# PFOA

## In this guide

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## *In vivo* toxicity data

### Conley *et al*, 2022

175. Conley *et al*. (2022) investigated the effects of PFOA exposure on TH in rats. In a developmental study, pregnant SD rats (5/group) were administered PFOA ammonium salt at doses 0, 10, 30, 62.5, 125 and 250 mg/kg bw/day by gavage from GD8 – PND2. Dams and offspring were sacrificed on PND2 and blood was collected for various analyses: TT4, TT3, FT3, FT4 and PFOS in dams, and TT4, TT3 and rT3 in offspring.

176. Mortality: In dams, due to a significant reduction in body weight at 250 mg/kg bw/day within 3-4 days of treatment, animals were euthanised. In offspring, survival was significantly reduced at 125 mg/kg bw/day, compared with controls.

177. General toxicity and body weight: No clinical signs of general toxicity were reported. In dams, significant weight loss was observed in 2 of the 5

dams at 125 mg/kg bw/day within 4 – 5 days treatment, and exposure was terminated for these animals. Body weight on GD22 and body weight gain on GD8-GD22 were significantly reduced at ≥62.5 mg/kg bw/day, while body weight on PND2 and body weight gain om GD8-PND2 were reduced at 125 mg/kg bw/day, compared with controls. In offspring, birthweights were significantly reduced at 10 and ≥ 62.5 mg/kg bw/day, while adjusted birthweights and body weights on PND2 were significantly reduced only at ≥62.5 mg/kg bw/day.

178. Thyroid hormone levels: In dams, TT4 and TT3 levels were significantly reduced at ≥10 mg/kg bw/day, compared with controls, while FT3 and FT4 levels were significantly reduced at 10, 62.5 and 125 mg/kg bw/day. In offspring, TT3 and TT4 levels were significantly reduced at ≥10 mg/kg bw/day while rT3 was significantly reduced at 10 and 30 mg/kg bw/day but significantly increased at 125 mg/kg bw/day.

179. Serum PFOA concentrations: In dams, mean PFOA concentrations were 0.16 µg/mL (controls), 31.8 µg/mL (10 mg/kg bw/day), 96.1 µg/mL (30 mg/kg bw/day), 168.9 µg/mL (62.5 mg/kg bw/day) and 280.0 µg/mL (125 mg/kg bw/day).

180. The authors concluded PFOA reduced serum TH concentrations, which occurred at nearly all doses depending on the specific hormone and life stage (maternal or neonatal).

## NTP, 2022a

181. NTP (2022a) investigated the effects of PFOA on thyroid weight, histopathology and TH levels in rats. In a repeated dose study, SD rats (10/sex/group) were administered PFOA at doses 0, 0.625, 1.25, 2.5, 5 or 10 mg/kg bw/day) for males, or 0, 6.25, 12.5, 25, 50, or 100 mg/kg bw/day for females by gavage for 28 days. At necropsy on day 29, blood samples were collected for TT4, TT3, FT4, TSH and PFOA analysis, and thyroids were removed for histopathological evaluation.

182. Mortality: One female rat at 100 mg/kg bw/day died, all other rats survived to scheduled necropsy.

183. General toxicity and body weight: One female rat at 100 mg/kg bw/day which subsequently died was lethargic, ataxic and thin prior to death. No clinical signs of general toxicity were observed in the remaining rats. In males, terminal body weights were significantly reduced at ≥ 2.5 mg/kg bw/day,

compared with controls. In females, terminal body weights were unaffected by treatment.

184. Gross pathology: In males, thyroid weights were significantly increased at 2.5 mg/kg bw/day, compared with controls and relative thyroid weight: body weight was significantly increased at ≥1.25 mg/kg bw/day. In females, thyroid weights and relative thyroid weight: body weight was unaffected by treatment.

185. Histopathology: In males, there was a non-significant increase in the incidence of thyroid gland follicular cell hypertrophy of minimal severity at 10 mg/kg bw/day, compared with controls. In females, there was a significant increase in the incidence of thyroid gland follicular cell hypertrophy of minimal severity at 100 mg/kg bw/day.

186. Thyroid hormone levels: In males, TT4 and FT4 levels were significantly decreased at ≥ 0.625 mg/kg bw/day, and TT3 levels were significantly decreased at 0.625 mg/kg bw/day, 1.25 mg/kg bw/day, 2.5 mg/kg bw/day and 5 mg/kg bw/day, compared with controls. TSH levels were significantly decreased at 5 and 10 mg/kg bw/day. In females, TT4 and FT4 levels were significantly decreased at 100 mg/kg bw/day and TSH levels were significantly increased at ≥ 6.25 mg/kg bw/day. TT3 levels were unaffected by treatment.

187. Plasma PFOA concentrations: In males, mean plasma PFOA concentrations on day 29 were 0.098 µg/mL (control), 50.690 µg/mL (0.625 mg/kg bw/day), 73.480 µg/mL (1.25 mg/kg bw/day), 95.430 µg/mL (2.5 mg/kg bw/day), 110.720 µg/mL (5 mg/kg bw/day) and 148.570 µg/mL (10 mg/kg bw/day). In females, mean plasma PFOA concentrations on day 29 were ND (control), 0.491 µg/mL (6.25 mg/kg bw/day), 1.153 µg/mL (12.5 mg/kg bw/day), 2.960 µg/mL (25 mg/kg bw/day), 9.326 µg/mL (50 mg/kg bw/day) and 23.444 µg/mL (100 mg/kg bw/day).

188. Overall, TT4 and FT4 were decreased in males and females, while TSH was decreased in males but increased in females. Thyroid gland follicular hypertrophy was observed in males and females.