Liver Weight

In this guide

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21. For PFCAs, absolute and/or relative liver weight was measured in 40 of the 50 studies reviewed (four of the 10 acute studies, 33 of the 37 repeated dose studies and all three developmental studies).

22. In the acute studies, three of the four studies reported an increase in liver weight. Das et al. (2017) reported an increase in absolute and relative liver weight with PFOA and PFNA in male mice, whereas Kawashima et al. (1995) only reported an increase in relative liver weight with PFDA, but not PFOA, in male mice.

23. In the repeated dose assays, an increase in liver weight was seen in 19 of the 33 assays.

24. An increase in absolute liver weight was seen in male, but not female, rats following exposure to PFBA for 28 and 90 days (Butenhoff et al., 2012a). PFOA also increased absolute and/or relative liver weight in male mice (Botelho et al., 2015; Guo et al., 2019; Soltani et al., 2023; Son et al., 2008; Wu et al., 2018), rats (Butenhoff et al., 2012a; Elcombe et al., 2010; Li et al., 2019; NTP., 2022b; Qazi et al., 2010b), male and female mice (Kennedy Jr, 1987) and male Cynomolgus monkeys (Butenhoff et al., 2002). An increase in absolute liver weight was also seen in male and female mice following exposure to PFNA (Kennedy Jr, 1987; NTP., 2022b) and absolute and relative liver weight was increased in male and female rats with PFDA (NTP., 2022b). PFDA also increased relative liver weight in female rats (Frawley et al., 2018).

25. Increased relative liver weights in male rats were also reported with PFunDA (Takahashi et al., 2014) and in male and female rats with PFDoDA (Kato et al., 2014), whereas both absolute and relative liver weight was increased following exposure to PFHxDA (Hirata-Koizumi et al., 2015), PFTeDA (Hirata-Koizumi et al., 2015) and PFODA (Hirata-Koizumi et al., 2012).

26. No effects were seen on liver weight with PFHxA, (Chengelis et al., 2009; Loveless et al., 2009; NTP., 2022b), PFBA (Foreman et al., 2009), PFNA (Hadrup et al., 2016) or PFDoDA (Zhang et al., 2008).

27. In the developmental studies, increased liver weights were also increased in female rats with PFBA (Das et al., 2017) and PFOA (Xu et al., 2022; Zhang et al., 2021).

28. Where both male and female rats were included in repeated dose studies, increased liver weights were seen in males but not females with PFBA (Butenhoff et al., 2012a), PFOA (Butenhoff et al., 2012a; NTP., 2022b), PFUnDA (Takahashi et al., 2014), PFDoDA (Kato et al., 2014), PFHxDA and PFODA (Hirata-Koizumi et al., 2012).

29. Various authors measured the hepatic DNA content to help the mechanism by which the increased liver weights occurred following exposure to PFAS. Elcombe et al. (2010) reported a decrease in liver DNA content, when expressed as mg/g liver but not as mg/whole liver, in male rats following exposure to PFOA for 7 and 28 days. This was accompanied by an increase in absolute and relative liver weight at both time points.

30. Butenhoff et al. (2002) showed a dose-dependent decrease in liver DNA content in male Cynomologus monkeys, although it only reached statistical significance at the top dose of 30 mg/kg bw/day (reduced to 20 mg/kg bw/day) whereas increased absolute liver weight was seen at 3 mg/kg bw/day.

31. For PFSAs, absolute and/or relative liver weight was measured in 17 of the 25 repeat dose toxicity studies reviewed, and an increase in absolute and/or relative liver weight was seen in 11 of the 17 studies.

32. An increase in absolute and relative liver weight was seen in male, but not female, rats following exposure to PFBS (Lieder et al., 2009b). PFBS also increased relative liver weight in male rats after 28 days exposure (NICNAS., 2005) and relative liver weight in male and female rats (NTP., 2022a).

33. PFHxS increased absolute liver weight in male mice (Bijland et al., 2011) and absolute and relative liver weights in male, but not female rats (NTP., 2022a).

34. PFOS also increased absolute liver weight in male mice (Bijland et al., 2011), relative liver weight in male rats (Elcombe et al., 2012), male and female rats (Kim et al., 2011) and male mice (Huck et al., 2018) and absolute and relative liver weights in male and female rats (NTP., 2022a) and female monkeys (Seacat et al., 2002).

35. No effects were seen on liver weight with PFBS (Bijland et al., 2011; Lieder et al., 2009a; NTP., 2022a), PFBS following 90 days exposure (NICNAS., 2005), PFHxS (Chang et al., 2018) and PFOS.

36. Where both male and female animals were included in repeated dose studies, increased liver weights were seen in male, but not female, rats with PFBS (Lieder et al., 2009b; NICNAS., 2005) and PFHxS (NTP., 2022a), and female, but not male, monkeys (Seacat et al., 2002).

Recovery

37. For both PFBA and PFOA, the increase in absolute liver weight seen in male rats after the 28- (PFBA and PFOA) and 90-day (PFBA only) exposure was comparable to controls following the 3-week recovery period (Butenhoff et al., 2012a). Butenhoff et al. (2002) also reported a transient increase in liver weight in Cynomolgus monkeys following a 90-day recovery period.

38. For PFBS, the increase in absolute and relative liver weights seen in male rats after a 28-day exposure was comparable to controls after a 14-day

recovery period (NICNAS., 2005). For PFOS, liver weight was still greater than controls in male rats after 84 days recovery, although on days 28 and 56 liver weight was comparable to controls (Elcombe et al., 2012).