TOX/2020/36

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

Conclusions of the Overarching Statement and Addendum on the potential risks from contaminants in the diet of infants aged 12 to 60 months – Summary tables for SACN

Background

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 0-5 years, in support of a review by the Scientific Advisory Committee on Nutrition (SACN) of Government recommendations on complementary and young child feeding. The work has been completed and both the Overarching Statement (2019) and Addendum to the Overarching Statement have been published (2020).

2. To date, the Secretariat has provided SACN with the conclusions (in table format) of the COT from the Overarching Statement, for their report on infant feeding (0 to 12 months).

3. The SACN Secretariat have now asked for tabled conclusions for their report on young children (12 to 60 months); Table 1 provides summaries of the COT conclusion for children aged 12 to 60 months, on all chemicals included in the Overarching Statement and Addendum. The SACN Secretariat have further asked if it would be possible to provide an overview of the separate statements published, including conclusions by the COT for children aged 12 to 60 months. These can be found in Table 2.

4. In the style of the SACN reports, sections of the conclusions have been highlighted in bold in both tables by the SACN Secretariat. Both Committee Chairs have seen the tabled conclusions and highlighted sections and felt it would be helpful to get a view of the Committee.

5. The Secretariat is not asking for a review of the conclusions themselves, but the Committee are invited to comment on the highlighted sections in the tables and whether they agree that the text highlighted is the most appropriate in the concluding text.

Secretariat
July 2020

1 Risks of chemical toxicity

1.1 To complement the SACN review of the scientific evidence underpinning current dietary recommendations for infants and young children in the UK, COT was asked to examine the risks of toxicity from chemicals in the diet of infants and young children and to consider whether current advice to Government should be revised.

1.2 In 2015, COT identified a number of dietary chemicals that might pose a risk to infants and young children on the basis of their known or suspected adverse effects and for which advice might be needed.

1.3 Consequently, COT published an overarching statement on the potential risks from extraneous chemicals in the diet of infants aged 0 to 12 months and young children aged 12 to 60 months (COT, 2019). In 2020, the COT published an addendum to the overarching statement on the potential risk of the remaining chemicals (COT, 2020). Table 1 provides an overview of the conclusions for all chemicals for children aged 12 – 60 months.

1.4 A number of chemicals identified for review were not included in the overarching statement or the addendum. Some of these have been subject to a full review, while others were considered to be either outside the remit of the COT or for it to be unnecessary to change COT's existing advice to government in the absence of any new data. A full list of all chemicals identified by the Committee, with the respective links to the discussion papers or statements where applicable, can be found in Table 2.

Table 1. Summary of the substance evaluations included in the 2019 COT overarching statement and the 2020 COT addendum to the overarching statement on potential chemical risks from the diet of young children (12 – 60 months)

Chemical considered	Summary of COT conclusions
Contaminants and process contaminants	
Chlorate (COT, 2019)	The data collected by the FSA on chlorate has been submitted to, and forms part of, the evaluation performed by EFSA. While further data collection has been undertaken, the data are unlikely to change the (UK) exposure assessment undertaken by EFSA or conclusions drawn therefrom. The COT therefore did not consider it necessary to undertake a full risk assessment itself. The COT agrees with the overall conclusion by EFSA. **Chronic dietary exposure to chlorate is of potential concern for high**

	consumers, particularly to individuals with mild to moderate iodine deficiency. Drinking water was the major contributor, at up to 40 to 60%. Single acute exposures to chlorate at levels found in food and drinking water, however, are unlikely to cause adverse effects, including in vulnerable individuals.
Furan and methylfurans (COT, 2019)	Non-neoplastic effects of furan are not of toxicological concern, the combined exposures of furan and methylfurans however are of potential toxicological concern. Neoplastic effects of furan for young children[1] for ready-to eat-meals and total exposure are of **potential toxicological concern**. However, there is a level of uncertainty concerning the carcinogenic MoA of furan and whether it is directly genotoxic and the COT acknowledges that its assessment is based on worst case assumptions. The lack of occurrence data for methylfurans add to the uncertainties for the summed exposure and could therefore lead to an over- as well as underestimation of risk.
Hexachlorocyclohexanes (COT, 2020)	The COT concluded that the exposures in the diet of young children aged 12 to 60 months are **not of toxicological concern.**
Legacy chemicals* (COT, 2019)	Although these chemicals are persistent in the environment, their levels have decreased since their use was banned. **As the levels for legacy chemicals are expected to further decline,** the COT confirmed the conclusions of its previous assessments, that **there is no indication of concern** for health from the presence of these chemicals in the diet of young children.
Monochloropropanediol (MCPD), its fatty acid and glycidol (COT, 2020)	Given the limited UK-specific occurrence data, the COT assessed 3-MCPD, its fatty acid esters and glycidol, based on the latest EFSA evaluation. Overall, the COT agreed that some of EFSA's MOE values for glycidol and exceedances of the TDI for 3-MPCD are of **potential concern** for young children aged 12 to 60 months. However, as concluded by EFSA, there are a number of uncertainties in these risk assessments such as uncertainty in the reference point used as a basis for the calculation of the MOE values for glycidol, and the long-term effects of 3-MCPD

[1] Following EFSAs approach the exposure estimates were calculated using age categories of 4 to 18 months and 18 to 60 months for furan and methylfurans. The latter have been used to cover the conclusions for this report.

	on the male reproductive system, as well as in the occurrence data.
Perchlorate (COT, 2019)	The data collected by the FSA on perchlorate have been submitted to, and are part of, the evaluation performed by EFSA. The COT therefore did not consider it necessary to undertake a full risk assessment itself. In agreement with EFSA, the COT concluded that while there are considerable uncertainties in the assessment, the chronic and short term estimated exposures for young children are of **potential concern**, particularly in the case of a mild to moderate iodine deficiency.
Polycyclic aromatic hydrocarbons (PAHs) (COT, 2020)	The COT concluded that the intakes of PAHs (BaP and PAH4) from human breast milk and food are of **low concern** for health for children aged 12 to 60 months. Intakes from soil and dust are not expected to contribute markedly to lifetime exposure.
Tetrabromobisphenol (COT, 2020)	Given the absence of genotoxicity, tumours only at high doses, large MOEs, and conservatism of exposure estimates based on non-detects, a MOE of 100 was considered to be sufficiently protective for human health. Thus, the calculated MOEs for UK chronic dietary exposures were considered **not to be cause for concern** for children aged 12 to 60 months.
Food Additives	
Food additives (COT, 2019)	The additives regulation applies to all foods produced, including foods specifically for young children. Therefore, the COT deemed it not necessary to assess food additives again in these age groups.
Sweeteners (COT, 2020)	The COT concluded that the exposures in the diet of children aged 12 – 60 months of the most commonly used sweeteners in the UK (aspartame, acesulfame K, saccharine, sorbitol and xylitol, stevia and sucralose) were **not of toxicological concern**.
Natural Toxins - Mycotoxins	
Aflatoxin (COT, 2020)	Aflatoxin levels in all samples in the TDS were below their respective LOQ. However, **given that aflatoxins are genotoxic and carcinogenic** their presence in food is always undesirable and when exposure was estimated based on their LOQs, it was **not possible to exclude a safety concern**.

Citrinin (COT, 2020)	The COT concluded that exposures to citrinin are **not of toxicological concern for nephrotoxicity**. However, it was noted that due to lack and limitations of the available data, **a concern for genotoxicity and carcinogenicity cannot be excluded**.
Cyclopiazonic acid (COT, 2020)	The COT concluded that the exposures in the diet of children aged 12 to 60 months are **not of toxicological concern.**
Diacetoxyscirpenol (COT, 2020)	The COT concluded that the exposures in the diet of children aged 12 to 60 months are **not of toxicological concern.**
Deoxynivalenol (DON) and its acetylated/modified forms (COT, 2020)	The COT concluded that exposures to DON, 15-Ac-DON, 3-Ac-DON, and the sum of all three forms in the diets of children aged 12 to 60 months are **unlikely to be of toxicological concern**. However, the COT noted that the sum of all forms is not based on individual measured values but on summing the respective averages of the concentrations provided. Therefore, the estimated exposures could be an overestimation of the actual values.
Ergot alkaloids (COT, 2020)	The COT concluded that the exposures in the diet of children aged 12 to 60 months are **not of toxicological concern**.
Fumonisins (COT, 2020)	The COT concluded that the exposures in the diet of children aged 12 to 60 months are **not of toxicological concern**.
Fusarenon-X (COT, 2020)	The COT concluded that exposures to fusarenon-X in the diets of young children aged 12 to 60 months are **not of toxicological concern**. However, the COT noted that there were some uncertainties involved in the extrapolation of the data. The Committee agreed that the likelihood of co-occurrence of fusarenon-x with other type B trichothecenes, deoxynivalenol and nivalenol, at the reported levels is low and that acute co-exposure was unlikely to result in adverse toxicological effects.
Moniliformin (COT, 2020)	The COT concluded that the exposures in the diet of young children aged 12 to 60 months are **not of toxicological concern**.

Nivalenol (COT, 2020)	The COT concluded that the exposures in the diet of young children aged 12 to 60 months are **not of toxicological concern**.
Patulin (PAT) (COT, 2020)	The COT concluded that exposures to PAT in the diets of young children aged 12 to 60 months are **not of toxicological concern**, but this is **contingent on resolution of the genotoxic potential of PAT**.
Sterigmatocystin (COT, 2020)	The COT concluded that the exposures in the diet of young children aged 12 to 60 months are **not of toxicological concern**.
Zearalenone (COT, 2020)	The COT concluded that the exposures in the diet of young children aged 12 to 60 months are **not of toxicological concern**.
Natural Toxins – other than mycotoxins	
Alcohol (COT, 2019)	As children aged 12 to 60 months would not be consuming alcohol directly, any further assessment of alcohol in this age group is not required.
Caffeine (COT, 2019)	As children aged 12 to 60 months would not be expected to be consuming high-caffeine beverages, the COT concluded that no further assessment of caffeine for this age group is required.
Soya phytoestrogens ** (COT, 2019)	In the absence of any more recent data, the COT decided to base its conclusion on its previous evaluation, that there is no scientific basis for a change in the current advice for children aged 0 to 12 months and that soy formula should be used only in exceptional circumstances. There are also potential concerns for children up to 5 years of age consuming soy drinks. A full statement will be available in due course.
Tropane alkaloids (TAs) (COT, 2020)	Overall, all estimated acute exposures of young children aged 12 to 60 months to (-)-hyoscyamine and (-)-scopolamine or the sum of **(-)-hyoscyamine and (-)-scopolamine are unlikely to be of toxicological concern**. However, the COT noted that a number of other TAs of unknown potency were present at higher concentrations than (-)-hyoscyamine and (-)-scopolamine, with some of these reported at detectable levels in up to 26% of the cereal-based samples. In the absence of any toxicological data and HBGVs on these TAs there is a **high degree of uncertainty to the risks associated with total TAs** in the diet.

Nutrient	
Chromium (COT, 2019)	Chromium is present in food and the environment largely as Cr(III). EFSA has established a TDI for Cr(III) of 300 µg/kg bw. Estimated dietary exposures for young children aged 12 to 60 months indicate chromium intake well below the TDI and is therefore considered **not to be of toxicological concern**. Environmental exposure to Cr(III) from dust, soil and air was calculated to be at most 0.038, 0.15 and 0.036% of the EFSA TDI, respectively and is therefore considered not to be of toxicological concern.
Selenium (COT, 2019)	Overall the COT concluded that estimated dietary exposures to selenium for young children aged 12 to 60 months were below the UL and are therefore **unlikely to be of toxicological concern**.
Vitamin A (COT, 2019)	Following its update in 2017, the COT concluded that the **possibility of adverse effects cannot be excluded in high consumers, primarily those who regularly eat liver**. However, if effects did occur it would be in a small proportion of consumers. The COT found no scientific basis for a change in current Government advice.
Zinc (COT, 2019)	The COT concluded, that overall, estimated dietary exposures do not indicate excessive zinc intakes and are therefore **unlikely to be of toxicological concern**. However, the COT did note that all HBGVs and UL are derived from adults and it is therefore difficult to identify a HBGV or UL that is applicable to young children.

*(including aldrin, dieldrin, endrin, chlordane, heptachlor, hexachlorobenzene, mirex, toxaphene, DDT, endosulfan, pentachlorobenzene, chlordecone)

** Update since the overarching statements publication: Soya phytoestrogens are currently undergoing a separate review, with emphasis on soya drink consumption in children aged 6 months to 5 years.

Table 2. Summary of evaluations for chemical that underwent a separate full COT review

Chemical considered	Summary of COT conclusions	Web link
Acrylamide	For exposure of young children to acrylamide from infant formula and food, the COT concluded that the MOEs did not suggest **any concern regarding neurotoxicity**. Although human studies do not prove that acrylamide causes cancer, there is a **potential concern regarding (genotoxic) carcinogenicity** relating to exposures in this age group based on extrapolations from experimental studies.	https://cot.food.gov.uk/sites/default/files/finalacrylamidestatement.pdf
Aluminium	Whilst there are some uncertainties in the overall risk assessment surrounding the potential aggregated exposure, including exposures from soil and dust, the COT concluded that estimated exposures of young children to aluminium from the diet, including soya-based infant formula, **do not indicate toxicological concerns** or a need for any modification in advice to Government.	https://cot.food.gov.uk/sites/default/files/finalaluminiumaddendum_0.pdf
Arsenic	The COT concluded that the total exposure to inorganic arsenic, from dietary and non-dietary sources, in young children aged 12 to 60 months was of **potential concern** to health. Dietary sources generally contribute more significantly to exposure in these age groups than non-dietary sources such as soil and dust.	https://cot.food.gov.uk/sites/default/files/finalstatementonarsenic_0.pdf
Bisphenol A	The COT is awaiting EFSAs new scientific opinion to conclude if a new COT evaluation is required.	
Copper	The COT concluded that intake of copper by young children aged 12 to 60 months through consumption of breast milk, infant formula, food and drinking water was	https://cot.food.gov.uk/sites/default/files/cotstatementoncopper.pdf

	below the safe upper level derived by the EVM and thus that there was **no toxicological concern** to the health of infants and young children with normal copper homeostasis.	
Cadmium (Cd)	Although the EFSA TWI of Cd was exceeded in some cases, these exceedances were small in magnitude and would not be expected to remain at this level over the decades of bioaccumulative exposure considered by EFSA in setting the HBGV. The COT concluded that this was therefore **not a major cause for concern**.	https://cot.food.gov.uk/sites/default/files/cotstatementoncadmium.pdf
Dioxins and dioxin-like compounds	EFSA confirmed its conclusion in 2018 that the dietary exposure to dioxin and dioxin-like PCBs is a health concern. Data from European countries indicate an exceedance of the new TWI across all age groups, including young children. The COT questioned the applicability of the new TWI to the whole population, and after recent discussions with the industry, the FSA has been asked to give a more detailed consideration of the new TWI and an assessment by the COT is currently ongoing,	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5333
Hexabromocyclododecane (HBCDDs)	The COT concluded that while the **level of HBCDDs in the diet of young children was not a cause for concern**, the possibility of high levels in household dust continues to be so. Levels in dust should be monitored in houses to determine whether they decrease, now that production and usage of HBCDDs has largely ceased.	https://cot.food.gov.uk/sites/default/files/finaladdendumonhbcdds.pdf
Iodine	The COT concluded that at current intakes, excess iodine is **unlikely to pose a toxicological risk to health**.	https://cot.food.gov.uk/sites/default/files/statementiodine0to5.pdf

Lead	The COT concluded that for young children, the **risk from dietary exposure alone is small** and there is no need for specific dietary advice relating to lead. However, when the possible contribution from soil and dust was taken into account, the possibility of adverse health effects cannot be excluded.	https://cot.food.gov.uk/sites/default/files/finaladdendumonlead.pdf
Manganese	The COT was **unable to draw firm conclusions** on the potential effects of dietary exposure on the neurodevelopment of children ages 12 to 60 months because it was not possible to relate the adverse effects observed in humans to dietary exposures. Further data is required to refine this risk assessment, although any risk at current dietary exposures is likely to be low.	https://cot.food.gov.uk/cotstatements/cotstatementsyrs/cot-statements-2018/statement-on-the-health-effects-of-manganese-in-the-diets-of-infants-aged-0-12-months-and-children-aged-1-5-years
Methylmercury	The COT concluded that when taking into consideration the high degree of conservatism in the exposure modelling, there was **low risk to health** from the potential minor exceedance of the TWI in children aged 12 to 60 months However, it would be prudent to maintain existing advice regarding consumption of large predator fish.	https://cot.food.gov.uk/sites/default/files/cotstatementonmethylmercury.pdf
Nickel	The COT concluded that **chronic exposure to nickel from food was of no toxicological concern** to the long-term health of young children aged 12 to 60 months. Acute dietary exposure to nickel in sensitised individuals could trigger or exacerbate potentially unpleasant dermal effects.	https://cot.food.gov.uk/sites/default/files/statementonpotentialrisksofnickel.pdf
Ochratoxin A (OTA)	The COT concluded that in young children consuming commercial foods for these age groups, exposures were well below the TWI and hence there was **no toxicological concern**.	https://cot.food.gov.uk/sites/default/files/cotstatement-ota.pdf

Perfluorooctan esulfonic (PFOS) acid and Perfluorooctan oic (PFOA) acid	The EFSA panel concluded that, for both compounds, exposures in a considerable proportion of the population exceed the proposed TWIs and these exceedances at the upper level of the estimates are of concern to human health. However, EFSA also noted that the present exposure assessment is highly uncertain as analytical methods are currently not sufficiently sensitive Furthermore, it is unclear what impact processing has on exposure as well as the impact of co-exposure to multiple PFAS on health-related outcomes. The COT agreed with the uncertainties surrounding PFOS and PFOA and concluded to await EFSAs publication on perfluoroalkyl substances (PFAS)[2]. The COT[3] have reviewed the recently published EFSA draft scientific opinion on 'the risks to human health of perfluoroalkyl substances (PFAS) in food' for public consultation and an updated COT statement will be published in due course.	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5194 PFAS opinion for public consultation http://www.efsa.europa.eu/en/consultations/call/public-consultation-draft-scientific-opinion-risks-human-health
Phthalates	EFSA (2019) establish a group TDI for DINP with DEHP, DBP, BBP in a low tier cumulative risk assessment, based on the reproductive effects and a plausible common mode of action. Exposures were below the TDI for European consumers of any age, including the most sensitive groups. The COT considered it reasonable to group those four phthalates and that the group TDI and the relative potency factors were appropriate for DEHP, DBP and BBP. Furthermore, the COT were content that the exposures estimated by EFSA did not	http://www.efsa.europa.eu/sites/default/files/consultation/consultation/Phthalates_in_plastic_FCM_draft_opinion_for_public_consultation.pdf

[2] INSERT COT meeting minutes March
[3] INSERT COT meeting minutes May

	indicate a health concern using the group TDI but noted that the uncertainty assessment in the draft opinion did not adequately reflect on the conclusions on DINP.	
Polybrominated biphenyls (PBBs)	The COT concluded that, taking into account all of the uncertainties surrounding the exposure estimates, the contributions made by planar PBBs to the TDI for dioxin-like compounds were minor, and the large margins of exposure in the assessment of non-planar PBBs **did not indicate a cause for concern**.	https://cot.food.gov.uk/sites/default/files/tox2015-34.pdf
Polybrominated diphenyl ethers (PBDEs)	The COT concluded that the **exposures from breast milk** (12 to 18 months of age) **and dust and soil** (12 to 60 months) **are of potential concern. Exposure from food was unlikely to be of concern.** However, given that PBDEs are no longer used commercially, the levels are therefore expected to decrease and are the sources of PBDEs for exposure in young children, the options for risk management are limited. The **COT however recommended for monitoring to be continued to ensure levels are declining as expected**.	https://cot.food.gov.uk/sites/default/files/statementpbdes.pdf
T-2 toxin, HT-2 toxin and neosolaniol	Whilst an effect on health cannot be entirely excluded at the 97.5th percentile exposure, it is doubtful that children would be regularly exposed to these levels. Overall, the COT therefore concluded that dietary exposure levels of T2, HT2 or NEO were **unlikely to be of any toxicological concern** in young children.	https://cot.food.gov.uk/sites/default/files/cotstatement-t2ht2andneosolaniol.pdf

Conclusions

1.5 The COT assessed a number of chemicals and their potential risk from the diet of infants (aged 0 to 12 months) and young children (age 12 to 60 months). The following paragraphs provide the conclusions for the latter age group; conclusions for

infants aged 0 to 12 months can be found in the SACN report ‘Feeding in the first year of life’ (SACN, 2018).

1.6 The COT refers to and confirms its previous evaluations for legacy chemicals, soya phytoestrogens, and vitamin A. As children aged 12 to 60 months would not be expected to be consuming high-caffeine beverages or alcohol, the COT concluded that no further assessment for these two chemicals in this age group is required.

1.7 The additives regulation applies to all foods produced, including foods specifically for young children. Therefore, the COT deemed it not necessary to assess food additives again in these age groups.

1.8 The data collected by the FSA on perchlorate and chlorate have been submitted to, and form part of, EFSAs evaluations. While further data collection has been undertaken for chlorate, the data are unlikely to change the (UK) exposure assessment undertaken by EFSA or conclusions drawn from them. The COT therefore did not consider it necessary to undertake a full risk assessment for either chemical itself. In agreement with EFSA, the COT concluded that while there are considerable uncertainties in the assessment there is potential concern from dietary exposure to chlorate and perchlorate.

1.9 Given the limited UK-specific occurrence data, the COT assessed 3-MCPD, its fatty acid esters and glycidol based on the latest EFSA evaluation. Overall, the Committee agreed that some of EFSA’s MOE values for glycidol and exceedances of the TDI for 3-MPCD are of potential concern. However, as concluded by EFSA, the impacts of the uncertainties in these risk assessments for glycidol and 3-MCPD are high, for example uncertainty in the reference point used as a basis for the calculation of the MOE values for glycidol, and the long-term effects of 3-MCPD on the male reproductive system, as well as in the occurrence data.

1.10 There have been efforts to reduce concentrations of furan (and methylfurans) in food over recent years but the evidence so far is not sufficient to demonstrate whether there has been a decrease in dietary exposure. The exposures in the COT’s assessment are of potential toxicological concern and efforts to reduce furan and methylfurans should therefore continue. However, there are numerous uncertainties in the assessment and the COT acknowledges that its assessment is based on worst case assumptions.

1.11 For exposure of young children to acrylamide from infant formula and food, the COT concluded that there was no cause for concern regarding neurotoxicity. Although human studies do not prove that acrylamide causes cancer, there is a potential concern regarding carcinogenicity relating to exposures in this age group based on extrapolations from experimental studies.

1.12 Aflatoxin levels in all samples in the FSA's TDS survey were below their respective LOQ. However, given that aflatoxins are genotoxic and carcinogenic their presence in food is always undesirable and when exposure was estimated based on their limit of quantifications (LOQs), it was not possible to exclude a safety concern.

1.13 The COT concluded that the total exposure to inorganic arsenic, from dietary and non-dietary sources, in young children aged 12 to 60 months was of potential concern to health.

1.14 Given the data gaps and limitations in the information for deoxynivalenol and its acetylated/modified forms, citrinin, patulin, manganese and tropane alkaloids, a potential health effect currently cannot be excluded.

1.15 For bisphenol A, dioxins, phthalates and perfluorooctanesulfonic acid perfluorooctanoic acid and perfluoroalkyl substances the COT decides to wait for EFSA's re-evaluation or is in the process of commenting on said publications.

1.16 Exposures to aluminium, cadmium, chromium, copper, iodine, lead, nickel, selenium, zinc, hexachlorocyclohexane, hexabromocyclododecane, methylmercury, ochratoxin A, polybrominated biphenyls, polycyclic aromatic hydrocarbons, tetrabromobisphenol, tropane alkaloids, T-2 toxin, HT-2 toxin, the five most common sweeteners in the UK (aspartame, acesulfame K, saccharine, sorbitol and xylitol, stevia and sucralose) and several mycotoxins (cyclopiazonic acid, diacetoxyscirpenol, ergot alkaloids, fumonisins, fusarenon-X, moniliformin, nivalenol, sterigmatocystin and zearalenone) are not of toxicological concern.