Statement on the EFSA Opinion on the risks to human health related to the presence of perfluoroalkyl substances in food

# Summary of 2020 EFSA evaluation

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# Hazard identification and characterisation

# Toxicokinetics

20. This new Opinion reviews data on the toxicokinetics of PFASs in animals and humans. PFOS and PFOA toxicokinetics studies published prior to 2017 are included in previous EFSA Opinions. Additional studies published since 2017 are analysed and reported in the 2020 Opinion.

# **Experimental animals**

21. Most of the information on the fate of PFASs and PFCAs is based on PFOS and PFOA, respectively. These compounds are readily absorbed in the gastrointestinal (GI) tract in mammals and distribute predominantly to the plasma as well as other parts of the body, and depending on the PFAS, they tend to accumulate in the liver. PFOS and PFOA are not metabolised and are excreted in both urine and faeces. They may be subject to extensive enterohepatic recirculation. Serum elimination half-lives for PFOS in rats and mice were slightly higher than one month whereas in rabbits and monkeys they were 3-4 months. Significant sex differences are observed in the elimination of PFOA in some species such as rats, for which half-lives may vary from a few hours in females, to several days in males. These differences in biological half-lives are mainly due to differences in renal clearance. For both PFOS and PFOA, maternal transfer occurs prenatally to the foetus through placental transfer and postnatally through the consumption of maternal milk.

#### Humans

22. Most of the human data published on the toxicokinetics of PFASs other than PFOS and PFOA are related to their distribution and elimination.

23. PFOS and PFOA have been reported to be extensively absorbed in humans and mainly distributed in plasma (predominantly bound to albumin), liver and kidney. PFOS and PFOA do not undergo metabolism and are eliminated in urine and bile. Biliary excretion of PFOS and PFOA is significantly higher than elimination via the urine, but does not predominantly contribute to overall elimination, due to high biliary reabsorption. Humans have a high percentage of PFOA renal tubular reabsorption, due to the high affinity of PFOA for human uptake transport proteins.

24. Several studies estimated half-lives of 2 and 6 years in humans for PFOS and PFOA respectively. Shorter chain PFCAs are preferentially excreted in urine, whereas PFNA and longer chain PFASs are preferentially eliminated through the bile and subsequently the faeces.

25. Extensive uptake from enterohepatic circulation and reabsorption by organic anion transport proteins (OATs) in the kidneys are believed to be more active processes in humans compared to rodents, slowing down the excretion of these substances. However, it is not clear which specific OAT(s) is/are responsible for this species difference.

26. Short-chain PFASs were found to have half-lives ranging from a few days (PFBA) to approximately 1 month (PFBS, PFHxA), whereas for PFHxS, PFOS, PFOA, PFNA, PFDA and PFUnDA, estimated half-lives can exceed 3 years and be up to approximately 8 years.

27. PFOS and PFOA have been detected in umbilical cord blood, breast milk and from the plasma of breastfed toddlers indicating that maternal transfer occurs pre- and postnatally. Longer fluoroalkyl chain length and a terminal sulfonate group are associated with lower fetal/maternal ratios.

28. Reports of high levels of PFASs in blood of individuals exposed to contaminated water indicate that gastrointestinal absorption of these compounds had occurred (Frisbee et al., 2009; Gyllenhammar et al.,2015).

29. No studies of metabolism of PFASs in humans were identified.

30. However, similar to experimental animals, humans are able to transform precursors to PFCAs and PFSAs.

31. Limited data were identified on the toxicokinetics of FTOHs and other precursors in humans. The FTOH metabolites FTCAs and FTUCAs were detected in the blood from ski wax technicians exposed through inhalation to high levels of 8:2 FTOH, suggesting metabolism of FTOH to PFOA and PFNA (Nilsson et al.,

2013).