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TOX/2018/31

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

Review of potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Introduction

1. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) was asked to review the risk of toxicity of chemicals in the diets of infants and young children aged 1-5 years, in support of a review by the Scientific Advisory Committee on Nutrition (SACN) of Government recommendations on complementary and young child feeding. The reviews will identify new evidence that has emerged since the Government's recommendations were formulated,and will appraise that evidence to determine whether the advice should be revised.

2. A scoping paper (TOX/2015/32) "COT contribution to SACN review of complementary and young child feeding; proposed scope of work for 0 to 5 year old children" was reviewed by the COT in 2015. The members requested a more detailed look at a number of chemicals and a first scoping paper (part I) providing an overview for tropane alkaloids (TAs), zinc, selenium and phthalates was reviewed in May 2018.

3. The following scoping paper (part II), provides an overview of perchlorate, chlorate and furan.

4. The data collected by the Food Standards Agency (FSA) on perchlorate has been submitted to and is part of the evaluation done by the European Food Safety Authority (EFSA). Therefore, Annex 1 provides a summary of the EFSA opinion on perchlorate from 2014 and the newest occurrence data from the 2017 scientific report, focusing on the derivation of the health based guidance values (HBGVs), exposure assessment and risk characterisation and conclusions with emphasis on UK data.

5. The data collected by the Food Standards Agency (FSA) on chlorate has been submitted to and forms part of the evaluation done by the European Food Safety Authority (EFSA) in 2015. Whilst further data collection has been undertaken, the data are unlikely to change the (UK) exposure assessment undertaken by EFSA. Therefore, Annex 2 provides a brief summary of the EFSA opinion on chlorate, giving the derivation of the HBGVs and focusing the exposure assessment, risk characterisation and conclusions on UK data.

6. Annex 3 provides a brief overview of furan, describing the MOE approach taken by EFSA and providing an exposure assessment, risk characterisation and conclusions on recent UK data. The Committee is asked to keep in mind while evaluating the information on furan, that the data is part of an on-going monitoring programme and the exposures presented here are based on limited data; the findings are in line with previous findings by EFSA, which are based on a larger data set for Europe and the UK.

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The Committee is asked to consider the chemicals and data presented in the scoping paper and to comment on the individual Annexes.

Secretariat

September 2018

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Abbreviations

ADI	Acceptable daily intake
AFC	EFSA Panel on Food, Additives, Flavourings, Processing Aids and Materials in Contact with Food
ALARA	As low as reasonably achievable
ARfD	Acute reference dose
BDA	cis-but-2-ene-1,4-dialdehyde
BMD	Benchmark dose
BMDL	Benchmark dose modelling
bw	body weight
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
DNSIYC	Diet and Nutrition Survey of Infants and Young Children
EC	European Commission
EU	European Union
EFSA	European Food Safety Authority
FSA	Food Standards Agency
GI	Gastrointestinal tract
GSH	Glutathione
HBGV	Health based guidance value
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LB	Lower bound
LOAEL	Lowest observed adverse effect level
LOD	Limit of detection
LOQ	Limit of quantification
MoA	Mechanism of action
MOE	Margin of exposure
MRL	Maximum residue limit
NDNS	National Diet and Nutrition Survey
NIS	Sodium-iodide symporter
NOAEL	No observed adverse effect level
NTP	National Toxicology Program
PMTDI	Provisional maximum tolerable daily intake
PRiF	Expert Committee on Pesticide Residues in Food
SACN	Scientific Advisory Committee on Nutrition

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TDI	Tolerable daily intake
TSH	Thyroid stimulating hormones
UB	Upper bound
UF	Uncertainty factor
UK	United Kingdom
WHO	World Health Organisation

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

Review of potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Perchlorate

7. The data collected by the Food Standards Agency (FSA) on perchlorate has been submitted to and is part of the evaluation done by the European Food Safety Authority (EFSA). The following scoping paper provides a brief summary of the EFSA opinion on perchlorate from 2014 and the newest occurrence data from the 2017 scientific report.

Background

8. Perchlorate is a chemical contaminant which is released into the environment from both, natural and anthropogenic sources.

9. Natural sources of perchlorate include nitrate and potash deposits and its natural formation in surface water and the atmosphere and its precipitation into soil and groundwater. Anthropogenic sources include the manufacture and use of fertilisers, especially of natural origin such as Chilean nitrate and the use and disposal of ammonium perchlorate in rocket propellants, explosives, fireworks, flares, air bag inflators and other industrial processes. Perchlorate is further formed during the degradation of sodium hypochlorite which is used for the disinfection of water and can contaminate the water supply. Water, soil and fertiliser are considered the most likely sources for perchlorate contamination of food.

10. Perchlorate has been reported in a wide range of foods, including vegetables, fruit, milk and dairy products, juice, beer, wine and bottled water and is rapidly and extensively absorbed from the gastrointestinal (GI) tract in humans and rats. It can be found in human serum, plasma, urine, saliva and breast milk; the available information to date indicates that the majority of perchlorate is excreted unmodified via urinary excretion. Breast milk has also been indicated as a route of excretion for humans and rats.

Toxicity

11. The main adverse effects of perchlorate are on the thyroid.

12. Changes in thyroid hormones and thyroid stimulating hormone (TSH) levels as well as an increased thyroid weight have been reported in rats after repeated exposure to perchlorate. Histopathological changes included changes in the thyroid and mammary glands. Chronic exposure lead to thyroid tumours in rats and mice.

13. Perchlorate competitively inhibits the uptake of iodine via the sodium-iodide symporter (NIS) in humans and rodents and therefore can possibly cause disruption

of thyroid hormone synthesis and consequently lead to the development of hypothyroid symptoms.

14. In humans, severe iodine deficiency can lead to hypothyroidism; mild to moderate iodine deficiency can lead to the development of toxic multinodular goitre, which can subsequently result in hypothyroidism.

15. Data from rodent toxicological studies is of limited use for the extrapolation to humans due to the difference in thyroid hormone physiology; no data are available on acute toxicity in humans. A single treatment with potassium perchlorate at a concentration of 10 mg perchlorate iron/kg (assuming a 70kg adult) used for diagnostic purposes showed no adverse effect. However, in vulnerable subpopulations such as foetuses and infants, an adverse effect has been suggested due to the lack of reserve capability that exists in adult humans and the key role of thyroid hormones in foetal/neonatal neurological development.

HBGVs

16. In 2011, the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2011) performed benchmark dose (BMD) modelling and derived a provisional maximum tolerable daily intake (PMTDI) of 0.01 mg/kg bw per day by applying an uncertainty factor (UF) of 10 to account for sensitive population subgroups to a $BMDL_{50}$ of 0.11 mg/kg bw per day.

17. In 2014, EFSA performed BMD modelling on human dose-response data looking at thyroid iodine uptake inhibition. The EFSA Panel concluded in their evaluation, that prolonged 50% inhibition of thyroid iodine uptake by perchlorate may lead to goitre and multinodular goitre, even if short term exposure does not alter the thyroid function test. Therefore, using the $BMDL_{05}$ of 0.012 mg/kg bw as a reference point and applying an UF of 4 to allow for inter-human differences in toxicokinetics, EFSA derived a tolerable daily intake (TDI) of 0.3 µg/kg bw.

18. EFSA concluded that an acute reference dose (ARfD) was not warranted on the basis that a single day acute exposure to perchlorate at concentrations found in food and drinking water is unlikely to cause an adverse effect in healthy humans and more vulnerable groups. Based on the limited information available, even the complete inhibition of thyroid iodine uptake would not deplete the thyroid iodine content in infants with mild to moderate iodine deficiency.

19. EFSA revised their scientific opinion on perchlorate in 2015 due to a technical error and re-assessed the dietary exposure, however this has not affected the derivation of the HBGVs.

Exposure Assessment

Dietary exposure

20. The newest European data on perchlorate has been submitted to EFSA for the 2017 scientific report. EFSA received 18,217 analytical results from 16 European member states and food business operators, including the UK. Analytical results with a limit of quantification (LOQ) > 50 µg/kg were excluded due to method sensitivity;

analytical results originating from suspect samples were excluded from the chronic dietary assessment.

21. Data submitted included analytical results on foods for infants and small children, infant formula (powder) and follow on formula (powder).

22. Following the approach in the 2014 scientific opinion, the use of suspect samples was considered an overestimation of the mean concentration of perchlorate for the chronic exposure assessments and were therefore only considered to assess uncertainties for the different sampling strategies. For short-term exposures, the EFSA Panel included suspect samples as a conservative approach; a single lot of highly contaminated food could be consumed over a short time period.

23. Table 1 and Table 2 provide the mean and 95th percentile estimated chronic and short-term exposures to perchlorate based on the total European data and UK data only.

Table 1 Estimated mean and 95th percentile short-term and chronic exposure to perchlorate (µg/kg bw per day) based on total European data submitted to EFSA for the 2017 scientific report, excluding suspect samples.

Age group	Exposure (µg/kg bw per day)			
	Short-term		Chronic	
	Mean (min LB-max UB)	95th percentile (min LB-max UB)	Mean (min LB - max UB)	95th percentile (min LB – max UB)
Infants	0.4-2.1	1.0-6.0	0.04-0.61	0.09-0.81
Toddlers	0.62-2.3	1.5-6.5	0.08-0.54	0.15-1.0
Other children*	0.41-1.7	0.94-5.4	0.06-0.42	0.12-0.79

* ≥ 36 months to < 10 years old

Table 2 Estimated mean and 95th percentile short-term and chronic exposure to perchlorate (µg/kg bw per day) based on UK data only, submitted to EFSA for the 2017 scientific report, excluding suspect samples.

Age group	Exposure (µg/kg bw per day)			
	Short-term		Chronic	
	Mean (min LB-max UB)	95th percentile (min LB-max UB)	Mean (min LB - max UB)	95th percentile (min LB – max UB)
Infants	0.90-1.70	2.29-3.35	0.09-0.49	0.23-0.81
Toddlers DNSIYC*	0.92-1.41	2.05-2.67	0.11-0.43	0.22-0.66
Toddlers NDNS**	0.81-1.23	1.78-2.38	0.10-0.35	0.20-0.60
Other children***	0.55-0.81	1.28-1.68	0.07-0.21	0.14-0.38

* Diet and Nutrition Survey of Infants and Young Children
** National Diet and Nutrition Survey
*** ≥ 36 months to < 10 years old

Human breast milk

24. No breast milk data for perchlorate were available for the UK or Europe. Based on data from the US, EFSA derived estimated exposure concentrations for exclusively breastfed infants of 0.76 to 4.3 µg/kg and 1.1 to 6.5 µg/kg bw per day for average and high-level consumptions of breast milk, respectively.

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Risk characterisation

25. In 2014 EFSA derived a TDI of 0.3 µg/kg bw; an ARfD was not deemed necessary.

26. In 2017, EFSA published a scientific report, including chronic exposure assessments based on the most recent occurrence data on perchlorate from 16 member states.

27. No acute exposure estimate was carried out, as adverse effects are not expected in any population group following a single-day exposure to perchlorate at the levels relevant for dietary exposure.

28. Short-term exposure was included in the assessment to take into account possible adverse effects in vulnerable groups, if exposed to relatively high levels of perchlorate for a short period (two to three weeks).

29. The estimated short-term exposure was increased by up to 64% (mean) and 53% (95th percentile) in infants and toddlers, if suspect samples were included in the assessment.

30. For the total of European data, the UB mean and 95th percentile estimated short-term and chronic estimated exposures exceeded the TDI of 0.3 µg/kg bw in all age groups. Both, the chronic and short-term exposures to perchlorate are therefore of potential concern for high consumers with mild to moderate iodine deficiency and/or low iodine intake.

31. For UK data only, the UB mean and 95th percentile estimated short-term exposure exceed the TDI in all age groups. UB chronic estimated exposures exceed the TDI for infants and toddlers, however are below the TDI in other children. Comparing the actual exposure values, estimated exposures from the total European data and UK data only are comparable. The only exception can be found in the 95th percentile short-term estimated exposure; UK exposures are approximately half of the overall European exposure. Nevertheless, both the chronic and short-term exposures based on UK data only, are of potential concern for high consumers with mild to moderate iodine deficiency and/or low intake.

32. Based on data available in the literature, the estimated exposures for breastfed infants exceeded the TDI for both, average and high-level consumption of breastmilk. This could possibly be of concern for breastfed infants of mothers with low iodine intake.

Uncertainties in the risk characterisation

33. Short-term exposure to perchlorate at concentrations higher than the TDI could be critical in breastfed infants and young children with mild to low iron deficiency. However, no data are available to derive an ARfD.

34. Limitations in the analytical data set in terms of coverage across Europe and representation of all relevant food groups, add uncertainty to the exposure assessment.

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Conclusions

35. The estimated exposures in all age groups, based on the total European data and UK data only, are of potential concern in case of a mild to moderate iodine deficiency, both for chronic and short-term exposures.

Questions to be asked to the Committee

i) Do the Committee agree with the approach taken by EFSA and the subsequent conclusions?

ii) Do the Committee agree, that the conclusions drawn by EFSA on the total of European data available, are also applicable to the submitted UK data?

iii) Are the Committee content with a summarizing paragraph on perchlorate in the overarching statement, referring to the EFSA opinion?

iv) Do the Committee have any other comments?

Secretariat

September 2018

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References

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

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Chlorate

36. The data collected by the Food Standards Agency (FSA) on chlorate has been submitted to and forms part of the evaluation done by the European Food Safety Authority (EFSA) in 2015. Whilst FSA and the Expert Committee on Pesticide Residues in Food (PRiF) have undertaken further data collection, also to inform the discussion on possible future maximum residue levels (MRLs) under the pesticide legislation, the data are unlikely to change the (UK) exposure assessment undertaken by EFSA or conclusions drawn and therefore it was not considered appropriate to undertake a full risk assessment. The following scoping paper therefore provides a brief summary of the EFSA opinion on chlorate.

Background

37. Chlorate is no longer permitted as a pesticide in the European Union (EU) (Commission Decision No 2008/865/EC). It can be formed as a by-product when using chlorine, chlorine dioxide or hypochlorite as a disinfectant for drinking water, water for food production and surfaces in contact with food. The direct treatment of animal derived food with chlorinated water is not permitted in the EU (although the washing of plant derived food with chlorine disinfected water is allowed).

38. No MRLs for chlorate have been set under the European Commission regulation (EC) No 396/2005 and therefore the default MRL of 0.01 mg/kg is applicable; no maximum level for chlorate in drinking water has been set by the EU, although the World Health Organisation (WHO) set a guideline level of 0.7 mg/L.

39. Chlorate residues in food have been shown to arise from the use of chlorinated water for food processing (for example washing) and the disinfection of surfaces and food processing equipment, although in many cases they may occur simply due to the presence of chlorate in potable water used for food production. There is no evidence that they are present as a result of illegal use of chlorate as a herbicide

40. In rats, following oral exposure, chlorate is rapidly absorbed and widely distributed throughout the body, metabolised to chloride and eliminated via urinary excretion.

Toxicity

41. The primary targets of chlorate toxicity are the thyroid gland and haematological system.

42. Chlorate, like perchlorate, acts as competitive inhibitor of iodine uptake in the thyroid leading to chronic effects such as multinodular goitre, especially in populations with mild to moderate iodine deficiency.

43. Chlorate has a high acute toxicity in humans; acute effects are the induction of methaemoglobinemia, followed by the lysis of red blood cells which can lead to renal failure. Acute toxicity in humans has been reported after oral exposure to chlorate concentrations of 11 to 23 mg/kg bw; lethality has been reported after oral exposure at doses of approximately 50 mg chlorate/kg bw.

HBGVs

44. The Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2008) and the EFSA Panel on Food, Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel, 2006) identified chlorite and chlorate as the main residues of acidified sodium chlorite, which is applied as an antimicrobial agent. JECFA applied a total uncertainty factor (UF) of 100 (10 for intraspecies variation, 10 for database deficiencies) to a $BMDL_{10}$ of 1.1 mg/kg bw based on non-neoplastic effects on the thyroid in male rats exposed to sodium chlorate (NTP, 2005) and derived an acceptable daily intake (ADI) of 0-0.01 mg/kg bw.

45. EFSA established a tolerable daily intake (TDI) of 3 µg/kg bw for chlorate based on a read across from perchlorate. The TDI for perchlorate (0.3 µg/kg bw) was multiplied by a factor of 10 to account for the different potencies of chlorate and perchlorate in rats (perchlorate appearing to be the more potent).

46. No long term or adequate epidemiological studies in humans were identified by EFSA; no long term or appropriate epidemiological studies in humans have been identified in a more recent literature search for this assessment.

47. EFSA identified the formation of methaemoglobin as a critical acute effect of chlorate and derived an acute reference dose (ARfD) of 36 µg/kg bw from the no observed adverse effect level (NOAEL) of 36 µg/kg in a controlled human study. No UF for more vulnerable individuals was applied in the derivation of the ARfD as EFSA concluded the difference between the NOAEL and the effect in poisoning cases to be sufficiently large.

Exposure Assessment

Dietary exposure, including drinking water

48. EFSA received analytical results of 8028 samples from European member states, including data from the UK. Approximately 5% of the results submitted were for drinking water.

49. Chronic exposure assessments were based on 35 dietary surveys carried out in 19 European member states; acute exposure assessments were based on 41 dietary surveys carried out in 23 European member states. All drinking water was included in the dietary exposure assessment.

50. For calculating the chronic dietary exposure to chlorate, food consumption and body weight data at the individual level were accessed in the Comprehensive

Database. Occurrence data and consumption data were linked at the lowest FoodEx level possible. In addition, the different food commodities were grouped within each food category to better explain their contribution to the total dietary exposure to chlorate. For each country, exposure estimates were calculated per dietary survey and age class.

51. In each dietary survey considered by EFSA, total acute dietary exposure was estimated for each individual and reporting day by multiplying the total daily consumption for each food by their mean occurrence level (UB estimate), except for one food where the highest reliable percentile (UB estimate) was used as occurrence value. This food refers to that with the highest contribution to the exposure when using highest reliable percentile occurrence levels. To estimate the acute dietary exposure food by food, the highest reliable percentile (UB estimate) was selected as occurrence value for each food at the appropriate FoodEx level, and linked to individual consumption data of that food in one single day.

52. EFSA discussed whether it was necessary to apply, in its acute exposure assessments, variability factors for residues in fruit and vegetables with a large unit weight (> 25 g) as is commonly performed for pesticides to account for variation within composite samples (EFSA, 2005). EFSA considered that in some instances where measurements of contaminants were carried out with composite samples of foods with a large unit size and depending on the route by which the contaminant enters the food, application of variability factors could be appropriate in acute exposure assessments.

53. In their evaluation EFSA considered two additional exposure scenarios 1) acute and chronic exposure assessments in which all occurrence data above a hypothetical MRL[1] of 0.7 mg/kg were excluded; and 2) acute exposure assessments where all food items were assumed to contain a level of 0.7 mg/kg.

54. Tables 1-3 give the estimated mean and 95th percentile acute and chronic exposures to chlorate based on the total data submitted to EFSA, providing all three scenarios. Table 4 gives the estimated mean and 95th percentile chronic exposure for UK data only.

Table 1 Estimated mean and 95th percentile acute and chronic exposure to chlorate (µg/kg bw per day) based on total data submitted to EFSA.

Age group	Exposure (µg/kg bw per day)			
	Acute		Chronic	
	Mean (min-max UB)	95th percentile (min-max UB)	Mean (min LB- max UB)	95th percentile (min LB- max UB)
Infants	4.8-13.2	13.9-30.9	1.6-4.1	3.3-6.6
Toddlers	5.5-10.6	10.9-18.0	2.1-3.5	3.2-5.4
Other children*	2.5-7.0	4.9-16.9	1.3-2.8	2.5-5.0

* ≥ 36 months to < 10 years old

[1] 0.7 mg/kg is the current guidance value set by the WHO (2005) for chlorate in drinking water

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Table 2 Estimated mean and 95th percentile acute and chronic exposure to chlorate (µg/kg bw per day) based on total data submitted to EFSA, excluding occurrence values above 0.7 mg/kg.

Age group	Exposure (µg/kg bw per day)			
	Acute		Chronic	
	Mean (min-max UB)	95th percentile (min-max UB)	Mean (min LB- max UB)	95th percentile (min LB- max UB)
Infants	3.7-12.3	10.0-28.9	1.3-3.9	2.6-6.2
Toddlers	4.2-9.6	9.6-16.5	1.8-3.1	2.8-5.1
Other children*	2.0-4.5	3.9-14.6	1.1-2.4	2.2-4.4

* ≥ 36 months to < 10 years old

Table 3 Estimated mean and 95th percentile acute exposure to chlorate (µg/kg bw per day) based on total data submitted to EFSA; occurrence values for all food items were set at 0.7 mg/kg.

Age group	Exposure (µg/kg bw per day)	
	Mean (min-max UB)	95th percentile (min-max UB)
Infants	20.7-68.9	45.7-110.8
Toddlers	20.9-36.0	37.4-62.2
Other children*	8.7-21.4	21.2-53.6

* ≥ 36 months to < 10 years old

Table 4 Estimated mean and 95th percentile chronic exposure to chlorate (µg/kg bw per day) based on UK data only.

Age group	Exposure (µg/kg bw per day)	
	Mean (LB-UB)	95th percentile (LB-UB)
Infants	1.6-2.0	3.4-4.1
Toddlers (NDNS)*	2.6-3.2	4.3-5.2
Toddlers (DNSIYC)**	2.3-2.9	4.0-4.8
Other children***	2.0-2.4	3.2-3.8

* National Diet and Nutrition Survey
** Diet and Nutrition Survey of Infants and Young Children
*** ≥ 36 months to < 10 years old

Human breast milk

55. No information on concentrations of chlorate in breast milk was available, therefore it was not possible to perform an exposure assessment.

Infant formula

56. The analytical data on infant formula/follow-on milk were received at a very late stage and at the time of publication of the scientific opinion, EFSA was still awaiting confirmation of the levels; further analysis was still ongoing. If the high levels reported (2.5 mg/kg dry weight) are accurate, these levels would result in a substantial increase in acute and chronic exposures in infants and toddlers.

57. However, some of the adverse effects in infants might be mitigated by the fortification of infant formula with iodine in the UK.

Risk characterisation

58. EFSA derived a TDI of 3 µg/kg bw and an ARfD of 36 µg/kg bw.

59. The TDI was exceeded for the UB 95th percentile estimated chronic exposure in all age groups; the UB mean estimated chronic exposure exceeded the TDI in infants and toddlers. The maximum exceedance was in infants (approximately 2-fold).

60. The estimated chronic exposure for UK data only is lower than the exposures estimated for the total European data. Nevertheless, the 95th percentile estimated chronic exposure for UK data only (Table 4) exceeded the TDI in all age groups; the highest exceedance was in toddlers (approximately 2-fold). All mean estimated chronic exposures were below the TDI, except for toddlers at the UB level (3.2 µg/kg bw).

61. In all population groups exceeding the TDI, drinking water was the major contributor, with up to 60%, 50% and 40% in infants, toddlers and other children, respectively.

62. Individuals with sufficient iodine intake are less likely to suffer adverse effects from exceedances of the TDI than fetuses, neonates and individuals with low iodine intake or individuals genetically predisposed to develop hyperthyroidism. The chronic dietary exposure is therefore of potential concern for high consumers in these age groups with mild to moderate iodine deficiency. The effects could furthermore be exacerbated in combination with other anti-thyroid substances.

63. The mean and 95th percentile estimated acute exposures for all age groups are below the ARfD. The highest exposure reported is 30.9 µg/kg bw for infants at the UB 95th percentile. Single acute exposure to chlorate at levels found in food and drinking water are therefore unlikely to cause adverse effects, including vulnerable individuals. No data for acute estimated exposures on UK data only were available.

64. Removing foods and drinking water containing levels > 0.7 mg/kg chlorate from the exposure assessment showed minimal impact on the acute and chronic exposure estimates as most of the occurrence data for chlorate were substantially below 0.7 mg/kg.

65. Assuming a level of 0.7 mg/kg for chlorate for all food commodities could lead to an acute exposure of up to five times the ARfD of 36 µg/kg bw, primarily due to drinking water and cows' milk. However, as it is implausible for all foods consumed in a single day to contain chlorate concentrations of 0.7 mg/kg, such exceedances are highly unlikely. However, if drinking water would contain concentrations of 0.7 mg/L,

mean water consumption could lead to mean (infants) and 97.5th percentile (toddlers) estimated exposures similar to the ARfD, high water consumption could lead to an exceedance of up to three times the ARfD.

Uncertainties in the risk characterisation

66. All uncertainties incurred with the derivation of the HBGV for perchlorate also apply to the derivation of the HBGV for chlorate and are described in the perchlorate opinion. In addition, the TDI established for chlorate is derived using read across from perchlorate; no human studies on inhibition of iodine uptake by chlorate were available. Different rat strains have been used for tests of the two compounds, adding additional uncertainty.

67. An ARfD was set based on a NOAEL of 36 µg/kg bw per day in a human repeat study, the NOAEL being the highest dose tested, and it is unclear as to how much higher a lowest observed adverse effect level (LOAEL) would be. No UF was applied as the NOAEL was at least 300 times lower than the toxic concentration in a poisoning case without induction of methemoglobinemia. However, this difference was derived from a single poisoning case.

Conclusions

68. Chronic dietary exposure to chlorate is of potential concern for high consumers in all age groups with mild to moderate iodine deficiency. The effects could furthermore be exacerbated in combination with other anti-thyroid substances.

69. Single acute exposure to chlorate at levels found in food and drinking water are unlikely to cause adverse effects, including vulnerable individuals.

70. Drinking water was the major contributor, at up to 40 to 60%.

Questions comments from policy to the COT

v) What are the health implications, especially if it proves impossible to reduce chlorate levels in food, including infant formula and baby food, sufficiently to get exposures to below the TDI (notwithstanding the possibility that the EU will set unachievable MRLs)?

vi) Are the Committee able to draw any conclusions on the relative risk posed by chlorination of drinking water compared to total exposure?

Questions to be asked to the Committee based on the above

vii) Do the Committee agree with the approach taken by EFSA and the derivation of the HBGVs?

viii) Do the Committee agree that the conclusions drawn by EFSA for the total of European data are also appropriate for UK data only?

ix) Is the Committee content with a summarizing paragraph on chlorate in the overarching statement, referring to the EFSA opinion?

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x) Are there points the Committee specifically wants to stress in the overarching statement

xi) Do the Committee have any other comments?

Secretariat

September 2018

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

Review of potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Furan

71. Unless stated otherwise, the following background information was derived from the European Food Safety Authority's (EFSA) scientific opinion on furan and methylfuran in food (EFSA, 2017).

72. The UK occurrence data used in the following assessment are results obtained from the Food Standards Agency's (FSA) 2017 survey, which forms part of a long-term surveillance programme (2014-2018). UK data from previous years was considered by EFSA in the 2017 EFSA opinion, however at the time the 2017 data was not yet available. The 2017 data have since been published in the final FSA report and used to derive the exposures presented in this paper.

73. EFSA concluded that current levels of dietary exposure to furan and its methyl analogues indicate a potential human health concern and should be reduced to as low as possible achievable (ALARA). The UK exposure presented in this paper are based on a smaller data set, the findings/exposures are however in line with the previous findings by EFSA.

Background

74. Furan and methylfurans (2-methylfuran, 3-methylfuran and 2.5-methylfuran) are volatile compounds that are formed in foods during thermal processing. Food characteristics, processing and cooking conditions, especially the preparation of the food at the level of the consumer, determines the final concentration of furan in foods as consumed. Furan can be found in a variety of foods, including coffee and canned and jarred goods.

75. Industrially produced furan is used in the production of pharmaceuticals, agricultural chemicals, stabilisers and as a solvent for resins. 2-methylfuran is produced as a side product in furfuryl alcohol production and used as a solvent and in antimalarial drugs. 2,5-dimethylfuran, as well as furan and 2-methylfuran are a potential source of biofuel.

76. After oral exposure of rats, furan is rapidly and extensively absorbed by the gastrointestinal (GI) tract and distributed throughout the body. Furan is extensively metabolised and elimination of unchanged furan occurred via exhalation, urine or bile/faeces. After 24 hours, no unchanged furan was detected in the liver or blood; the half-life of radioactive furan was approximately 40 minutes in the liver and approximately 1.3 hours in blood. No half-life could be established for kidneys.

77. Data from in vitro studies suggest that 2-methylfuran and 3-methylfuran become associated with lung and liver microsomal proteins but no oral studies have

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been performed. Inhalation studies in dogs indicate that the three alkylated furans are absorbed from the gastrointestinal tract but the extent of this is unclear.

Toxicity

Furan

78. Although not directly measured, results with trapping agents and identification of urinary and biliary metabolites provide strong evidence that cis-but-2-ene-1,4-dialdehyde (BDA) is a prime reactive intermediate in the metabolism of furan. BDA has a high reactivity with amino acids, glutathione (GSH) and protein and non-protein amino and thiol residues.

79. The binding of BDA to a range of molecules leads to cell and tissue damage, mitochondrial dysfunction and fibrosis, primarily in the liver. There is limited evidence of a direct mechanism of action (MoA) for furan; epigenetic changes, oxidative stress/DNA damage and regenerative hyperplasia, accompanied by tissue damage are however involved in an indirect MoA.

80. In short term rodent studies (< 90 days), furan showed strong hepato- and nephrotoxicity; changes in serum markers related to hepatotoxicity, significant increases in serum thyroid hormones and severe histopathological damage in the liver were observed. In long term studies, furan was associated with toxicity in the liver. Histopathological changes in testes, prostate gland, Lydig cells and seminal vesicles were observed in weaning/post puberty rats; no histopathological effects in the reproductive organs were observed in adult rodents.

81. Furan was unable to induce gene mutations in bacteria and results in mammalian cells in vitro were contradictory. In contrast, BDA, was observed to induce DNA adducts and possibly crosslinks in vitro and to directly induce mutations in bacteria and mammalian cells. In vivo, furan was observed to induce the formation of low levels of DNA adducts in the liver and kidney; the chemical structure of these adducts could not be defined but were different to the adducts induced in vitro by BDA. Data on the induction of DNA breaks in the liver were conflicting. The available data suggests that the potency of covalent binding in vivo is either not very high or the reaction products are very short-lived and that BDAs reactivity with proteins could restrict its access to the DNA.

82. Chronic exposure to furan induced chromosomal damage in rodents. A single mouse study suggested weak mutagenic activity; it is uncertain if the mutation is the result of oxidative damage or a pre-existing spontaneous mutation.

83. Limited information is available on furan levels in humans. The studies available show a variety of inconsistencies and therefore do not allow for conclusions regarding the reported levels of blood and urinary furan and whether or not furan has an effect on the liver.

Methylfurans

84. As with BDA the reactive intermediate of 2,5-dimethylfuran reacts with amino acids and GSH. Limited to no information is available for the intermediates of 2-methyl and 3-methylfuran. However, based on structure and reactivity, it may be

anticipated that these will react with tissue components in a similar way to the primary metabolites of furan and 2,5-dimethylfuran.

85. The liver has been identified as the primary target for acute and short term (< 90 days) toxicity of methylfurans in rodents; 3-methylfuran also showed indications of nephrotoxicity after long term exposure. The toxic potency of methylfurans were reported to be in the same order of magnitude as for furan.

86. No information on the genotoxicity of 3-methylfuran are available. 2-methylfuran and 2,5-dimethylfuran showed negative results in bacteria; some evidence however points to chromosome damage in mammalian cells in vitro. Some evidence furthermore points to DNA strand breaks in vivo as a result of 2,5-dimethylfuran.

HBGV

87. Based on the very limited data available on the effects of furan on humans, EFSA used experimental animal data to derive Health Based Guidance Values (HBGVs) in their scientific opinion of 2017.

88. For non-neoplastic effects of furan, EFSA selected a bench mark dose ($BMDL_{10}$) of 0.064 mg/kg bw per day as a reference point, based on the induction of cholangiofibrosis in male rats after two years.

89. Combined data from two studies on the incidences of hepatocellular adenomas and carcinomas after two years in female mice was considered the most robust data set for neoplastic effects of furan. A $BMDL_{10}$ of 1.31 mg/kg bw per day was derived as reference point.

90. EFSA found it not appropriate to establish a tolerable daily intake (TDI) due to clear evidence of indirect mechanisms in the carcinogenic MoA of furan and some indications of direct genotoxic mechanisms and therefore used the margin of exposure (MOE) approach.

91. Based on the available toxicity data and taking inter- and intraspecies variations into consideration, EFSA concluded a MOE of 100 or higher to be of low health concern for non-neoplastic effects. For substances that are both genotoxic and carcinogenic, EFSA concluded a MOE of 10,000 or higher to be of low health concern, if based on a $BMDL_{10}$ from an animal carcinogenicity study.

92. EFSA concluded the available information to be insufficient to identify a reference point for methylfurans; it was however considered to assume additivity of hepatotoxicity of furan, 2-methyl and 3-methylfuran in the rat.

Exposure Assessment

Dietary exposure

93. The occurrence data are results from a FSA retail survey conducted in 2017 and are included in the final report on monitoring of furan in food samples. Samples were taken from a number of food groups (breakfast cereal, biscuits, coffee, ready to eat meals for children, popcorn, dried prunes) and analysed for furan, 2-methylfuran

and 3-methylfuran. More detailed information on the number of samples as well as the occurrence of furan and methylfurans in the different food groups can be found in Appendix 1.

94. No data on breast milk was available.

95. Consumption data (on a body weight basis) for the estimated dietary exposure are from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013) and from years 1-8 of the National Diet and Nutrition Survey (NDNS) (Bates et al., 2014, 2016 & 2018).

96. Breakfast cereals and ready-to-eat meals for children were the main food groups that contributed to the total exposure to furan and methylfurans. This is in line with the findings reported by EFSA for infants and toddlers. Breakfast cereal and ready-to-eat meals analysed as part of the FSA retail survey were 'as purchased' rather than 'as consumed' samples. Therefore, concentrations of furan and methylfurans could potentially be reduced as a result of heating the meal, due to evaporation, or as a result of dilution with water, milk or other consumer behaviours prior to consumption.

97. EFSA therefore considered a scenario where all ready-to-eat meals for infants and small children were assumed to be reheated in a hot-water bath without a lid as this technique leads to the highest losses of furan. Hence, in view of this scenario, furan concentrations in ready-to-eat meals for infants and small children were divided by reduction factors (1.3 to 1.5) derived from the literature prior to estimating exposure in this paper.

98. Tables 1-4 give the estimated chronic exposures to furan, 2-methylfuran, 3-methylfuran and the sum of all three for children aged 4 to 60 months.

Table 1 Estimated chronic exposures to furan for children aged 4 to 60 months, using occurrence data from the 2017 FSA retail survey.

Food Group	**Exposure LB-UB (µg/kg bw per day)**					
	4 to 18 months			**18 to 60 months**		
	Number of consumers	**Mean**	**97.5th percentile**	**Number of consumers**	**Mean**	**97.5th percentile**
Breakfast cereal	1134	0.036-0.046	0.17-0.21	981	0.025-0.032	0.11-0.15
Biscuits	1472	0.018-0.02	0.06-0.067	1014	0.021-0.024	0.07-0.077
Coffee[a]	4	0.0001	0.0001-0.0002	7	0.0001	0.0001-0.0002
Ready to eat meals for children	1668	0.17	0.58	94	0.066	0.29
Popcorn	14	0.018	0.097	43	0.023	0.076
Dried prunes	38	0.007	0.019	1	0.003	0.003
Total Exposure	**2455**	**0.14-0.15**	**0.54-0.56**	**1297**	**0.04-0.048**	**0.15-0.17**

[a] investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed instant coffee. Therefore, only furan measured in the six instant coffee samples were used in the exposure estimates.

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NOTE: Please note that consumption or exposure estimates made with a small number of consumers may not be accurate. In particular, estimates of the 97.5th percentile based on less than 60 consumers should be treated with extreme caution, as they may not be as representative for larger number of consumers.

Table 2 Estimated chronic exposures to 2-methylfuran for children aged 4 to 60 months, using occurrence data from the 2017 FSA retail survey.

Food Group	**Exposure LB-UB (µg/kg bw per day)**					
	4 to 18 months			**18 to 60 months**		
	Number of consumers	**Mean**	**97.5th percentile**	**Number of consumers**	**Mean**	**97.5th percentile**
Breakfast cereal	1134	0.02032	0.092	981	0.014	0.062
Biscuits	1472	0.017-0.018	0.058-0.063	1014	0.021-0.022	0.068-0.072
Coffee[a]	4	0.0002	0.0007	7	0.0002	0.0006
Ready to eat meals for children	1668	0.003	0.011-0.033	94	0.0012-0.0037	0.0055-0.017
Popcorn	14	0.01	0.053	43	0.012	0.041
Dried prunes	38	n/a	n/a	1	n/a	n/a
Total Exposure	**2455**	**0.012-0.026**	**0.052-0.086**	**1297**	**0.016-0.029**	**0.064-0.092**

[a] investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed instant coffee. Therefore, only furan measured in the six instant coffee samples were used in the exposure estimates.

NOTE: Please note that consumption or exposure estimates made with a small number of consumers may not be accurate. In particular, estimates of the 97.5th percentile based on less than 60 consumers should be treated with extreme caution, as they may not be as representative for larger number of consumers.

Table 3 Estimated chronic exposures to 3-methylfuran for children aged 4 to 60 months, using occurrence data from the 2017 FSA retail survey.

Food Group	**Exposure LB-UB (µg/kg bw per day)**					
	4 to 18 months			**18 to 60 months**		
	Number of consumers	**Mean**	**97.5th percentile**	**Number of consumers**	**Mean**	**97.5th percentile**
Breakfast cereal	1134	n/a	n/a	981	n/a	n/a
Biscuits	1472	0	0	1014	0	0
Coffee[a]	4	n/a	n/a	7	n/a	n/a
Ready to eat meals for children	1668	0.0042-0.0083	0.014-0.029	94	0.0017-0.0033	0.0074-0.015
Popcorn	14	n/a	n/a	43	n/a	n/a
Dried prunes	38	n/a	n/a	1	n/a	n/a
Total Exposure	**2455**	**0.0028-0.0056**	**0.013-0.026**	**1297**	**0.0001-0.0002**	**0.0015-0.003**

[a] investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed

instant coffee. Therefore, only furan measured in the six instant coffee samples were used in the exposure estimates.

NOTE: Please note that consumption or exposure estimates made with a small number of consumers may not be accurate. In particular, estimates of the 97.5th percentile based on less than 60 consumers should be treated with extreme caution, as they may not be as representative for larger number of consumers.

Table 4 Estimated chronic exposures to the sum of furan, 2-methylfuran and 3-methylfuran for children aged 4 to 60 months, using occurrence data from the 2017 FSA retail survey.

Food Group	**Exposure LB-UB (µg/kg bw per day)**					
	4 to 18 months			**18 to 60 months**		
	Number of consumers	**Mean**	**97.5th percentile**	**Number of consumers**	**Mean**	**97.5th percentile**
Breakfast cereal	1134	0.056-0.066	0.26-0.30	981	0.039-0.046	0.17-0.21
Biscuits	1472	0.035-0.038	0.12-0.13	1014	0.042-0.046	0.14-0.15
Coffee[a]	4	0.0003	0.0008-0.0009	7	0.0003	0.0007-0.0008
Ready to eat meals for children	1668	0.18	0.61-0.64	94	0.069-0.073	0.30-0.32
Popcorn	14	0.028	0.15	43	0.035	0.12
Dried prunes	38	0.007	0.019	1	0.003	0.003
Total Exposure	**2455**	**0.16-0.18**	**0.61-0.67**	**1297**	**0.056-0.077**	**0.22-0.27**

[a] investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed instant coffee. Therefore, only furan measured in the six instant coffee samples were used in the exposure estimates.

NOTE: Please note that consumption or exposure estimates made with a small number of consumers may not be accurate. In particular, estimates of the 97.5th percentile based on less than 60 consumers should be treated with extreme caution, as they may not be as representative for larger number of consumers.

99. The EFSA opinion included an assessment of exposures to furan in different population groups from UK DNSIYC and NDNS surveys. The total mean LB-UB exposures to furan reported for UK infants and toddlers were in the region of 0.42 to 0.53 µg/kg bw per day. The corresponding LB-UB 95th percentile exposures were 0.85 to 1.02 µg/kg bw per day. The exposures for furan in this assessment (Table 1) were derived from a very limited number of samples (Appendix 1) and are considerably below the exposures reported by EFSA for the UK.

100. The exposure assessments for 2- methylfuran and 3- methylfuran reported in Tables 2 and 3 are also based on a very limited number of samples (Appendix 1). However, it is apparent that exposure to 2-methyfuran is considerably higher than from 3-methylfuran.

101. No data on concentrations of methylfurans were available to EFSA at the time of the assessment and therefore the baseline exposure assessments reported by EFSA did not take account of the contribution of methylfurans. EFSA noted that indicative ratios for 2- and 3-methylfuran over furan were reported in some studies

for coffee beverages, breakfast cereals, cereal-based food for infants and young children, and ready-to-eat meals for infants and young children, the literature data were too limited to derive such ratios for 2,5-dimethylfuran. EFSA applied these ratios for adding exposures from methylfurans with furans in a scenario based approach.

102. Estimates for adults, elderly and very elderly showed the highest increase in the exposure scenario for the sum of furan, 2-methylfuran and 3-methylfuran conducted by EFSA, compared to the baseline scenario for furan alone. This exposure was mainly driven by the high concentrations of 2-methylfuran in coffee (four times higher than furan). However, coffee makes a minimal contribution to total exposure from furans and methylfurans in infants and young children.

Margin of exposure (MOE)

103. Table 5 and 6 show the MOEs for furan using the reference point of a) 0.064 mg/kg (equivalent to 64 µg/kg) bw per day for the induction of cholangiofibrosis in male rats for 2 years (non-neoplastic effects) and b) 1.31 mg/kg bw per day for induction of hepatocellular adenomas and carcinomas in female mice after 2 years (neoplastic effects). Calculation of the MOEs used the corresponding estimated chronic exposures given in Table 1.

104. Following EFSAs approach, Table 7 shows the MOEs for the sum of furan, 2-methylfuran and 3-methylfuran for non-neoplastic effects using the reference point of 0.064 mg/kg.

Table 5 Margin of Exposure (MOE) for non-neoplastic effects of furan in children aged 4 to 60 months old, using the exposure estimates provided in Table 1.

Food Group	**Margin of Exposure (MOE)**			
	4 to 18 months		**18 to 60 months**	
	Mean	**97.5th percentile**	**Mean**	**97.5th percentile**
Breakfast cereal	1778-1391	376-305	2560-2000	582-427
Biscuits	3556-3200	1067-955	3048-2667	914-831
Coffee	640000	640000-320000	640000	640000-320000
Ready to eat meals for children	376	110	970	221
Popcorn	3556	660	2783	842
Dried prunes	9143	3368	21333	21333
Total Exposure	**457-427**	**119-114**	**1600-1333**	**427-376**

Table 6 Margin of Exposure (MOE) for neoplastic effects of furan in children aged 4 to 60 months old, using the exposure estimates provided in Table 1.

Food Group	**Margin of Exposure (MOE)**			
	4 to 18 months		**18 to 60 months**	
	Mean	**97.5th percentile**	**Mean**	**97.5th percentile**
Breakfast cereal	36389-28478	7706-6238	52400-40938	11909-8733

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Biscuits	72778-65500	21833-19552	62381-54583	18714-17013
Coffee	13100000	13100000-6550000	13100000	13100000-6550000
Ready to eat meals for children	7706	2259	19848	4517
Popcorn	72778	13505	56957	17237
Dried prunes	187143	68947	436667	436667
Total Exposure	**9357-8733**	**2426-2339**	**32750-27292**	**8733-7706**

Table 7 Margin of Exposure (MOE) for non-neoplastic effects of the sum of furan, 2-methylfuran and 3-methylfuran in children aged 4 to 60 months old, using the exposure estimates provided in Table 4.

Food Group	**Margin of Exposure (MOE)**			
	4 to 18 months		**18 to 60 months**	
	Mean	**97.5th percentile**	**Mean**	**97.5th percentile**
Breakfast cereal	1143-970	246-213	1641-1391	376-305
Biscuits	1829-1684	533-492	1524-1391	457-427
Coffee	213333	80000-71111	213333	91429-80000
Ready to eat meals for children	356	105-100	928-877	213-200
Popcorn	2286	427	1829	533
Dried prunes	9143	3368	21333	21333
Total Exposure	**400-356**	**105-96**	**1143-831**	**291-237**

Risk characterisation

105. EFSA found it not appropriate to establish a TDI due to an (indirect) carcinogenic MoA and some indications for direct genotoxic mechanisms. EFSA therefore used the MOE approach and concluded a MOE of 100 or higher to be of low health concern for non-neoplastic effects and a MOE of 10,000 or higher for neoplastic effects.

106. All MOEs for non-neoplastic effects of furan are greater than 100 and are therefore not of toxicological concern. The MOEs at the 97.5th percentile for ready-to-eat meals for both age groups (110 and 121) and the MOEs for total exposure at the 97.5th percentile for children aged 4 to 18 months (119-114) are however close to the MOE of 100. Given the uncertainties in the exposure assessment, these concentrations could be a potential concern for human health.

107. The mean and 97.5th percentile MOEs for neoplastic effects of furan for children ages 4 to 18 months and the 97.5th percentile MOEs for children aged 18 to 60 months, for both ready-to eat meals and total exposure are below 10,000. The MOEs at the 97.5th percentile in children aged 4 to 18 months are especially low with values of < 2500. These exposures are of toxicological concern.

108. All other MOEs for neoplastic effects of furan are greater than 10,000 and are therefore not of toxicological concern.

109. All MOEs for non-neoplastic and neoplastic effects of 2-methylfuran and 3-methylfuran are greater than 100 and 10,000, respectively. The levels of 2- and 3-methylfurans are therefore not of toxicological concern.

110. The 97.5th percentile MOEs (105-96) for non-neoplastic effects of the sum of furan and the two methylfurans for children ages 4 to 18 month, for both ready-to-eat meals and total exposure, are at/below the MOE of 100. These exposures are of potential toxicological concern. Given the uncertainties surrounding the sum of furan and methylfurans, these values could be an over- as well as underestimation of risk. The 97.5th percentile MOEs for ready-to-eat meals (213-200) for children aged 18 to 60 months, breakfast cereal in both age groups (246-213; 376-305) and total exposure for children aged 18 to 60 months (291-237) are close enough to the MOE of 100, that a potential underestimation of the risk based on the uncertainties could be of potential concern.

Uncertainties in the risk characterisation

111. The estimated exposures of infants and young children to furan and methylfuran is based on a very limited number of samples from an FSA retail survey. Samples analysed were ‘as purchased’ and not ‘as consumed’, leading to further uncertainties about the concentration of furan as a result of culinary practices prior to consumption. The effect of different cooking practises on the levels of methylfurans is furthermore uncertain.

112. EFSA considered indicative occurrence values for 2-methylfuran and 3-methylfuran in food groups with the highest contribution to the exposure and calculated exposure based on the sum of furan and methylfuran in a scenario based approach. Based on the limited occurrence data available for this risk assessment on 2-methylfuran and 3-methylfuran, an exposure assessment and MOEs for non-neoplastic effects were calculated for the sum of all three chemicals. However, the approach taken is conservative. No occurrence data was available for 2,5-dimethylfuran. The lack of information regarding the contribution of 2-methylfuran and 3-methylfuran, as well as the lack of data on 2,5-dimethylfuran and the potential contribution add to the uncertainty and may lead to an overestimation or underestimation of risk.

113. There is a level of uncertainty concerning the carcinogenic MoA and whether or not furan is directly genotoxic and to what extent this might contribute to the overall effect.

114. Limited information is available on the toxicity and adverse effects of methylfurans. EFSA therefore concluded the available information to be insufficient to identify a reference point for methylfurans; it was however considered to assume additivity of hepatotoxicity of furan, 2-methyl and 3-methylfuran in the rat.

Conclusions

115. EFSA concluded a MOE of 100 or higher to be of low health concern for non-neoplastic effects and a MOE of 10,000 or higher for neoplastic effects.

116. Based on the MOEs for neoplastic effects, the total exposure of children aged 4 to 60 months to furan is of toxicological concern, with MOEs smaller than 10,000. Ready-to-eat meals made the main contribution to the total exposure from furan, which is in line with the conclusions drawn by EFSA. Breakfast cereals were the main contributor to the total exposure from 2-methylfuran.

117. The MOEs for non-neoplastic effects are greater than 100 and are therefore not of toxicological concern; some of the MOEs are however close to 100. Given the uncertainties in the exposure assessment, these concentrations could be a potential concern for human health.

118. No MOEs could be derived for methylfurans due to the lack of reference points.

119. Based on the available data exposures and MOEs for non-neoplastic effects were calculated for the sum of furan the two methylfurans. Most MOEs were > 100, with the exception of ready-to-eat meals and the total exposure at the 97.5th percentile for children aged 4 to 18 months; some other food groups are close to the MOE of 100. However, the exposure is conservative and there is a high degree of uncertainty in the assessment due to the lack of information on the contribution of 2-methylfuran and 3-methylfuran and the complete lack of information on 2,5-dimethylfuran.

120. Some of the exposures and MOEs presented in this assessment are a cause for concern to health, however, they are based on a limited data set for the UK. In addition, the findings in this assessment are in line with the findings by EFSA, based on a larger data set for Europe and the UK.

Questions to be asked to the Committee

i) Do the Committee agree with the approach taken by EFSA in 2017 and applied to the recent UK data from 2017?

ii) Do the Committee consider it sufficient to include a brief summary of the important points (HBGVs, exposure, conclusions) in the overarching statement?

iii) Do the members have any other comments?

Secretariat

September 2018

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https://www.gov.uk/government/statistics/ndns-results-from-years-7-and-8-combined

This is a background paper for discussion.
It does not reflect the views of the Committee and should not be cited.

Dietary occurrence data

Furan

Breakfast cereals

121. Furan was measured in 8 (33.3%) of the 24 samples of breakfast analysed, ranging from 29 to 116 µg/kg. The remaining 16 (66.7%) of the samples were below the limit of quantification (LOQ) of 25 µg/kg; of these 9 (37.5%) were below the limit of detection (LOD) of 10 µg/kg and 7 (29.2%) were at, or between the LOD and LOQ.

Biscuits

122. Furan was measured in 15 (50%) of the 30 samples analysed, ranging from 25 to 108 µg/kg. Furan was not detected in one sample. The remaining 14 samples were below the LOQ of 25 µg/kg; of these, 10 (33.3%) were below the LOD of 10 µg/kg and 4 (13.3%) were between the LOD and LOQ.

Coffee

123. Furan was measured in 13 (65%) of the 20 samples which were analysed "as prepared for consumption"; six of these samples were instant coffee samples. Investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed instant coffee. Therefore, only furan measured in the six instant coffee samples, ranging from 1 to 4 µg/kg, were used in the exposure estimates. Two of the 6 samples (33%) were below the LOQ of 2.5 µg/kg; of these, 1 was at the LOD of 1 µg/kg and the other was 2 µg/kg.

Ready-to-eat meals for children

124. Furan was measured in 16 (72.7%) of the 22 samples analysed, ranging from 2 to 98 µg/kg. Furan was not detected in 2 samples (9.1%). Four (18.2%) of the samples were below the LOQ of 5 µg/kg; and either at the LOD of 2 µg/kg or between the LOD and LOQ.

125. In line with EFSA's approach (EFSA, 2017), the dietary exposure from ready-to-eat meals was refined by assuming that all ready-to-eat meals for infants and small children were reheated in a hot-water bath without lid. The furan and methylfuran concentration results were therefore divided by reduction factors (ranging from 1.3 to 1.5) influencing furan and methylfuran levels in commercially heat-processed foods as reported in the scientific literature (EFSA, 2017).

Popcorn

126. Only 2 samples of popcorn were analysed for furan. Furan was measured in both (limit of quantification of 25 µg/kg); one at 31 µg/kg and the other at 36 µg/kg. The average value, 33 µg/kg, was used to estimate exposures.

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Dried prunes

127. Only 2 samples of dried prunes were analysed for furan. Furan was measured (limit of quantification of 5 µg/kg); one at 9 µg/kg and the other at 15 µg/kg. The average value, 12 µg/kg, was used to estimate exposures.

2-methylfuran

Breakfast cereals

128. 2-methylfuran was measured in 10 (41.7%) of the 24 samples analysed, ranging from 37 to 69 µg/kg; six between the LOD of 10 µg/kg and 4 (16.7%) above the LOQ of 25 µg/kg. The remaining 14 (58.3%) samples were non-detects.

Biscuits

129. 2-methylfuran was measured in 18 (60%) of the 30 samples analysed, ranging from 25 to 136 µg/kg; one (3.3%) at the LOD of 10 µg/kg, 3 (10%) above the LOD but below the LOQ of 25 µg/kg LOQ and 14 (46.7%) at or above the LOQ.

Coffee

130. 2-methylfuran was measured in 16 (80%) of the 20 samples which were analysed "as prepared for consumption"; six of these samples were instant coffee samples ranging from 3 to 16 µg/kg. As previously stated for furan, investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed instant coffee. Therefore 2-methylfuran measured in only the six instant coffee samples were used in the exposure estimates. One of the six samples (33%) was between the LOQ of 2.5 µg/kg and the LOD of 1 µg/kg.

Ready-to-eat meals for children

131. 2-methylfuran was measured in 2 (9.1%) of the 22 samples analysed; one at 6 µg/kg and the other at 6 µg/kg. Five of the samples (22.7%) were below the LOQ of 5 µg/kg but above the LOD of 2 µg/kg. 2-methylfuran was not detected in 15 samples (68.2%).

132. In line with EFSA's approach (EFSA, 2017), the dietary exposure from ready-to-eat meals was refined by assuming that all ready-to-eat meals for infants and small children were reheated in a hot-water bath without lid. The furan and methylfuran concentration results were therefore divided by reduction factors (ranging from 1.3 to 1.5) influencing furan and methylfuran levels in commercially heat-processed foods as reported in the scientific literature (EFSA, 2017).

Popcorn

133. Only 2 samples of popcorn were analysed for 2-methylfuran; it was measured in both samples between the LOD of 10 µg/kg and LOQ of 25 µg/kg; one at 17 µg/kg and the other at 19 µg/kg. The average value, 18 µg/kg, was used to estimate UB exposures.

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Dried prunes

134. Only 2 samples of dried prunes were analysed for 2-methylfuran. There were no detects.

3-methylfuran

Breakfast cereals

135. 3-methylfuran was not detected in any of the 24 samples that were analysed.

Biscuits

136. 30 samples were analysed; there was only one detect (14 µg/kg) which is above the LOD (10 µg/kg) but below the LOQ (25 µg/kg).

Coffee

137. 3-methylfuran was measured in 8 (40%) of the 20 samples analysed "as prepared for consumption"; none of these samples were instant coffee samples. As previously described for furan and 2-methylfuran, investigation of DNSIYC and NDNS data showed that for the age group under consideration (children aged 4 to 60 months), all the 11 respondents who recorded coffee consumption, consumed instant coffee. Since 3-methylfuran was not detected in any of the six instant coffee samples, no exposures have been estimated.

Ready-to-eat meals for children

138. 3-methylfuran was measured in 1 (6.7%) of the 15 samples analysed. 3-methylfuran was not detected in 11 samples (73.3%). Three (20%) of the samples were between the LOD of 2 µg/kg and the LOQ of 5 µg/kg.

139. In line with EFSA's approach (EFSA, 2017), the dietary exposure from ready-to-eat meals was refined by assuming that all ready-to-eat meals for infants and small children were reheated in a hot-water bath without lid. The furan and methylfuran concentration results were therefore divided by reduction factors (ranging from 1.3 to 1.5) influencing furan and methylfuran levels in commercially heat-processed foods as reported in the scientific literature (EFSA, 2017).

Popcorn

140. Only 2 samples of popcorn were analysed for 3-methylfuran. There were no detects.

Dried prunes

141. Only 2 samples of dried prunes were analysed for 3-methylfuran. There were no detects.

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TOX/2018/31 Appendix 2

Literature search terms

The focus of this scoping paper was a first comparison of estimated exposures in UK children aged 1-5 years to the current EFSA opinion (2017).

EFSA did not consider breast milk in the assessment due to a lack of available data. To confirm no new data was available since the last EFSA opinion, a literature search was carried out using PubMed.

No specific time period was covered by the search.

Search terms

Furan	and	breast milk human milk breastfeeding
Methylfuran	and	breast milk breastfeeding human milk
2-methylfuran	and	breast milk breastfeeding
3-methylfuran	and	breast milk breastfeeding

No appropriate literature was retrieved for furan and no literature was available for methylfurans.