

Table 1 Lowest POD for PFAS based on liver effects - PFCAs

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This is a paper for discussion. This does not represent the views of the Committee and should not be cited.

*Derived by contractor; NA – not applicable.

| Substance / reference / table | Sex, strain and species (Duration) | NOAEL/LOAEL mg/kg bw/day | Effect at LOAEL |
|-------------------------------------|--|-----------------------------|-----------------|
|-------------------------------------|--|-----------------------------|-----------------|

| | | | |
|--------------------------|---|--------------------|--|
| | | | <p>↑ absolute liver weight</p> <p>↑ ALP</p> <p>↓ TP</p> <p>↓ bilirubin</p> <p>↑ hepatocellular hypertrophy</p> |
| PFBA | Male and female Sprague-Dawley rats, | Males: 6 / 30. | |
| Butenhoff et al. (2012a) | 90 days. | Recovery 30 / NA*. | <p>↑ mRNA of Acox, UGT1A1, CYP4A1, malic enzyme and Por</p> |
| Table 7 | Recovery group: 3 weeks. | | <p>↓ mRNA for Cyp1A1 in liver.</p> <p>Recovery:</p> <p>Absolute liver weight, TP, bilirubin and hepatocellular hypertrophy comparable to controls.</p> |
| PFHxA | Male and female Crl:CD Sprague-Dawley rats, | | |
| Loveless et al. (2009) | 28 days. | Males: NA / 20. | <p>↑ ALT</p> |
| Table 8 | Recovery group: 30 and 90 days. | | |

| | | | |
|--------------------------------|-----------------------------|----------------------|---|
| | | | ↑ relative liver weight, |
| PFOA | Male Balb/c mice, | | ↑ TP |
| Guo et al. (2019) | 28 days. | Males: NA / 0.4. | ↑ albumin |
| Table 9 | Recovery not assessed. | | ↑ globulin |
| | | | ↑ hepatocellular hypertrophy. |
| PFNA | Male Wistar rats, | | |
| Hadrup et al. (2016) | 14 days. | Males: 0.25 / 5. | ↓ mRNA of AKR1C1, Ugt 2B15, Cyp2C11, Cyp1A2 and Cyp2B6. |
| Table 10 | Recovery not assessed. | | |
| PFDA | Female Sprague-Dawley rats, | | |
| Frawley et al. (2018) Table 11 | 28 days. | Females: NA / 0.125. | ↑ relative liver weight. |
| | Recovery not assessed. | | |
| | | | Males |
| | | | ↑ relative liver weight |
| | | | ↓ total cholesterol |
| PFUnDA | Crl:CD (SD) rats, | Males and | ↑ albumin/globulin ratio |
| Takahashi et al. (2014) | 41-46 days, | females: 0.1 / 0.3, | ↑ hepatocyte centrilobular hypertrophy, |
| Table 12 | Recovery not assessed, | | Females: |
| | | | ↓ total cholesterol |
| | | | ↑ hepatocyte centrilobular hypertrophy, |

| | | | |
|--------------------------|---|----------------|---|
| | | | Males |
| | | | ↑ relative liver weight |
| PFDODA | Male and female Crl:CD (SD) rats, | Males and | ↑ ALP |
| Kato et al. (2014) | 42 days (males), | females: 0.1 / | ↓ total cholesterol. |
| Table 13 | 41-46 days (females), | 0.5, | Females: |
| | | | ↑ albumin/globulin ratio |
| | | | ↑ relative liver weight |
| | | | ↑ focal necrosis. |
| | Male and female Crl:CD (SD) rats, | | |
| PFTeDA | Males: 42 days beginning 14 days prior mating. | | ↑ absolute liver weight |
| Hirata-Koizumi (2015) | Females: 14 days prior to mating, gestation and to PND5. | Males: 1 / 3. | ↑ relative liver weight |
| Table 14 | | | ↑ centrilobular liver hypertrophy and steatosis. |
| | Male and female Crl:CD (SD) rats | | ↓ body weight |
| | | | ↑ absolute liver weight |
| PFHxDA | Males: 42 days beginning 14 days prior mating. | Males and | ↑ relative liver weight |
| Hirata-Koizumi (2015) | | females: 20 / | ↑ centrilobular liver hypertrophy. |
| Table 15 | Females: 14 days prior to mating, gestation and to PND5. | 100. | Females: |
| | | | ↑ centrilobular liver hypertrophy. |

| | | | |
|--|---|------------------------------------|--|
| PFODA (Hirata-Koizumi et al., 2012) Table 16 | Male and female Crl:CD (SD) rats | | Males |
| | Males: 42 days beginning 14 days prior mating. | Males and females: 40 / 200. | ↑ absolute liver weight |
| | Females: 14 days prior to mating, gestation and to PND5. | | ↑ relative liver weight ↑ centrilobular hypertrophy. |
| | | | Females ↑ relative liver weight. |