

In vivo thyroid toxicity studies - PFAS/2023/04

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6. For perfluorosulfonic acids (PFSAs), *in vivo* acute toxicity studies are available for perfluorooctane sulfonic acid (PFOS) and are presented in Annex A Table 3; for perfluoroalkyl carboxylic acids (PFCAs) *in vivo* acute toxicity studies are available for perfluorodecanoic acid (PFDA) and are presented in Annex A Table 4.

7. For PFSAs, repeated dose toxicity studies are available for perfluorobutane sulfonic acid (PFBS), perfluorohexanesulfonic acid (PFHxS) and PFOS presented in Annex A Table 5 to Table 7, and for PFCAs repeated dose studies are available for perfluorobutanoic acid (PFBA), perfluorohexanoic acid (PFHxA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), PFDA, perfluorotetradecanoic acid (PFTeDA) and perfluorohexadecanoic acid (PFHxDA) and are presented in Annex A Table 8 to Table 13.

8. For PFSAs, developmental toxicity studies are available for PFBS, PFHxS and PFOS, and are presented in Annex A Table 15 to Table 17, and for PFCAs developmental toxicity studies are available for PFOA and are presented in Annex

A Table 18.

9. From the 34 published sources, a total of 50 studies were carried out on 10 PFAS. Annex A Table 3 to Table 18 present no observed adverse effect levels (NOAELs) and lowest observed adverse effect level (LOAELs) based on thyroid effects.

10. The current paper considers effects in adult animals following exposure to PFAS by gavage, intraperitoneal (i.p) injection, diet or drinking water.

11. Data for 10 PFAS were identified, although most of the data relate to three PFAS: PFOS and PFHxS (PFSA) and PFOA (PFCA).

12. Eight acute studies have been identified, for PFOS and PFDA.

13. Of the 26 repeated dose studies identified, 13 were carried out with PFSA (PFHxS, PFOS) and 13 with PFCA (PFBA, PFHxA, PFOA). Only one study was carried out with PFBS, PFNA, PFDA, PFHxDA and PFTeDA.

14. Of the 16 development toxicity studies identified, three were carried out on PFSA (PFBS, PFHxS, PFOS) and one on PFCA (PFOA). Only effects in the dam are discussed in the endpoint summaries below. Developmental effects in offspring, as a result of exposure during gestation and/or lactation, will be evaluated in subsequent papers.

15. The majority of acute and repeated dose studies were conducted in rats, with the exception of a single acute study in mice, and two acute studies and two repeated dose studies that were carried out in Cynomolgus monkeys. Developmental studies were carried out in mice and rats.

16. An overview of the PFAS chemical structure and molecular weight is presented in Annex C to this paper. Depending on the PFAS, studies have investigated the acid form, or a sodium, ammonium or potassium salt.

Endpoints investigated

17. Exposure to PFAS caused a number of thyroid effects in animals including effects on thyroid hormone (TH) levels, effects on thyroid histopathology and thyroid weight, impacts on gene transcription and associated process in the thyroid and other tissues.

18. Thirty-eight of the 50 studies (reported in the 34 published sources) measured THs, although not all THs were measured in each study, 25 included histopathology, 17 measured thyroid weight, and six included gene expression related to thyroid effects.

19. Observed effects at the LOAEL are based on statistically significant results. Effects seen at higher doses are not included. Abbreviations used in the tables are not spelled out.