and x 2 since it was a sub-chronic study).

Occurrence data of HT-2 and T-2

6. A number of brands of oat drink are sold in the UK, for example Alpro and Plenish. Due to differences in their production processes, there are slight differences in the oat content of these drinks. The mean average oat content across the brands of oat drink is 108 grams of oats per litre of oat drink (COT, 2020).

7. Oat drink consumed in the UK is made from European-harvested oats. Therefore, occurrence data of T-2 and HT-2 in oats were taken from EFSA's database which comprises of samples of unprocessed oats taken from across the European Union. The concentrations ranged from 234 (mean LB) to 236 µg/kg (mean UB) for the sum of T-2 and HT-2 in unprocessed oat grains (COT, 2020).

8. Schwake-Anduschus *et al.* (2010) demonstrated that T-2 and HT-2 toxins are mostly attached to the outer hull of oat grains, as the "de-hulling of oats led to a mean T-2/ HT-2 reduction of 98 %, where the reduction varied between 93.8 % and 100 %". This substantial reduction in the concentration of T-2 and HT-2 by de-hulling oat grains is recognised by EFSA and the Agriculture and Horticulture Development Board (AHDB). For example, the "normal cleaning and dehulling during mill processing can reduce these levels by 80-95 %" (EFSA, 2011). Furthermore, on their website, the AHDB states that "there is good evidence that at least 90 % of mycotoxins are removed during dehulling"[2]. These results explain why studies in the UK have shown high levels of mycotoxins in oats at harvest but generally low concentrations in consumer products.

9. Using the upper bound mean concentration of 236 µg/ kg for the sum of T-2 and HT-2 toxins in unprocessed oats, and a mean concentration reduction of 98 % after de-hulling as reported by Schwake-Anduschus *et al.* (2010), 4.72 µg of T-2 and HT-2 is expected to remain in 1 kg of groats after cleaning and de-hulling. Assuming

that 108 grams of processed oats are required to produce 1L of oat drink (paragraph 6), 0.51 µg of T-2 and HT-2 is estimated to be present in 1 kg of oat drink. This mean concentration was used for a UK exposure assessment (COT, 2020).

Exposure to HT-2 and T-2

10. To refine the exposure estimations, several sources of information were considered; the First Steps Nutrition Trust Eating Well: vegan infants and under 5s (2020), Vegan Society Food tips for vegan children (2017) and Public Health England's (PHE) published Example menus for Early Years Settings (EYS) (2017). The above sources provided guidance for frequency and portion sizes for children under 5 and considering the lack of consumption information for the groups of interest they were deemed the most representative scenarios for the diet of children following dairy-free or plant-based diets. It must be noted that the recommendations from these sources were for soya-alternatives to milk, these have been used in absence of representative consumption information for oat drinks. Soya-milk has been recommended due to its similar nutritional value and monetary cost to cow's milk, so these are conservative assumptions but are considered to be a more relevant proxy than cow's milk. Additionally, it should be noted that as children under 1 year are not recommended to consume dairy alternatives as their main milk drink, the assumption made here for the 6 – 12 month age group is that up to 200 ml of oat drink may be used in cooking infant food. Soya drink consumption for those wishing to avoid dairy products, individuals with an intolerance to lactose or another component of milk or those following a plant-based diet is likely to be significantly greater than for the general public, therefore these exposure estimates may be overestimating exposure in the general population.

Exposure to HT-2 and T-2 from oat drinks in the UK

11. The "sum of T-2 and HT-2" was used for estimating exposure which is consistent with what has been done previously for other mycotoxins. To calculate UK infant and young children exposures to T-2 and HT-2 from oat drink consumption, the estimated concentration of 0.51 µg T-2 and HT-2/ kg oat drink from occurrence data in European-harvested oats was used (see paragraph 9).

12. Due to insufficient consumption data from the DNSIYC survey (DH, 2013; Lennox *et al*., 2013; for infants aged 3 ≤ 18 months) and the NDNS survey (Bates *et al.,* 2014; Bates *et al*., 2016; Roberts *et al.,* 2018; for ages >18 months), consumption assumptions for soya drink are used as a proxy for oat drink (Table 1).

Table 1: Estimated chronic exposure to the sum of HT-2 and T-2 from consumption of oat drink for 6 to 60-month olds in the UK (**ng/kg b.w./day**)**

Age group	**Minimum***	**Maximum***
6 to < 12 months	11	---

12 to ≤ 18 months	14	23
18 to < 24 months	13	21
24 to < 48 months	10	17
48 to < 60 months	8.3	13

* Uses soya drink consumption rates (minimum & maximum) from a review of recommendations derived from the First Steps Nutrition Trust, Vegan Society and Public Health England as a proxy for oat drink consumption. Values rounded to 2 s.f.
** Uses estimated concentration of 0.51 µg T-2 & HT-2/ kg oat drink. Does not consider exposure to HT-2 and T-2 from other food sources.

Amount of oat drink required to exceed HBGV for HT-2 and T-2

13. The amount of oat drink that needs to be consumed, for exposure to approach the TDI was estimated (Table 2). This calculation does not take into account background dietary exposure to HT-2 and T-2. Although EFSA (2017) have reported background dietary exposure levels to the HT-2 and T-2 toxins, these data were not used because 1) their assessment is for the general diet (which includes dairy products, processed oats and possibly oat drinks) and thus does not consider children following a plant-based diet or avoid dairy, and 2) the age groups reported by EFSA are not aligned with the age groups reported in Table 3.

Table 2: Estimated quantity of oat drink required in **L** or **Kg*** to exceed the HBGV for HT-2 and T-2 mycotoxins for 6 to 60-month olds in the UK

Age group	**ARfD**	**TDI**
6 to < 12 months	5.4	0.36
12 to ≤ 18 months	6.4	0.43
18 to < 24 months	7.1	0.47
24 to < 48 months	8.9	0.60
48 to < 60 months	11	0.72

* Uses soya drink consumption rates (minimum & maximum) from a review of recommendations derived from the First Steps Nutrition Trust, Vegan Society and Public Health England as a proxy for oat drink consumption. Uses estimated concentration of 0.51 µg T-2 & HT-2/ kg oat drink. Does not consider exposure to HT-2 and T-2 from other food sources. Values rounded to 2 s.f.

Dietary exposure to HT-2 and T-2 from processed oats in the general diet in the UK

14. For this exposure assessment for 6 to 60-month olds, consumption data from the DNSIYC survey (DH, 2013; Lennox *et al.,* 2013; for infants aged 3 <18 months) and the NDNS survey (Bates *et al.,* 2014; Bates *et al.,* 2016; Roberts *et al*., 2018; for ages >18 months) were used. An estimated concentration of 4.72 µg HT-2 & T-2/ kg processed oats was used (see paragraph 9).

Table 3: Estimated acute and chronic exposure to the sum of HT-2 and T-2 mycotoxins from consumption of processed oats in the general diet for 6 to 60-month olds in the UK.

Age group	Number of consumers	Acute exposure (ng/kg bw/day)*		Chronic exposure (ng/kg bw/day)*	
		Mean	97.5th %ile	Mean	97.5th %ile
6 to < 12 months	632	5.2	19	2.4	9.0
12 to ≤ 18 months	713	6.1	20	2.8	11
18 to < 24 months	89	5.4	17	2.4	9.9
24 to < 48 months	347	4.8	15	2.1	7.6
48 to < 60 months	151	4.1	11	1.9	5.8

* Recipes were used for this assessment with oat content > 5% and 'oat-based alternatives to milk' were removed from the assessment. The assumption was made that all oats consumed were processed and had a concentration of 4.72 µg HT-2 & T-2/ kg processed oats. Values rounded to 2 s.f.

Exposure to HT-2 and T-2 from oat drinks and processed oats in the general diet (combined) in the UK

Table 4: Estimates of chronic exposure to the sum of HT-2 and T-2 mycotoxins from consumption of oat drinks and processed oats in the general diet combined for 6 to 60-month olds in the UK **(ng/kg b.w./day)***

Age group	Minimum	Maximum
6 to < 12 months	24	--**
12 to ≤ 18 months	17	26
18 to < 24 months	15	23
24 to < 48 months	12	19
48 to < 60 months	10	15

*The mean chronic exposure to HT-2 and T-2 from processed oats in the general diet has been summed with the minimum and maximum exposure from oat drinks. The assumption was made that all oats consumed were processed and had a concentration of 4.72 µg HT-2 & T-2/ kg processed oats. Uses estimated concentration of 0.51 µg T-2 & HT-2/ kg oat drink. Values rounded to 2 s.f.
** One value presented based on a consumption of 200 mL

Background dietary exposure to HT-2 and T-2 in the general diet

15. HT-2 and T-2 mycotoxins are not exclusively found in oats. For example, these mycotoxins also occur in bread, pasta, and breakfast cereals. EFSA (2017) have collated occurrence data from various foodstuffs across Europe and estimated total exposure to HT-2 and T-2 mycotoxins in the general diet (which includes dairy products, processed oats and possibly oat drinks). It was possible to distinguish the

UK data from this EFSA dataset: for infants (<12 months old) HT-2 exposure values were 11-34 (mean LB-UB), and 33-79 ng/kg b.w. per day (95th percentile LB-UB), and T-2 exposure values were 4.3-24 (mean LB-UB), and 12-54 ng/kg b.w. per day (95th percentile LB-UB); for toddlers (≥12 months to < 36 months) HT-2 exposure values were 14-49 (mean LB-UB), and 34-91 ng/kg b.w. per day (95th percentile LB-UB), and T-2 exposure values were 6.8-34 (mean LB-UB), and 14-64 ng/kg b.w. per day (95th percentile LB-UB); for other children (≥36 months to < 10 years old) HT-2 exposure values were 12-42 (mean LB-UB), and 26-71 ng/kg b.w. per day (95th percentile LB-UB), and T-2 exposure values were 6.1-31 (mean LB-UB), and 12-50 ng/kg b.w. per day (95th percentile LB-UB). However, these national estimates may overestimate the background diet exposure of UK children following a plant-based diet, or those avoiding dairy because it considers dairy products which they are unlikely to consume and oats (possibly including oat drinks) which have been considered separately here.

Risk characterisation for T-2 and HT-2

16. Estimated exposure to the sum of HT and HT2 from chronic consumption of oat drinks ranged from 42-70 % (minimum range) to 65-120 % (maximum range) of the TDI across the age groups for 6 to 60-month olds in the UK (COT, 2020).

17. Estimated exposure to the sum of HT and HT2 from consumption of processed oats in the UK general diet ranged from 9.5 to 14 % of the TDI across the age groups for 6 to 60-month olds (COT, 2020).

18. Estimated exposure to the sum of HT and HT2 from consumption of processed oats in the UK general diet and oat drinks combined ranged from 50-120 % (minimum range) to 75-130 % (maximum range) of the TDI across the age groups for 6 to 60-month olds (COT, 2020).

19. Chronic health risks were calculated from UK dietary exposures to T-2 and HT-2 toxins in the general diet of young children taken from EFSA (2017). For infants (<12 months old) HT-2 exposure values were 56-170 (mean LB-UB), and 160-400 % of TDI (95th percentile LB-UB), and T-2 exposure values were 21-120 (mean LB-UB), and 61-270% of TDI (95th percentile LB-UB). For toddlers (≥12 months to < 36 months) HT-2 exposure values were 72-240 (mean LB-UB), and 170-450 % of TDI (95th percentile LB-UB), and T-2 exposure values were 34-170 (mean LB-UB), and 70-320 % of TDI (95th percentile LB-UB). For other children (≥36 months to < 10 years old) HT-2 exposure values were 59-210 (mean LB-UB), and 130-360 % of TDI (95th percentile LB-UB), and T-2 exposure values were 31-150 (mean LB-UB), and 59-250 % of TDI (95th percentile LB-UB). These data take into account exposure to HT-2 and T-2 from processed oats in the general diet in addition to other major dietary sources. In their exposure assessment, EFSA noted that foods within the ‘Grains and Grain-based products’ category had the highest levels of the sum of HT-2 and T-2 mycotoxins, specifically ‘Grains for human consumption’ and ‘Breakfast cereals’, and in particular oat-containing commodities within these groups (EFSA,

2017). However, it can be seen that a substantial amount of 'left-censored' data is included in their assessment, leading to some overestimation of the upper-bound estimates of exposure. In addition, these age groups do not align fully with those used in the exposure assessments performed for this paper and, the consumption and occurrence data are from multiple European sources including the UK. Furthermore, the EFSA exposure assessment included dairy products so therefore did not consider children on plant-based diets or those avoiding dairy for various reasons, and it may also include oat drinks. Therefore, these figures would be expected to be lower for the background diet of children following a plant-based or dairy-free diet in the UK.

Toxicity of OTA

20. An opinion on OTA was published by the EFSA panel on contaminants in the food chain (CONTAM) in 2020. In this opinion, it was concluded that OTA is genotoxic both *in vitro* and *in vivo*, though the mechanisms of genotoxicity are unclear (EFSA, 2020). Direct and indirect genotoxic and non-genotoxic modes of action might each contribute to tumour formation. Since recent studies have raised uncertainty regarding the mode of action for kidney carcinogenicity, EFSA (2020) concluded that it was inappropriate to establish a health-based guidance value (HBGV) and agreed to apply a margin of exposure (MOE) approach.

21. For the characterisation of non-neoplastic effects, EFSA (2020) used a BMDL10 of 4.73 µg/kg bw/day (calculated from kidney lesions observed in pigs). For characterisation of neoplastic effects, EFSA (2020) used a BMDL10 of 14.5 µg/kg bw/day (calculated from kidney tumours seen in rats). In this paper, both of these BMDLs are used, separately, to calculate margins of exposure (MOEs) to assess the health risk of exposure to OTA.

22. For neoplastic effects, an MOE of ≥10,000 would indicate low concern. This MOE was derived following EFSA guidance for substances that are both genotoxic and carcinogenic. The opinion states that "In the interpretation of the MOE for the neoplastic risks, the CONTAM panel considered that the MOE of 10,000 for substances that are genotoxic and carcinogenic could be particularly conservative in this case because the evidence for a direct interaction of OTA with the DNA is inconclusive." For characterisation of chronic non-neoplastic effects, an MOE of ≥ 200 was considered as being of low health concern. This MOE was derived by applying a default uncertainty factor (UF) of 100 for intra- and interspecies toxicokinetic and toxicodynamic differences combined with an additional UF of 2 to account for extrapolation of a 3-month study in pigs to a chronic situation in that species (EFSA, 2020).

Occurrence data of OTA

23. Oat drink consumed in the UK is made from European-harvested oats. Therefore, occurrence data of OTA in oats were taken from JECFA's database which comprises of samples of unprocessed oats taken from across the European Union. JECFA (2001) have reported maximum concentrations of OTA measured in processed oats intended for human consumption across European countries which ranges from 0.05 - 56.6 µg/kg. The value of 56.6 µg/kg has been used because it is considered more representative and was found in 'oat kernels' which have been 'de-hulled'. This was the maximum value for these 'oat kernels' and has been used to give an estimate of worst-case scenario in the exposure assessment.

24. To produce one litre of oat drink, 108 grams of processed oats are required (paragraph 6). Thus, the estimated concentration of OTA in oat drink is 6.11 µg/ kg oat drink (COT, 2020).

Exposure to OTA

Exposure to OTA from oat drinks in the UK

25. To estimate UK infant and young children exposures to OTA from oat drink consumption, the estimated concentration of 6.11 µg OTA/ kg oat drink from occurrence data in European-harvested oats was used (see paragraph 24). This estimated concentration was derived from the maximum concentration value and has been used to give an estimate of worst-case scenario in the exposure assessment.

26. There was no representative consumption data for oat drinks from the DNSIYC survey (DH, 2013; Lennox *et al*., 2013; for infants aged 3 ≤ 18 months) and the NDNS survey (Bates *et al.,* 2014; Bates *et al*., 2016; Roberts *et al.,* 2018; for ages >18 months). Therefore, in this chronic exposure assessment, consumption assumptions for soya drink are used as a proxy for oat drink (Table 5).

Table 5: Estimated chronic exposure to OTA from consumption of oat drink for 6 to 60-month olds in the UK **(ng/kg b.w./day)****

Age group	Minimum*	Maximum*
6 to < 12 months	130	---
12 to ≤ 18 months	170	280
18 to < 24 months	150	250
24 to < 48 months	120	200
48 to < 60 months	100	170

* Uses soya drink consumption rates (minimum & maximum) from a review of recommendations derived from the First Steps Nutrition Trust, Vegan Society and Public Health England as a proxy for oat drink consumption. Values rounded to 2 s.f.
** Uses estimated concentration of 6.11 µg OTA/ kg oat drink. Does not consider exposure to OTA from other food sources.

27. The 2020 EFSA risk assessment of OTA in food states that using the HBGV is not suitable and proposed an approach using the MOE approach (EFSA, 2020).

Therefore, calculations for the amount of oat drink required to exceed the HBGV could not be calculated for OTA.

Dietary exposure to OTA from processed oats in the general diet in the UK

28. For this exposure assessment for 6 to 60-month olds, consumption data from the DNSIYC survey (DH, 2013; Lennox *et al.,* 2013; for infants aged 3 <18 months) and the NDNS survey (Bates *et al.,* 2014; Bates *et al.,* 2016; Roberts *et al*., 2018; for ages >18 months) were used. An estimated concentration of 56.6 µg OTA/ kg processed oats was used (see paragraph 23). Acute exposures ranged from 49 to 73 (mean) and 130-240 ng/kg bw/day (97.5th percentile) across the age groups. Chronic exposure estimates ranged from 23 to 34 (mean) and 69-140 ng/kg bw/day (97.5th percentile) across the age groups (COT, 2020).

Exposure to OTA from oat drinks and processed oats in the general diet (combined) in the UK

Table 6: Estimates of chronic exposure to OTA from consumption of oat drinks and processed oats in the general diet combined for 6 to 60-month olds in the UK (**ng/kg b.w./day**)*

Age group	**Minimum**	**Maximum**
6 to < 12 months	160	--**
12 to ≤ 18 months	200	310
18 to < 24 months	180	280
24 to < 48 months	150	230
48 to < 60 months	120	190

*The mean chronic exposure to DON from processed oats in the general diet has been summed with the minimum and maximum exposure from oat drinks. The assumption was made that all oats consumed were processed and had a concentration of 56.6 µg OTA/ kg processed oats. Uses estimated concentration of 6.11 µg OTA/ kg oat drink. Values rounded to 2 s.f.
** One value presented based on a consumption of 200 mL

Background dietary exposure to OTA in the general diet

29. OTA is not exclusively found in oats. For example, these mycotoxins also occur in other grains. EFSA (2020) have collated occurrence data from various foodstuffs across Europe and estimated total chronic exposure to OTA in the general diet (which includes dairy products, processed oats and possibly oat drinks). It was possible to distinguish the UK data from this EFSA dataset, and these UK data are presented in Table 7. These estimates may overestimate background diet exposure of UK children following a plant-based diet, or those avoiding dairy because it considers dairy products which they are unlikely to consume.

Table 7: Summary statistics of the chronic dietary exposure to OTA in the general diet for young children in the UK (EFSA, 2020) (**ng/kg b.w. per day**)*

Age group**		**Mean dietary exposure**	**95th percentile diary exposure**
Infants (<12 months old)	**LB**	1.9	6.1
Infants (<12 months old)	**UB**	6.2	14

Toddlers (≥12 months to < 18 months	**LB**	4.5	10
Toddlers (≥12 months to < 18 months	**UB**	11	20
Toddlers (≥18 months to < 36 months	**LB**	5.4	10
Toddlers (≥18 months to < 36 months	**UB**	12	21
Other children (≥36 months to < 10 years old)	**LB**	4.8	9.3
Other children (≥36 months to < 10 years old)	**UB**	10.8	19

Risk characterisation for OTA

30. Chronic health risks were assessed based on estimated chronic dietary exposures to OTA in the general diet for young children in the UK that were taken from EFSA (2020). These health risks are expressed as margins of exposure (MOE). Using a BMDL10 of 4.73 µg/kg bw/day, the MOEs ranged from 390-760 (range of minimum) to 880-2500 (range of maximum) across the age groups. Using a BMDL10 of 14.5 µg/kg bw/day, the MOEs ranged from 1200-2300 (range of minimum) to 2700-7600 (range of maximum) across the age groups (COT, 2020).

31. Chronic health risks were assessed based on consumption of oat drink for 6 to 60-month olds in the UK and expressed as MOEs. Using a BMDL10 of 4.73 µg/kg bw/day, the MOEs ranged from 19-36 (range of minimum) to 28-47 (range of maximum) across the age groups. Using a BMDL10 of 14.5 µg/kg bw/day, the MOEs ranged from 52-112 (range of minimum) to 85-145 (range of maximum) across the age groups (COT, 2020).

32. Chronic health risks were assessed based on estimated exposure to OTA from consumption of processed oats in the general diet for 6 to 60-month olds in the UK and expressed as MOEs. Using a BMDL10 of 4.73 µg/kg bw/day, the MOE ranged from 34-69 (range of minimum) to 140-210 (range of maximum) across the age groups. Using a BMDL10 of 14.5 µg/kg bw/day, the MOE ranged from 100-210 (range of minimum) to 430-630 (range of maximum) across the age groups (COT, 2020).

33. Chronic health risks were calculated from estimated exposure to OTA from consumption of oat drinks and processed oats in the general diet combined for 6 to 60-month olds in the UK and expressed as MOEs. Using a BMDL10 of 4.73 µg/kg bw/day, the MOEs ranged from 15-30 (range of minimum) to 24-39 (range of

maximum) across the age groups. Using a BMDL10 of 14.5 µg/kg bw/day, the MOEs ranged from 47-90 (range of minimum) to 73-120 (range of maximum) across the age groups (COT, 2020).

Toxicity of DON

34. A group TDI for the sum of DON, 3-Ac-DON, 15-Ac-DON and DON-3-glucoside of 1 µg/kg bw/day has been used by EFSA (2017b). This group TDI is based on reduced bodyweight gain in mice. The CONTAM Panel identified vomiting as critical acute effect in humans. To assess acute human health risk, epidemiological data from mycotoxicoses were assessed and a group-ARfD of 8 µg/kg bw per eating occasion was calculated (EFSA, 2017b). In 2020, the health risks from exposure to DON in the diets of infants and young children aged 0-5 years old, as part of the Addendum to the Overarching Statement on the potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years (COT, 2020).

Occurrence data of DON

Estimation of DON concentration in oat drink

35. Oat drink consumed in the UK is made from European-harvested oats. Therefore, occurrence data of DON in oats were taken from EFSA's database which comprises of samples of unprocessed oats taken from across the European Union. EFSA (2013) have reported the mean concentration of DON in oat grains intended for human consumption across European countries as being 209 µg/kg (n = 203).

36. Using a concentration of 209 µg/ kg for DON in unprocessed oats, and a mean concentration reduction of 88.2 % after de-hulling as reported by Scudamore *et al.* (2007), 24.66 µg of DON would be expected to remain in 1 kg of groats after cleaning and de-hulling. Assuming that 108 grams of processed oats are required to produce 1L of drink (paragraph 6), the estimated concentration in oat drink is 2.66 µg of DON / kg oat drink (COT, 2020).

Exposure to DON

Exposure to DON from oat drinks in the UK

37. To estimate UK infant and young children exposures to DON from oat drink consumption, the estimated concentration of 2.66 µg DON/ kg oat drink from occurrence data in European-harvested oats was used (see paragraph 36).

38. There were no representative consumption data for oat drinks from the DNSIYC survey (DH, 2013; Lennox et al., 2013; for infants aged 3 ≤ 18 months) and the NDNS survey (Bates et al., 2014; Bates et al., 2016; Roberts et al., 2018; for ages >18 months). Therefore, in this chronic exposure assessment, consumption assumptions for soya drink are used as a proxy for oat drink (Table 8).

Table 8: Estimated chronic exposure to DON from consumption of oat drink for 6 to 60-month olds in the UK **(ng/kg b.w./day)****

Age group	Minimum*	Maximum*
6 to < 12 months	58	---
12 to ≤ 18 months	73	120
18 to < 24 months	66	110
24 to < 48 months	53	88
48 to < 60 months	43	72

* Uses soya drink consumption rates (minimum & maximum) from a review of recommendations derived from the First Steps Nutrition Trust, Vegan Society and Public Health England as a proxy for oat drink consumption. Values rounded to 2 s.f.
** Uses estimated concentration of 2.66 µg DON/ kg oat drink. Does not consider exposure to DON from other food sources.

Amount of oat drink required to exceed HBGV for DON

39. The amount of oat drink one would need to consume to approach the TDI and ARfD was estimated (Table 9). This calculation does not take into account background dietary exposure to DON. Although EFSA (2017) have reported background dietary exposure levels to DON, these data were not used because 1) their assessment is for the general diet (which includes dairy products, processed oats and possibly oat drinks) and thus does not consider children following a plant-based diet or those avoiding dairy, and 2) the age groups reported by EFSA are not aligned with the age groups reported in Table 9.

Table 9: Estimated quantity of oat drink required to exceed the HBGV for DON for 6 to 60-month olds in the UK **(L)***

Age group	ARfD	TDI
6 to < 12 months	28	3.5
12 to ≤ 18 months	33	4.1
18 to < 24 months	36	4.5
24 to < 48 months	46	5.7
48 to < 60 months	55	6.9

* Uses soya drink consumption rates (minimum & maximum) from a review of recommendations derived from the First Steps Nutrition Trust, Vegan Society and Public Health England as a proxy for oat drink consumption. Uses estimated concentration of 2.66 µg DON/ kg oat drink. Does not consider exposure to DON from other food sources. Values rounded to 2 s.f.

Dietary exposure to DON from processed oats in the general diet in the UK

40. For this exposure assessment for 6 to 60-month olds, consumption data from the DNSIYC survey (DH, 2013; Lennox *et al.,* 2013; for infants aged 3 <18 months) and the NDNS survey (Bates *et al.,* 2014; Bates *et al.,* 2016; Roberts *et al*., 2018; for ages >18 months) were used. An estimated concentration of 24.66 µg DON/ kg processed oats was used (see paragraph 36).

41. In the Addendum to the Overarching statement on the potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years (COT, 2020), the acute and chronic exposures were calculated using data from the TDS; measurements were performed for DON, 3-AC-DON and 15-AC-DON, no measurements were available for 3-DON-glycoside. 3-Ac-DON and 15-Ac-DON were not detected in any samples above the limit of detection (LOD). A combined concentration for the sum of 15-Ac-DON, 3-Ac-DON and DON was not provided to the FSA as part of the TDS, thus the sum used in the exposure assessment was estimated by summing the individual concentrations of all three forms.

42. Estimated acute exposures to DON from consumption of processed oats in the general diet for 6 to 60-month olds in the UK ranged from 21-32 ng/kg bw/day (mean) and 56-100 ng/kg bw/day (95.5th percentile) across the age groups (COT, 2020). Estimated chronic exposures to DON from consumption of processed oats in the general diet for 6 to 60-month olds in the UK ranged from 10-15 ng/kg bw/day (mean) and 30-60 ng/kg bw/day (95.5th percentile) across the age groups (COT, 2020).

43. Estimated acute exposures to DON from oat drinks and processed oats in the general diet (combined) in the UK ranged from 53-88 ng/kg bw/day (minimum) and 82-140 ng/kg bw/day (maximum) across the age groups (COT, 2020).

Background dietary exposure to DON in the general diet

44. DON is not exclusively found in oats. For example, these mycotoxins also occur in other grains. EFSA (2017) have collated occurrence data from various foodstuffs across Europe and estimated total acute exposure to DON in the general diet (which includes dairy products, processed oats and possibly oat drinks). It was possible to distinguish the UK data from this EFSA dataset. These estimates may overestimate background diet exposure of UK children following a plant-based diet, or those avoiding dairy because it considers dairy products which they are unlikely to consume and oats (possibly including oat drinks) which have been considered separately here. Estimated chronic dietary exposures to DON in the general diet for young children in the UK were taken from EFSA (2017). For infants (<12 months old), exposures ranged from 100-700 (LB-UB, mean) and 1000-2200 ng/kg b.w. per day (LB-UB, 95th percentile). For toddlers (≥12 months < 36 months), exposures ranged from 800-1600 (LB-UB, mean) and 1500-2700 ng/kg b.w. per day (LB-UB, 95th percentile). For other children (≥36 months to < 10 years old), exposures ranged from 800-1300 (LB-UB, mean) and 1300-2200 ng/kg b.w. per day (LB-UB, 95th percentile). COT (2020).

Risk characterisation for DON

45. The chronic health risks were assessed based on estimated exposure to DON from consumption of oat drink for 6 to 60-month olds in the UK. These health risks were 4.3-7.3 (range of minimum) to 7.2-12 % of TDI (range of maximum) across the age groups (COT, 2020).

46. The chronic health risks were assessed based on estimated exposure to DON from consumption of processed oats in the general diet for 6 to 60-month olds in the UK. These health risks were 1.0-1.5 (mean) to 3.0-6.0 % of TDI (97.5th percentile) across the age groups (COT, 2020).

47. The chronic health risks were assessed based on estimated exposure to DON from consumption of oat drinks and processed oats in the general diet combined for 6 to 60-month olds in the UK. These health risks were 5.3-8.8 (minimum) to 8.2-14 % of TDI (maximum) across the age groups (COT, 2020).

48. The chronic health risks were assessed based on UK dietary exposures to DON in the general diet for young children in the UK (data taken from EFSA, 2017). For infants (<12 months old), exposures were 40-110 (LB-UB, mean) and 100-220 (LB-UB, 95th percentile) % of the TDI. For toddlers (≥12 months to < 36 months), exposures were 80-160 (LB-UB, mean) and 150-270 (LB-UB, 95th percentile) % of the TDI. For other children (≥36 months to < 10 years old), exposures were 80-130 (LB-UB, mean) and 130-220 (LB-UB, 95th percentile) % of the TDI.

Conclusions

49. The exposure estimates for these mycotoxins are considered be generally conservative for children on a plant-based or dairy-free diet as consumption of oat drinks is likely to be lower for all age groups as, based on the existing advice from the Vegan society, First Steps Nutrition Trust and PHE, soya is the main recommended alternative drink to replace cow's milk. For children who are not following plant-based or dairy free diets, cow's milk is the main recommended milk drink. Therefore, all age groups are likely to be consuming less oat drink than estimated here. However, a small number of children exclusively consuming oat drinks in place of cow's milk cannot be excluded.

50. In terms of acute exposure to DON and the sum of HT-2 and T-2, large amounts of oat drink are required to exceed their ARfDs, thus acute exposure to Don, and sum of HT-2 and T-2 from consumption of oat drink was considered to be of low risk.

51. It was concluded there was no chronic health concern in respect of HT-2/T2 exposure, as intakes are below the TDI (except for 12-24-month olds, in whom exceedance of the TDI was only minor and the exposure estimates used were conservative). The TDI sets safe limits for exposures over a lifetime, and these minor exceedances will be transient with exposure per kg bw decreasing as these children grow up. Furthermore, there are several limitations of the risk calculations using EFSA's background dietary exposure assessment. The background diet includes dairy and oats and thus their estimated exposure to HT-2 and T2 may therefore be an overestimation for children following a plant based or dairy free diet. Although this is not UK data alone, it nevertheless provides an estimation of exposure to these mycotoxins from the total diet versus a high consumer of oat drinks. In 2018, the COT has previously assessed HT-2 and T-2 in in the diet of infants aged 0 to 12 months and children aged 1 to 5 years, and the Committee concluded here that it is unlikely that chronic dietary exposure levels of T-2 and HT-2 would be of any toxicological concern in infants and young children (COT, 2018).

52. Mean and 97.5th percentile acute exposures to 15-Ac-DON, 3-Ac-DON and DON and the sum of all three forms were below the group ARfD of 8.0 µg/kg bw, for all age groups and are therefore not of toxicological concern for infants and young children aged 0 to 5 years old. All mean and 97.5th percentile chronic exposures to the sum of all three forms were below the TDI of 1.0 µg/kg bw for all age groups, except the 97.5th percentile UB exposure in children > 12 months of age, which were at or up to 1.3-fold the TDI. This was considered unlikely to be of toxicological concern. It was noted that the sum of all forms was not based on individual measured values but on summing the respective averages of the concentrations provided. Therefore, exposure estimates might have been conservative (COT, 2020)

53. In respect of OTA, the Committee were unable to conclude whether the exposure estimates indicated a potential health concern. There were many uncertainties in the cancer endpoint used for risk characterisation, and furthermore, it was unclear whether or not OTA was a genotoxic carcinogen, and thus which MOE

threshold value would be applicable. Some age groups had MOEs lower than desirable for non-neoplastic effects while all age groups had MOEs lower than that considered of low concern for a genotoxic carcinogen.

54. Information on consumption is not currently available for young children who may be consuming a mixture of different plant-based drinks. Therefore, the current approach, which assumes that consumption was exclusively of a single plant-based drink, was most appropriate as young children are likely to develop a preference for one drink. It was noted that there are plans to obtain more consumption data for children who follow a dairy-free diet, as these diets are becoming more popular.

55. When monitoring the levels of relatively potent genotoxic carcinogens, measured levels are often below the LOD resulting in conservative estimations of exposure and preventing any assurance of low concern. Ideally there needs to be studies of at a least a few representative samples using a sufficiently reliable analytical method to determine the actual occurrence levels of these contaminants present in the UK diet.

56. Although this exposure assessment is for young children, it should be extended to adults, as there may be health risks for the general population. The exposure estimates make the best use of the available data but include a lot of assumptions relating to the use of soya milk consumption data and the concentrations in oat drink. Therefore, the MOEs should be interpreted with these uncertainties in mind. For example, the maximum reported concentration of OTA in “oat kernels” (i.e. groats) was used, however reported exposures ranged from 0.05 - 56.6 µg/kg for processed oats ready for human consumption. Furthermore, it is unclear whether further processing during oat drink manufacturing could further reduce OTA levels.

57. The intake assumptions for oat drinks are based on recommendations on soya, which is indicated as the preferable dairy milk alternative. It is therefore likely that the consumption could be lower than assumed and may occur in combination with other, more nutritious alternatives, such as soya milk. It is thus likely that exposures would be much lower, and any potential exceedances will be occasional and of very short duration. It should also be noted that based on EFSA’s recent evaluation, for neoplastic effects the MOEs are lower than 10,000 across most age groups. The MOE of 10,000 for substances that are directly genotoxic and carcinogenic may not be appropriate in this case because the evidence for a direct interaction of OTA with the DNA is inconclusive. The uncertainty in the assessment is high and it is likely that the risk is being overestimated.

Secretariat

July 2020

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

Glossary

ARfD – Acute reference dose

BMDL10 – benchmark dose level

b.w. – bodyweight

DNSIYC - diet and nutrition survey of infants and young children

DON – deoxynivalenol

HBGV – health-based guidance value

Kg - kilogram

LB – lower bound

LOD – limit of detection

MOE – margin of exposure

NDNS – National Diet and Nutrition Survey

OTA – ochratoxin A

TDI – tolerable daily intake

UB – upper bound

UF – uncertainty factor

References

Bates B., Cox L., Nicholson S., et al. (2016) National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 – 2013/2014) Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/551352/NDNS_Y5_6_UK_Main_Text.pdf

Bates B., Lennox A., Prentice A., *et al.* (2014) National Diet and Nutrition Survey Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012) Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/310995/NDNS_Y1_to_4_UK_report.pdf

COT (2018) COT statement of T-2 toxin (T2), HT-2 toxin (HT2) and neosolaniol (NEO) in the diet of infants aged 0 to 12 months and children aged 1 to 5 years. Available at: https://cot.food.gov.uk/committee/committee-on-toxicity/cotstatements/cotstatementsyrs/cot-statements-2018/cot-statement-of-t-2-toxin-t2-ht-2-toxin-ht2-and-neosolaniol-neo-in-the-diet-of-infants-aged-0-to-12-months-and-children-aged-1-to-5-years

COT (2020) Discussion paper on the health risk of mycotoxin contamination in oat drinks for children aged 6 months to 5 years of age. Available at: https://cot.food.gov.uk/sites/default/files/tox202003oatdrinks.pdf

DH (2013). Diet and Nutrition Survey of Infants and Young Children (DNSIYC), 2011. Available at: http://transparency.dh.gov.uk/2013/03/13/dnsiyc-2011/

EFSA (2011) Scientific Opinion on the risks for animal and public health related to the presence of T-2 and HT-2 toxin in food and feed. *EFSA Journal* 9(12): 2481 Available at: https://www.efsa.europa.eu/en/efsajournal/pub/2481

EFSA (2013) Deoxynivalenol in food and feed: occurrence and exposure. *EFSA Journal* 11(10):3379 Available at: https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/j.efsa.2013.3379

EFSA (2017) Human and animal dietary exposure to T-2 and HT-2 toxin.doi: 10.2903/j.efsa.2017.4972 Available at: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4972

EFSA (2017b) Risks to human and animal health related to the presence of deoxynivalenol and its acetylated and modified forms in food and feed. *EFSA Journal* **15(9)**:4718 Available at: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4718

EFSA (2020) Risk assessment of ochratoxin A in food. *EFSA Journal* **18(5)**:6113 Available at: https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2020.6113

First Steps Nutrition Trust (2018): *Good food choices and portion sizes for 1-4 years olds*, First Steps Nutrition Trust, Available online at: https://www.firststepsnutrition.org/

JECFA (2001) WHO Food Additives Series: 47 Safety evaluation of certain mycotoxins in food. Appendix A (p. 393). Available at: http://www.fao.org/3/a-bc528e.pdf

PHE (2017): Example menus for early years settings in England. Available at: https://www.gov.uk/government/publications/example-menus-for-early-years-settings-in-england

Rahman S., Sharma A.K., Singh N.D., *et al.* (2014). Clinico-haematological changes in T-2 toxicosis in Wistar rats. *Indian Journal of Veterinary Pathology* **38:** 22-28

Roberts C., Steer T., Maplethorpe N., *et al.* (2018) National Diet and Nutrition Survey Results from Years 7 and 8 (combined) of the Rolling Programme (2014/2015 – 2015/2016) Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/699241/NDNS_results_years_7_and_8.pdf

Schwake-Anduschus C., Langenkämper G., Unbehend G., *et al.* (2010) Occurrence of Fusarium T-2 and HT-2 toxins in oats from cultivar studies in Germany and degradation of the toxins during grain cleaning treatment and food processing. *Food Additives and Contaminants. Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment* **27:** 1253-1260

Scudamore K.A., Baillie H., Patel S., et al. (2007) Occurrence and fate of Fusarium mycotoxins during commercial processing of oats in the UK. *Food Additives & Contaminants* **24:** 1374-1385

Vegan Society (2017):A Nutrition Gide for vegans under five years old. Available at: https://www.vegansociety.com/sites/default/files/uploads/downloads/Under-fives%20PDF%202_0.pdf

Vegan Society(2016): Tips for vegan children:' Dietitian Heather Russell provides a kids' meal plan as well as fun ways to introduce the great fruit and vegetable adventure to young children', 18 November. Available at: https://www.vegansociety.com/whats-new/blog/food-tips-vegan-children#:~:text=Beans%2C%20chickpeas%2C%20lentils%2C%20tofu,are%20rich%20in%20vitamin%20C.

Wu W., Zhou H., Bursian S.J., *et al.* (2016). Emetic responses to T-2 toxin, HT-2 toxin and emetine correspond to plasma elevations of peptide YY3-36 and 5-hydroxytryptamine. *Archives of Toxicology* **90:** 997-1007

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

Annex C to TOX/2020/XX

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft statement on the potential risks from almond drink consumption in children aged 6 months to 5 years of age.

1. The first draft statement on almond drink consumption in children aged 6 months is attached for Members' comments. The conclusions are laid out in paragraphs 30 to 37.

Questions for the Committee:

i) Do the Committee have any comments on the structure and content of the first draft statement?

Secretariat

September 2020

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

First draft statement on the potential risks from almond drink consumption in children aged 6 months to 5 years of age.

Background

1. The Department of Health and Social Care (DHSC), Public Health England (PHE) and the Food Standards Agency (FSA) are receiving an increasing number of enquiries regarding the use of plant-based drinks in the diets of infants and young children. Therefore, we are asking the COT to consider the potential health effects of almond drinks in the diets of these age groups.

2. Currently the UK government advises that parents should only use infant formula as an alternative to breast milk in the first 12 months of a baby's life. It is also advised that whole cows' milk and unsweetened calcium-fortified milk alternatives, such as soya, almond and oat drinks can be given to children from the age of 1 as a part of a healthy, balanced diet (NHS, 2018)

3. The Committee considered a discussion paper on the potential risks from almond drink consumption in children aged 6 months to 5 years of age in March 2020.[5] With additional data being considered in July 2020[6]. The potential risks identified were the potential presence of cyanogenic glycosides and aflatoxin B1

Occurrence data

Cyanogenic glycosides

4. Eleven drinks containing raw vegetables and fruit, flax seeds, whole apples with seeds, raw almond drink and pasteurised almond drink were analysed for total cyanide. Total cyanide levels of 9.6, 41,134 and 272 µg/L were detected in smoothies containing almond. The two smoothies with the highest levels also contained flaxseed which is also high in cyanide-containing molecules (Baker et al, 2018).

5. There is a lack of data for total cyanide in almond drinks alone. Therefore, occurrence data of total cyanide in sweet and bitter almonds were taken from EFSA's database which comprises of analytical samples from across the European Union (Table 1).

Table 1. Total cyanide concentration of almonds (µg/kg)*

[5] https://cot.food.gov.uk/sites/default/files/tox202017almonddrinksseconddraft.pdf
[6] https://cot.food.gov.uk/sites/default/files/tox202033overarchingdiscussionpaper.pdf

Food commodity	Number of samples	Mean LB	Mean UB
Sweet almond	35	4500	4500
Bitter almond	3	1437000	1437000

LB: lower bound; UB: upper bound. EFSA 2019.
*Converted from mg/kg to µg/kg

Aflatoxin B1

6. Harmonised maximum levels for aflatoxins have been in place in the European Union (EU) since January 1999 and included in the Annex, Section 2 of Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for contaminants in food stuffs (EFSA, 2007). EU Maximum levels for aflatoxins have been set for almonds that are used for direct human consumption or for use as an ingredient in food. The levels are currently set at 8 µg/kg/AFB1 (almonds ready to eat) and 12 µg/kg/AFB1 (almonds for further processing) (Official Journal of the European Union, 2006). In the case of genotoxic carcinogens such as aflatoxins maximum levels should be set at a level which is as low as reasonably achieved.

7. In 2007, the scientific panel on contaminants in the food chain received a request from the Commission related to the potential increase of consumer health risk by possible increase of the existing maximum levels for aflatoxins in almonds, hazelnuts and pistachios and derived products. 40,000 analytical results on occurrence of aflatoxins in various food commodities were considered by the CONTAM Panel. Aflatoxins were not detected in about 75% of the samples tested i.e. if present they were below the limit of detection of the method used, which varied for different sets of data. The CONTAM Panel concluded that changing the maximum levels for total aflatoxins from 4 to 8 or 10 µg/kg in almonds, hazelnuts and pistachios would have negligible effects on the estimates of dietary exposure, cancer risk and the calculated MOEs. There were recommendations made for representative data for nuts and other foodstuffs, with the inclusion of total diet studies, to reduce uncertainties in the risk assessment. Methods should be applied that allow measurement of individual aflatoxins at concentrations well below the regulatory maximum levels (EFSA, 2007).

Cyanogenic glycosides

8. Cyanogenic glycosides in bitter apricot kernels were previously reviewed by COT in 2006 where a nominal acute reference dose of 5 µg/kg was established. More recently, cyanogenic glycosides in raw apricot kernels. were reviewed by EFSA (EFSA, 2016). An acute reference dose (ARfD) of 20 µg/kg body weight was established for cyanide. In the most recent EFSA opinion (EFSA, 2019), the panel concluded that the ARfD of 20 µg/kg body weight is applicable for acute effects of cyanide regardless the dietary source.

9. Once the almond is macerated, the cyanogenic glycosides interact

with ß-glucosidase. This enzyme hydrolyses the cyanogenic glycosides and can yield hydrogen cyanide, benzaldehyde, glucose and ketones (Haque, 2002). The quantity of intact cyanogenic glycoside present in almond drinks is unknown.

10. Exposure to large amounts of cyanide can lead to convulsions, loss of consciousness, dizziness, weakness, mental confusion and heart failure (Burns *et al*, 2012). The Committee had previously agreed that if only sweet almonds were used in the preparation of almond drinks, then there would be no health concern. However, Members had agreed that more information on the likelihood of bitter almond contamination of almond drinks and what precautions were taken by manufacturers to prevent their entry to the supply chain should be investigated.

11. Bitter almonds are not used in almond drinks because of the flavour profile. Most manufacturers do not want a flavour profile which differs significantly from dairy– the use of bitter almonds would impart an excessively almond-flavoured product which would more resemble marzipan in taste than milk. It should be noted that only sweet varieties of almonds are produced in Californian commercial orchards, a major supplier of almonds to Europe[7]. Additionally, information provided by an almond drink manufacturer has also confirmed that only sweet almonds are used in their drinks.[8]

Exposure assessment for cyanogenic glycosides

12. The sweet almond mean upper bound and lower bound concentration of 4500 µg/kg (EFSA, 2019) was used to estimate the amount of cyanide that could be present in 1 litre of almond drink assuming 6% (w/w) almond nuts in the drink. The value of 270 µg/kg was calculated. A similar value has not been calculated for bitter almonds as almond drink is highly unlikely to be made from this type of almond. The value of 6% has been assumed because information publicly available for almond drinks indicates a range from 1% to 6% almond content.

13. Due to the limited information on the consumption of almond drinks by these age groups, the chronic exposure estimates for cyanide exposure in children between 6 months and 5 years of age were originally calculated assuming that all milk was replaced with almond-based alternatives. To refine these exposures several sources of information were considered; British Nutrition Foundation (2019), the First Steps Nutrition Trust Eating Well: vegan infants and under 5s (2020), Vegan Society Food tips for vegan children (2017) and Public Health England's (PHE) published Example menus for Early Years Settings in England (EYS) (2017). The above sources provided guidance for frequency and portion sizes for children under 5 and considering the lack of consumption information for the groups of interest they were deemed the most representative scenarios for the diet of children following dairy-free or plant-based diets. It must be noted that the recommendations from these sources were for soya-alternatives to milk; these have been used in the

[7] Personal communication. Almond Board of California

[8] Personal communication from almond drink company.

absence of representative consumption information for almond drinks. Soya-milk has been recommended due to its similar nutritional value and monetary cost to cow's milk, so these are conservative assumptions but are considered to be a more relevant proxy than cow's milk. Hence, these are conservative assumptions but are considered a more relevant proxy than cow's milk. Additionally, it should be further noted that children under 1 year are not recommended to consume dairy alternatives as their main milk drink, the assumption made here for the 6 – 12 month age group was that up to 200 ml of almond milk may be used in cooking infant foods.

14. Table 2 gives the acute exposure estimates for total cyanide in children between the ages of 6 months and 5 years, with the assumption that all soya milk would be replaced with almond drink in a diet. Potential acute cyanide exposures were calculated using the estimated total cyanide concentration of 4500 µg/kg (sweet almond) combined with the consumption assumptions described in paragraph 16 below.

Table 2: The acute exposure estimates of the total cyanide in children between the ages of 6 months and 5 years, with an assumption that all soya milk would be replaced with almond drink containing 270 µg/kg CN in the diet (µg/kg bw/day*)

Age group (months)	**Acute exposure estimates for sweet almond (270 µg/kg CN)**	
	Minimum	**Maximum**
6 < 12	5.9[9]	--
12 ≤ 18	7.4	12
18 < 24	6.7	11
24 < 48	5.3	8.9
48 < 60	4.4	7.3

*rounded to 2s.f

Aflatoxin B1 (AFB1) in almonds

15. Aflatoxins are produced as a result of fungal contamination with *Aspergillus flavus* and *A. parasiticus* moulds under warm and humid conditions in tree nuts such as almonds. The degree of contamination is dependent on temperature, humidity, soil and storage conditions. AFB1 was identified as a common chemical contaminant of almonds which could be potentially transferred to almond drinks.

16. Aflatoxins have been previously reviewed by the Scientific Committee for Food (SCF) in 1996, the European Food Safety Authority (EFSA) in 2007 and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1998, 2001 (AFM1) and 2018. In the most recent EFSA opinion (EFSA, 2020) the panel considered the chronic endpoint of liver carcinogenicity in a rat performed in a study by Wogan *et al*, 1974 to be the most sensitive and adequate study for dose response modelling.

17. Groups of male Fisher rats were administered diets containing 0, 1, 5, 15, 50,

or 100 µg/kg diet of AFB1 (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 AFB1 into daily intakes assuming that an average adult male rat consumed 40 g diet per kg body 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 AFB1 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 $BMDL_{10}$ was 0.4 µg/kg bw per day.

18. AFB1 is considered to be genotoxic and carcinogenic so its maximum permitted levels set by the EU are set at a level which is based on the "as low as reasonably achievable" (ALARA) principle. The AFB1 maximum levels set by the EU are 8 µg/kg for ready to eat almonds and 12 µg/kg for almonds that require further processing (Official Journal of the European Union, 2006).

19. There are few data on the distribution of AFB1 levels below the maximum level. The Rapid Alert for Food and Feed (RASFF Portal)[10] is a tool that provides information on public health warnings issues by food safety authorities and food companies. It also provides the latest information on food recall notices. Between December 2019 to June 2020, there were two reported incidences whereby levels of AFB1 were detected in almond nuts (from EU member states) according to the RASFF Portal. A RASFF alert notification[11] was raised by the German authority for almonds that had originated from Spain, whereby an AFB1 level of 37.5 µg/kg was reported[12]. In the second incident, a RASFF information notification[13] was raised by the Dutch authority for almonds that had originated from the United States of America, whereby an AFB1 level of 2.9 µg/kg was reported.[14] However, the almond nut industry has programmes and procedures in place to ensure that almond nuts that exceed the set AFB1 EU maximum levels are rejected (Almond board of California, 2016).

[9] One value presented based on a consumption of 200 mL[10] European Commision (2020) – Food and Feed Safety Alerts. Available at: https://ec.europa.eu/food/safety/rasff_en

[11] RASFF Alert: are sent when a food or feed presenting a serious health risk is on the market when rapid action is required.

[12] EC RASFF Portal. Available at: https://webgate.ec.europa.eu/rasff-window/portal/?event=notificationDetail&NOTIF_REFERENCE=2020.1392

[13] RASFF information: are used when a risk has been identified about food or feed places on the market, but the other members do not have to take rapid action.

[14] EC RASFF Portal. Available at: https://webgate.ec.europa.eu/rasff-window/portal/?event=notificationDetail&NOTIF_REFERENCE=2020.1148

20. The almond drink industry has also confirmed that their almond nut suppliers test For aflatoxin levels to ensure that levels comply with the set EU maximum AFB1 levels. The almond drink production starts off with ingredients in reception/storage and water. The whole almonds are shelled, blanched, lightly roasted or unroasted and ground to produce a creamy almond paste. The almond paste is blended in water and other ingredients and nutrients are added to create the almond drinks.[15]

Exposure assessment for aflatoxin

21. An initial exposure assessment was performed using aflatoxin concentrations from the Riba et al paper along with cows' milk consumption as a proxy, i.e. assuming that cows' milk will be replaced with almond milk. On the basis of this assessment, the Committee had agreed that aflatoxin exposure from almond drinks were a potential concern but there were uncertainties. Overall, it was agreed that further work needed to be done to refine the aflatoxin exposure assessment.

22. No relevant data on aflatoxin contamination in almond drink were identified. Some limited data on AFB1 contamination of almonds was available, but this was not sufficiently robust to use for exposure assessment. The aflatoxin B1 maximum levels (MLs) set by the EU of 8 µg/kg for ready to eat almonds and 12 µg/kg for almonds that require further processing (see paragraph 18) were used to estimate the amount of AFB1 that could be present in 1 litre of almond drink assuming 6% (w/w) almond nuts in the drink. On this basis, the values of 0.48 µg/kg and 0.72 µg/kg aflatoxin were calculated using the values for ready to eat almonds and almonds that require further processing respectively.

23. There were very few or no almond milk consumers reported in the NDNS and DNSIYC surveys. Therefore, the exposure assessment for AFB1 also used soya milk recommendations as a proxy with the same assumptions and uncertainties described for cyanogenic glycosides. Table 3 gives the chronic exposure estimates for AFB1 in children between the ages of 6 months to 60 months, with the assumption that soya milk has been replaced with almond drink in the diet of a plant- based child or those that avoid dairy. Potential chronic AFB1 exposures were calculated using the estimated concentrations of 0.48 and 0.72 µg/kg combined with soya milk consumption data for children aged 6 – 60 months, respectively.

[15] Personal communication from an almond drink company

Table 3: Estimated chronic AFB1 exposure of children aged 6 months to 60 months based on an assumption that all soya milk would be replaced with almond drink in diet (excluding infant formula) (using estimated aflatoxin concentrations in almond drink). (µg/kg bw/day)*

Age group (months)	**0.48 µg/kg AFB1 – almonds ready to eat exposure range**	**0.72 µg/kg AFB1 – almonds for further processing exposure range**
6 < 12	0.010	0.016
12 ≤ 18	0.013 – 0.022	0.020 – 0.033
18 < 24	0.012 – 0.020	0.018 – 0.030
24 < 48	0.0095 – 0.016	0.014 – 0.024
48 < 60	0.0078 – 0.013	0.012 – 0.020

*rounded to 2 SF

24. There are very few data available on the levels of contaminants in almond drinks or on their consumption. The exposure assessment for aflatoxin is based on a worst-case scenario as it is assumed that almond drink will be consumed in the same way as soya milk since there are very few almond drink consumers to use in the exposure assessment.

25. The fate of aflatoxins during the processing of contaminated almonds was reported by (Zivoli et al, 2014). Four kg of shelled almonds purchased from a local market in Italy were inoculated with aflatoxin B1 and B2 strains. The blanching and peeling of almonds did not reduce aflatoxin levels. Peeled contaminated almond nuts were roasted for 30 – 120 minutes at 120°C and 150°C, respectively. Roasting and peeling almonds reduced aflatoxin levels by up to 84% as seen in table 4. Based on this data it appears that the roasting of almond nuts during the manufacturing process can further reduce aflatoxin levels.

Table 4. Effect of roasting on AFB1 in contaminated almonds

	Level (µg/kg)	**Mean reduction (%)**
Initial level	5558.7 ±4091.3	
120°C, 30 min	5258.6 ±2708.9	5
120°C, 60 min	2295.4 ±1376.6	58
120°C, 120 min	2571.4 ±458.4	54
150°C, 30 min	2500.4 ±974.8	55
150°C, 60 min	1465.8 ±1006.1	74
150°C, 120 min	907.1 ±611.9	84

Background diet

26. In the most recent EFSA opinion on aflatoxins (EFSA, 2020) the panel calculated the chronic dietary exposures for aflatoxins from a total diet as seen in Table 5. These exposure values give a good estimation on levels of AFB1 exposure that could come from a background diet. However, these age groups do not align fully with those used in the exposure assessments performed for this paper and, the consumption and occurrence data are from multiple European sources including the UK. Furthermore, the EFSA exposure assessment included dairy products so

therefore did not consider plant-based children or those avoiding dairy for various reasons, it may also not include almond drinks. Therefore, we would expect these figures to be lower for the background diet of children following a plant-based or dairy-free diet in the UK.

Table 5: EFSA mean and high chronic exposure to AFB1 (µg/kg bw per day)*

Age group		Minimum	Median	Maximum
Infants (<12 months old)	LB	0.000080	0.00018	0.00060
	UB	0.00058	0.0020	0.0049
Toddlers (≥12 months to < 36 months	LB	0.00043	0.00064	0.0011
	UB	0.0032	0.0054	0.0070
Other children (≥36 months to < 10 years old)	LB	0.00047	0.00076	0.0018
	UB	0.0035	0.0050	0.0061

AFB1: aflatoxin B1; bw: body weight; LB: lower bound;
*Converted from ng/kg/bw/day to µg/kg bw per day and rounded to 2s.f.

Risk characterisation

Cyanogenic glycosides

Acute reference dose (ARfD)

27. In the most recent EFSA opinion (EFSA, 2019) the panel concluded that the ARfD of 20 µg/kg body weight was applicable for the acute effects of cyanide regardless the dietary source. No chronic health-based guidance has been established for cyanide.

28. The estimated acute exposures in table 2 (µg/kg bw/day) were used to calculate the health risks as percentages of the ARfD (20 µg/kg body weight) These percentages are shown below in Table 6. All estimated exposures are below the ARfD.

Table 6: Calculation of acute risk (%) following total cyanide exposure of children aged 6 months to 5 years based on an assumption that all soya milk would be replaced with almond drink containing 270 µg/kg CN in the diet (µg/kg bw/day)

	Sweet almond	
	ARfD (%)*	
Age group (months)	**Minimum**	**Maximum**
6 < 12	29[16]	--
12 ≤18	37	62

18 < 24	33	56
24 < 48	27	44
48 < 60	22	37

[16] One value presented based on a consumption of 200 mL
*rounded to 2 SF

Conclusions

29. There are very few data available on contaminants in almond drinks or on their consumption.

30. The risk assessment for cyanide is based on a worst-case exposure scenario as it is used soya milk recommendations as a proxy that almond drink would be consumed in the same way. Although the use of bitter almonds in almond milk drinks cannot be completely ruled out, based on industry information, it seems highly unlikely that these will be used in the manufacture of these products.

31. Estimates of acute exposure to cyanide assuming sweet almonds were used to make the almond drink do not exceed the ARfD for infants and young children aged 6 months to 60 months.

32. The risk for cyanide is based on a worse-case scenario for sweet almonds used in almond drinks. In practice, bitter almonds would not be deliberately used in almond drinks. However, contamination with bitter kernels or the presence of almond kernels cannot be completely ruled out. However, although data on cross-contamination with bitter almonds are not available, it appears unlikely that it could occur.

33. Almond production includes either the light roasting or non-roasting of whole almonds. Although the roasting of almond nuts could further reduce AFB1 levels, no data on whether roasted or unroasted almonds are used has been provided by industry to indicate whether AFB1 levels are potentially lower in almond drinks. Almond drinks may also contain a lower quantity of almonds than the 6% estimated here suggesting that AFB1 levels may also be lower than estimated.

34. The exposure assessment for AFB1 assumes a high level of AFB1 as the EU maximum permitted levels were used. The exposure assessment uses a conservative approach as it uses AFB1 MLs (almond nuts) and the nutritional recommendations that are made for soya milk. AFB1 is considered to be a genotoxic carcinogen so the MLs set by the EU are set at a level that is “as low as reasonable possible”. When 40,000 analytical results on the occurrence of aflatoxins in various food commodities were considered by the EFSA Panel in 2007, aflatoxins were not detected in 75% of the samples tested so it is likely that the actual levels in almonds and estimated in almond drinks will be lower than the set MLs. However, RASSF

data shows that the MRL can also be exceeded on occasion. Actual data on AFB1 levels from almond drinks are not available and it is unclear whether processing during manufacturing might further reduce AFB1 levels in almond drinks. It is also unclear how much of an overestimate will occur from assuming all almonds are at the ML, but in the absence of data on the actual distribution of AFB1 levels in almonds it provides an upper value to the potential exposure. The potential for some drinks to contain almonds with higher AFB1 levels than the ML is expected to be low given the monitoring by growers.

35. The Committee noted that using the maximum levels set by the European Commission did not provide assurance that potential AFB1 contamination in almond drinks was not a concern since margins of exposures (MOEs) were well below 10,000. However, it was concluded that better information on actual exposure levels was needed to determine the risk posed by AFB1 exposure from this source.

36. Information on consumption is not currently available for young children who may be consuming a mixture of different plant-based drinks. Therefore, the current approach, which assumes that consumption was exclusively of a single plant-based drink, was most appropriate as young children are likely to develop a preference for one drink. It was noted that there are plans to obtain more consumption data for children who follow a dairy-free diet, as these diets are becoming more popular.

Secretariat

September 2020

This is a draft statement for discussion. It does not represent the final views of the Committee and should not be cited.

Glossary

AFB1– Aflatoxin B1

ALARA – As low as reasonably achievable

ARfD – Acute Reference Dose

CN – Cyanide

DHSC – Department of Health and Social Care

EC – European Commission

EFSA – European Food Safety Authority

EU – European Union

EYS – Early Year Settings

JECFA – Joint FAO/WHO Expert Committee on Food Additives

ML – Maximum Level

MOE – Margin of Exposure

PHE – Public Health England

RASFF – Rapid Alert for Food and Feed

SCF – Scientific Committee for Food

References

Almond Board of California (2016) Pre-Export Checks (PEC) Program Manual. Version 9.0. Available at: https://www.almonds.com/sites/default/files/pec_program_manual_version_9.0.pdf

Baker A, Garner MC, Kimberley KW, Sims DB, Stordock JH, Taggart RP and Walton DJ (2018) Cyanide Toxicity of Freshly Prepared Smoothies and Juices Frequently Consumed. European Journal of Nutrition and Food Safety, September 2018, 8(4)

Bates B., Cox L., Nicholson S., et al. (2016). National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 – 2013/2014). Available at: https://www.gov.uk/government/statistics/ndns-results-from-years-5-and-6-combined

Bates B., Lennox A., Prentice A., et al. (2014). National Diet and Nutrition Survey (NDNS): results from Years 1 to 4 (combined) of the rolling programme for 2008 and 2009 to 2011 and 2012. Available at: https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-resultsfrom-years-1-to-4-combined-of-the-rolling-programme-for-2008-and-2009-to-2011- and-2012

British Nutrition Foundation (2019): Healthy eating for toddlers. Accessible at: https://www.nutrition.org.uk/healthyliving/resources/healthyeatingtoddlers.html

Burns AE, Bradbury JH, Cavagnaro TR, Gleadow RM. Total cyanide content of cassava food products in Australia. Journal of Food Composition and Analysis. 2012;25(1):79–82.

Children. Available at: https://www.gov.uk/government/publications/diet-andnutrition-survey-of-infants-and-young-children-2011

COT (2016) statement on cyanogenic glycosides in bitter apricot kernels. https://cot.food.gov.uk/sites/default/files/cot/cotstatementapricot200615.pdf

DH (Department of Health) (2013). Diet and Nutrition Survey of Infants and Young

EFSA (2005). Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for Risk Assessment of Substances Which are both Genotoxic and Carcinogenic. The EFSA Journal. 282: 1-31.Available at: https://www.efsa.europa.eu/en/efsajournal/pub/282

EFSA (2007) Opinion of the scientific panel on contaminants in the food chain on a request from the Commission related to the potential increase of consumer health risk by a possible increase of the existing maximum levels for aflatoxins in almonds, hazelnuts and pistachios and derived products.

EFSA (2016) Scientific Opinion on acute health risks related to the presence of cyanogenic glycosides in raw apricot kernels and products derived from raw apricot kernels. Available at:

EFSA (2019) Scientific Opinion on the evaluation of the health risks related to the presence of cyanogenic glycosides in foods other than raw apricot kernels. Available at: https://www.efsa.europa.eu/en/efsajournal/pub/5662

EFSA (2020) Risk assessment of aflatoxins in food. Available at: https://www.efsa.europa.eu/en/efsajournal/pub/6040

Food and Agriculture Organization. Available at: http://www.fao.org/3/a-y5499e.pdf