Meeting

Initial paper on further work on PFAS

Introduction

1. The COT has previously considered per- or poly-fluoroalkyl substances (PFAS) on a number of occasions, and has recently published a statement on the European Food Safety Authority (EFSA) opinion "Risk to human health related to the presence of perfluoroalkyl substances in food" (see Annex A for information). The Committee is now asked to consider what further guidance can be provided to support human health risk assessments undertaken by UK Government Departments and Agencies.

Background

2. PFAS are a class of over 12,000 fluorinated substances (US EPA CompTox Dashboard 2022) that have been produced since the 1940s and which are or have been used in a broad range of consumer products and industrial applications (Glüge *et al*., 2020). There are differing definitions for PFASs, however they are predominantly substances with a hydrophobic alkyl chain of varying length (typically C4-C16), which is fully or partially fluorinated, and a hydrophilic end group. PFAS are highly persistent due to the strong covalent C-F bond. In addition many PFAS are potential precursors of others.

3. A range of health outcomes associated with PFAS have been studied. Human epidemiological data suggests effects on the immune system, increased cholesterol, increase in liver enzymes, and limited evidence for an association with cancer. Studies in laboratory animals have shown effects on the liver and immune system, neurodevelopmental effects, and effects on reproduction and development (COT, 2022).

4. In 2006, COT published statements on tolerable daily intakes (TDIs) for perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), recommending TDI values of 0.3 micrograms per kilogram bodyweight per day

(µg/kg bw/day) for PFOS and 3 µg/kg bw/day for PFOA (COT, 2006a; COT 2006b). In 2009, the COT re-evaluated PFOA in light of opinions from EFSA and the US Environmental Protection Agency (US EPA). At that time, COT recommended a TDI of 1.5 µg/kg bw/day for PFOA, as well as confirming its previous recommendation on PFOS (COT, 2009).

5. In 2014, the COT considered the potential risks from PFOS in the infant diet, and used both the 2006 COT TDI for PFOS, and a 2008 EFSA TDI, as part of the risk characterisation, but acknowledged newer data were available, which EFSA was at that time reviewing (COT, 2014).

6. EFSA has also undertaken a number of activities on PFAS, and most recently in 2020 published its opinion "Risk to human health related to the presence of perfluoroalkyl substances in food". EFSA considered the evidence for potential health effects for a number of PFAS substances, and established a Tolerable Weekly Intake (TWI) for the sum of four PFAS: PFOA, perfluorononanoic acid (PFNA), perfluorohexane sulfonate (PFHxS) and PFOS, of 4.4 nanograms per kilogram bodyweight per week (ng/kg bw/week) (EFSA, 2020).

7. COT considered the latest EFSA opinion both in draft form and following publications, and noted a number of uncertainties in the assessment. These included reservations about the choice of the critical study and the effect selected, while accepting it was the best available; about the model used and the benchmark dose (BMD) approach; noting that the BMDL and TWI were low and with a lot of uncertainty in the data used; concerns over the exposure estimates; and flagged that there are strong caveats in comparing exposure estimates with the TWI due to uncertainty in the appropriateness of the derivation of the TWI and of the biological significance of the response on which the EFSA TWI is based (COT, 2022).

8. A number of other health-based guidance values (HBGVs) and regulatory values from other countries and international bodies are also available (e.g. US EPA, Health Canada, the US Agency for Toxic Substances and Disease Registry (ATSDR), Australia). These are predominantly for PFOA, PFOS, PFNA, PFHxS as well as a few other PFAS. The choice of sensitive endpoints vary between the different organisations, and some have used animal data while others have used human data as the basis for the HBGVs. In addition, a number of organisations are considering PFAS and are expected to publish their findings in the coming years (e.g. World Health Organization (WHO)).

Current risk assessment challenges for FSA and UKHSA

9. The Food Standards Agency (FSA) and UK Health Security Agency (UKHSA) provide human health risk assessments in response to monitoring for PFAS in a variety of media (e.g. food, water, land), and support regulatory decision making on PFAS in these media. This has a number of challenges which will be outlined in this section.

10. As noted above, there are many possible PFAS substances. Analytical methods have been developed for a number of these substances, and as more methods for more compounds become available, the range of compounds being analysed for is increasing. For example, the Environment Agency is currently undertaking a monitoring programme of PFAS in surface and ground water and over 40 compounds are being assessed as part of this programme.

11. There are few PFAS substances for which HBGVs are available, and for most PFAS substances there is little or no available toxicity data either. As there are fewer HBGVs available than there are PFAS that can be measured, and multiple substances may be present in the same samples, risk assessors have to make pragmatic decisions on how best to approach the assessment of all the detected substances. This may be by summing all the PFAS present, or grouping substances with similar chemical structure, which brings uncertainty to the assessment. The EFSA TWI used an approach for consideration of the sum of PFOA, PFNA, PFHxS and PFOS, however no further guidance is provided on appropriate assessment of other PFAS which may be present in the same samples. Nor is it clear how a sample could be risk assessed if none of these four substances were present.

12. With the COT statement flagging some of the uncertainties with respect to the EFSA TWI, and awareness of a number of other available HBGVs, there are a number of values to which risk assessors can compare exposure estimates derived from monitoring data. It would be helpful to have either a HBGV or group of HBGV values for PFAS from COT, or a general view from COT on the suitability of the available values.

13. As noted in the COT 2022 statement on the EFSA opinion, there are uncertainties in the biological significance of the response on which the TWI is based. Risk assessors regularly estimate exceedances of the EFSA TWI, however, given the uncertainty in the biological significance, it is difficult to communicate

about what this might mean in terms of health risk to people exposed to the media of concern, and thus determine any appropriate measures required to protect public health.

14. Finally, in the EFSA assessment, it is noted that infant exposure via the mother following breastfeeding is taken into account during the derivation of the TWI for the rest of the population, and thus infant exposure should not be compared with the TWI. However, when assessing PFAS in drinking water for example, intakes are calculated for bottle-fed infants as part of the risk assessment, with caveats on the interpretation of the results.

Outline plan of series of papers for COT consideration

15. It is acknowledged that making a thorough evaluation of PFAS is likely to be a significant piece of work and take some time. Therefore it is suggested that in the more immediate term, it would be helpful to prepare an ‘interim’ position paper to provide some immediate advice to Government Departments and Agencies risk assessors on the interpretation and level of concern of exceedances of the EFSA TWI, including the applicability to children and non-breast-fed infants. In addition, any immediate guidance on consideration of other PFAS could also be provided*, e.g.* with a grouping or read across approach. This position paper would also note the longer review of the topic to support UK risk assessment.

16. In the longer term, there are a number of aspects to consider:

i). Which PFAS substances can be considered, and whether there is a means of ‘future-proofing’ for new substances.

ii). The available data on toxicity across PFAS substances, including: weight of evidence for health effects, as some epidemiology findings are not replicated across different populations, utilising a Joint COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence subgroup (SEES/SETE) approach; exploring toxicity of PFAS substances beyond those considered by EFSA and others; evaluating differences in data between substances, and consider whether NAMs could be used to extrapolate between different PFAS, and whether any distinction can be made on potential potency; and whether biomonitoring data can be used to support risk assessment, including accounting for analytical issues in utilising the data.

iii). Detailed review of available HBGVs, including the endpoints these are based on and whether from human or animal studies, and the basis for regulatory or other values in food, water and soil from other authorities, *e.g.* US EPA health advisories, EU Drinking Water Directive values.

iv). Consider the available exposure data, noting issues with analytical capability and the challenges of demonstrating compliance with standards, and whether these enable appropriate risk assessment. Data is likely to be available for ground and surface water and may be available for drinking water, food and soils. In addition, a search will be conducted for levels in breastmilk. Where possible data for different PFAS 'groups' will be presented.

17. In terms of strategy of work, it may be helpful to utilise a SETE approach for this consideration.

Questions on which the views of the Committee are sought

18. Members are invited to consider the following questions:

i). Is the Committee content with the proposal to draft an interim position statement initially and then continue with the longer series of papers?

ii). Are there any additional aspects that Members consider would be helpful to support the Committee's considerations

iii). Are there any endpoints in particular that should be focussed on, or can any be set aside, at this stage?

iv). Would a SETE approach be helpful for this consideration?

v). Would a subgroup be helpful for consideration of this topic?

vi). Are Members aware of any data gaps that could be filled with specific research projects?

vii). Do Members have any other comments?

Secretariat

October 2022

List of Abbreviations and Technical terms

ATSDR	US Agency for Toxic Substances and Disease Registry
EFSA	European Food Safety Authority
FSA	Food Standards Agency
HBGV	health-based guidance value
PFAS	per- or poly-fluoroalkyl substances
PFHxS	perfluorohexane sulfonate
PFNA	perfluorononanoic acid
PFOA	perfluoronooctanoic acid
PFOS	perfluorooctane sulfonate
SETE	Joint COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence subgroup
TDI	Tolerable Daily Intake

TWI	Tolerable Weekly Intake
UKHSA	UK Health Security Agency
WHO	World Health Organization

References

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TOX/2022/53 Annex A

COT statement on the EFSA opinion on the risks to human health related to the presence of perfluoroalkyl substances in food

This statement is available on the COT website:

TOX_2020_60_First draft statement on published EFSA PFAS Opinion (food.gov.uk)

Secretariat

October 2022