

Introduction and Background - PFAS/2023/03

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This is a paper for discussion.

This does not represent the views of the committee and should not be cited.

Introduction

1. This paper is part of a series of papers supporting the COT assessment of the toxicological assessment of PFAS. This paper provides the evidence on in vivo thyroid toxicity. Later papers will include new approach methodologies (NAMS) and human evidence, and other endpoints including developmental, liver toxicity and immunotoxicity.

Background

2. In 2020 the European Food Safety Agency (EFSA) published an opinion “Risk to human health related to the presence of perfluoroalkyl substances in food” in which tolerable weekly intake (TWI) for perfluoroalkyl substances (PFASs) of 4.4 ng/kg bw/week was determined (EFSA., 2020). This was based on a human study from which the lowest benchmark dose of 17.5 ng/mL serum was calculated for 1-year old children, based on the sum of four PFAS. This serum value was extrapolated to long-term maternal exposure of 0.63 ng/kg bw/day using PBPK modelling, which was converted to the TWI due to the accumulation of PFAS over time.
3. This TWI is lower than EFSA’s previous tolerable intake of 13 ng/kg bw/week for PFOS and 6 ng/kg bw/week for perfluorooctanoic acid (PFOA) (EFSA., 2018) based on increased serum cholesterol in adults and a decrease in antibody response at vaccination in children, and increased serum cholesterol, respectively. Liver toxicity and a reduction in birth weight were also considered for PFOA.
4. The COT has previously considered PFAS on a number of occasions (see summary in [TOX/2022/53](#)), and has recently published [a statement on the EFSA opinion](#). A paper summarising health-based guidance values (HBGV) was presented in December 2022 ([TOX/2022/67](#)) and following agreement in March 2023 the PFAS subgroup was established and [an interim position](#) published outlining future work.
5. This paper is the first in a series of papers supporting the COT subgroup on the risk assessment of PFAS.

Literature search

6. Search terms used previously by (EFSA, 2018) and EFSA (2020) were replicated. Such search terms, inclusion and exclusion criteria and the search results are presented in Annex A to this paper.

Toxicity of PFAS

7. *In vivo* thyroid toxicity data following acute exposure to perfluoroalkyl carboxylic acids (PFCAs) and perfluorosulfonic acids (PFSAs) are presented in Table 1 and Table 2, respectively, and thyroid toxicity effects following repeated exposure are presented in Table 3 and Table 4, respectively. Narrative summaries of the studies are provided below.

