

Revised TWI for PFASs: rationale and consequences

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*The content of this presentation reflects my
personal views and does not necessarily reflect
the views of EFSA or any other organisation*

Previous EFSA assessment for PFOS

- ▶ 2008, EFSA established a tolerable daily intake (TDI) of **150 ng/kg bw per day for PFOS**
- ▶ Based on a lowest no-observed-adverse-effect-level (NOAEL) of 0.03 mg/kg bw per day derived from a sub-chronic study on cynomolgus monkeys, where a decrease in serum total cholesterol and high-density lipoproteins (HDL), increased TSH levels and lowered triiodothyronine (T3) concentrations were observed.
- ▶ Uncertainty factor (UF) of 200 was applied to the NOAEL. A UF of 100 was used for inter and intra-species differences and an additional UF of 2 to compensate for uncertainties related to the duration of the key study and the elimination kinetics of PFOS. The EFSA CONTAM panel concluded that the exposure to the general population was well below the derived TDI

Previous EFSA assessment for PFOA

- ▶ For PFOA a benchmark dose for a 10% increase in increased liver weight (BMDL₁₀) of 0.3 mg/kg bw per day based on studies in mice and rats was used to derive a **TDI of 1.5 µg/kg bw per day** applying a UF of 200 to the BMDL₁₀



The EFSA Journal (2008) 653, 1-131

Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts

Scientific Opinion of the Panel on Contaminants in the Food chain¹

(Question N° EFSA-Q-2004-163)

Other risk assessments

- ▶ All use animal studies and all present TDIs in broadly the same range and conclude no adverse health effects for most of population as a result of dietary exposure based on normal occurrence levels
 - ▶ Federal Institute for Risk Assessment in Germany (BFR)
 - ▶ Swedish Environmental Protection Agency
 - ▶ United States Environmental Protection Agency (U.S. EPA)
 - ▶ Danish Environmental Protection Agency
 - ▶ Agency for Toxic Substances and Disease Registry (ATSDR),
 - ▶ etc

New Mandate of EFSA CONTAM Panel

- ▶ ORIGINAL: to prepare an opinion on the risks to human health related to the presence of perfluoroalkylated substances (PFASs) in food
- ▶ LATER: Following an agreement with EC, the CONTAM Panel decided to address the mandate in 2 separate opinions, one on perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) and another on other PFASs

2018 opinion

- ▶ 2018 EFSA opinion set separate TWIs
 - ▶ 13 ng/kg bw per week for PFOS
 - ▶ 6 ng/kg bw per week for PFOA
- ▶ 2018 opinion used increased cholesterol as the main critical effect, but noted other effects at around the same level

2020 opinion

- ▶ 2020 opinion takes into account:
 - ▶ more recent scientific knowledge
 - ▶ recent guidance for assessing combined exposure to multiple chemicals
- ▶ HBGV based on sum of 4 PFASs - perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorononanoic acid (PFNA), perfluorohexane sulfonic acid (PFHxS).
- ▶ Decreased response of the immune system to vaccination now considered to be the most critical human health effect
- ▶ **Draft 2020 opinion subject to public consultation which resulted in a lowering of the proposed TWI from 8 to 4.4 ng/kg body weight per week for sum of PFOA, PFNA, PFHxS and PFOS.**

Rationale behind 4 PFASs chosen

- ▶ Similar effects in animals
- ▶ Toxicokinetics
- ▶ Observed levels in human blood
- ▶ These 4 PFASs make up half of the overall dietary exposure, remainder primarily from PFASs with short half-lives

Critical effect

- ▶ 2018 opinion considered increased cholesterol as the critical effect for adults due to its link to cardiovascular disease, a common public health issue
- ▶ New data about the effects of PFAS in animals and humans have become available and new scientific studies have been published which question the direct link between exposure to PFAS and increased cholesterol level
- ▶ Not the case for effects on the decreased response of the immune system to vaccination, which was also identified as an important effect in the previous assessment.
- ▶ Proposed new TWI is also protective against other possible health effects, such as the increase of cholesterol in blood

Derivation of HBGV

- ▶ From a human study, a lowest $BMDL_{10}$ of 17.5 ng/mL for the sum of the four PFASs in serum was identified for 1-year-old children.
- ▶ Using PBPK modelling, this serum level of 17.5 ng/mL in children was estimated to correspond to long-term maternal exposure of 0.63 ng/kg bw per day.
- ▶ Since accumulation over time is important, a tolerable weekly intake (TWI) of **4.4 ng/kg bw per week** was established.

Dietary exposure

- ▶ Food can become contaminated through contaminated soil and water used to grow the food, through the concentration of these substances in animals via feed and water, through food packaging containing PFAS, or equipment that contained PFAS during food processing.
- ▶ Foods that contribute most to dietary exposure to these four PFASs are
 - ▶ drinking water,
 - ▶ fish,
 - ▶ fruit,
 - ▶ eggs

Exposure

- ▶ Mean LB exposure in adolescents and adult age groups ranged from 3 to 22 ng/kg bw per week
- ▶ 95th percentile from 9 to 70 ng/kg bw per week
- ▶ Double this for toddlers and ‘other children’.
- ▶ Upper bound exposure was 4- to 49- fold higher than LB levels, but the latter were considered more reliable due to the amount of data <LOD and high LODs.

Most exposed population groups

- ▶ Infants, toddlers and other children have highest dietary exposure.
- ▶ Pregnancy and breastfeeding are the main contributors to exposure for infants.
- ▶ The new TWI was set in such a way that it should protect infants against high exposure.

Basis for group TWI

- ▶ EFSA's 'MixTox' guidance was published in 2019
- ▶ Methodologies and tools to assess combined exposure to multiple chemicals.
- ▶ As a result, one single group TWI for PFOA, PFNA, PFHxS and PFOS, could be established based on effects observed in humans.

Exposure

- ▶ Previous data on food demonstrated that exposure was well below established (<2018) TDIs.
- ▶ Some analytical methods that have been used to date lack sensitivity and many data are left censored (i.e. <LOD) but this was not so problematic because it was possible to show that exposure was well below any level of concern; i.e. was fit for purpose
- ▶ To analyse food to demonstrate that exposure is below the new TWI means that this is no longer the case and more sensitive analytical methods are needed for measurement of PFASs

Knowledge gaps

- ▶ Occurrence data is needed for a broad range of food groups obtained with more sensitive analytical methods,
- ▶ More information on the relative *potencies* of the 4 PFAS (they were *assumed* equal)
- ▶ More information on other PFASs that are detected in food.

acknowledgements



Especially the WG on PFASs, and the
CONTAM Panel

The Panel on Contaminants in the Food Chain (CONTAM) provides scientific advice on contaminants in the food chain and undesirable substances such as natural toxicants, mycotoxins and residues of unauthorised substances.