PAN Europe's response to EFSA's Public Consultation

on consumer health-based guidance values

on trifluoroacetic acid

Overall

PAN Europe welcomes the opportunity to provide comments on the EFSA's *Draft statement on consumer health-based guidance values on trifluoroacetic acid*.

Our organisation is closely following the developments related to TFA, as it is a common degradation product of 30 PFAS pesticide active substances approved and used in numerous pesticide products across Europe. The use of PFAS pesticides has increased over the past 10 years, as shown by rising residue levels in fruit and vegetables, as well as sales data where available[1]. Most PFAS pesticides contain at least one -CF3 group and are a significant source of TFA contamination into the environment and water resources. Our preliminary work has shown that TFA is detected in water resources across all of Europe, including drinking water, both tap or mineral bottled water, as well as groundwater.[2] It is also detected in plant-based products such as wine[3], bread and cereals[4].

Scientific evidence clearly indicates that this very persistent and very mobile metabolite has the potential to cause liver toxicity, impair foetal development and fertility[5]. Because of its properties, scientist have warned that it must be considered a threat to our planetary boundaries[6]. Given that human and environmental exposure to TFA is already widespread and rapidly increasing, it is of utmost importance to conduct an objective, independent, and thorough investigation of the toxicity of this common pesticide metabolite and to establish truly protective health-based guidance values. The contribution of multiple PFAS sources should also be considered, as they result in background levels significantly above zero.

As this issue concerns multiple PFAS substances, the assessment process must be safeguarded against industry attempts to downplay the toxicity of the substance.

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[1] Pan Europe et al, Toxic Harvest: The rise of forever PFAS pesticides in fruit and vegetables in Europe, February 2024 [link].

[2] PAN Europe et al, TFA in Water: Dirty PFAS Legacy Under the Radar, May 2024 [link]. PAN Europe et al, TFA: The Forever Chemical in the Water We Drink, July 2024 [link]. PAN Europe et al, TFA: The 'Forever Chemical' in European Mineral Waters, December 2024 [link]

[3] PAN Europe et al. Message from the bottle: The rapid rise of TFA contamination across Europe, 2025.

[4] Global2000 et al. The forever chemical in our daily bread:The worrying rise of TFA in cereal prod, 2025.

[5] See ECHA's TFA hazard classification [link]

[6] Arp H.H P, Gredelj A et al. 2024. The Global Threat from the Irreversible Accumulation of Trifluoroacetic Acid (TFA). *Environmental Science & Technology* ***58****, 45, 19925–19935* *https://doi.org/10.1021/acs.est.4c06189*

Comments

PAN Europe welcomes the analysis carried out by EFSA. After reading the draft closely, we would like to raise our concerns regarding the selection of NOAEL and the proposed Adverse Daily Intake (ADI). We consider that, based on the available scientific evidence, the ADI for TFA is not protective enough and will fail to provide a high level of protection for the public from TFA, in line with the requirements of the EU law.

On the selection of NOAEL

We disagree with the NOAEL of 8.65 mg/kg/bw per day based on the observed changes in thyroid hormones (decreased T4 levels) in the EOGRTS (#100). Adverse effects were seen at this exposure and therefore a NOAEL cannot be derived from this study.

Indeed, following a close review of the **EOGRTS (#100),** we see that certain TFA alterations were observed in animals from all exposure groups, including the low exposure group. When taken together it is evident that a NOAEL cannot be established in this study. The TFA-induced effects across all doses are the following:

- **Thyroid**: In F1 animals, levels of TSH were increased at all doses in females (PND 22) and levels of total T4 decreased at all doses in males (cohort 1A, 13 weeks). In addition, relative thyroid weight decreased significantly throughout all exposures in males, and high exposure in females. These changes demonstrate an adverse effect on thyroid at all levels for offspring, which is more pronounced in males than females. Total T4 levels were also lower already at PND 22 both in males (medium and high) and females (high), an indication that effects increase with time. As thyroid was also affected on parental animals, it should be concluded that TFA has the potential to interfere with thyroid function in rats. Therefore, a NOAEL for thyroid cannot be derived by this study as effects in offspring were seen across all exposures.
- **Blood chemistry** was altered for certain parameters across all exposure groups: plasma glucose (males and females), triglycerides (males), non-esterified fatty acids (males).
- **Sperm parameters**: Sperm motility in offspring was affected even at low exposure, as in Cohort 1A the Average Path Velocity decreased across all exposure levels and Curvilinear Velocity decreased at low and high exposure levels. Other sperm parameters were also affected but they were measured only at the high exposure: a significant decrease was observed in the absolute weight of testis and testis spermatid counts. The absence of measurements in low and medium exposure levels should not be interpreted as an absence of effects.
- **Immunotoxicity:** As correctly identified by EFSA, immunophenotyping of T cells (including CD4+ and CD8+ T subsets), B cells, NK cells, monocytes and 330 neutrophils was performed on rat spleen leukocytes in offspring from F1 cohort 1A, week 13. A decrease in absolute cell counts in the spleen was observed in both sexes at all dose levels for all previously analysed cell populations. There was no shift in the CD4+/CD8+ ratio. A cohort for immunotoxicity was not included. It is a mistake to assume that these effects should not be considered adverse, considering that TFA is a PFAS and many PFAS are known to be immunotoxic as it has been reported in

scientific literature (citation). Once again, the absence of additional studies on immunotoxicity should not be interpreted as the absence of adverse effects.

Assembling the alterations observed across all exposures in the offspring of the EOGRTS it is evident that a NOAEL cannot be established. The approach of EFSA to examine the evidence one by one and dismiss the findings at the lower exposure group as non-adverse is not only misleading but also dangerous, considering that TFA is already a widespread pollutant.

Regarding the NOAEL, EFSA should consider the derivation of the health-based value by the German Environment Authority UBA following a close examination of the 52-week rat repeated dose toxicity study (#109). Based on this study, UBA had set the NOAEL at 1.8 mg/kg/d. According to UBA, Solvay Hannover, who had commissioned the chronic toxicity study had set the NOAEL at the highest exposure level of 37.8 mg/kg (600 ppm). After an examination of the study report, UBA identified that ALT (alanine aminotransferase), which is a biomarker for liver damage, showed a dose-dependent increase under TFA exposure. Liver toxicity has been reported in other studies (*citation, 90 day*). Medium and high exposures were significantly different from the control group and therefore UBA has set a NOAEL of 1.8 mg/kg bw.

Therefore, considering all the available scientific studies, the NOAEL should be established at 1.8 mg/kg bw.

Establishing the ADI

PAN Europe disagrees with the WG's suggestion for setting the Acceptable Daily Intake (ADI) at 0.03 mg/kg bw per day (expressed as sodium trifluoroacetate) based on the NOAEL of 8.65 mg/kg bw per day from the EOGRTS, and an uncertainty factor (UF) of 300. Considering the available scientific evidence, the lowest NOAEL is the one from the 52-week rat study, and therefore the ADI should be set at least at 1.8 µg/kg bw per day, following an UF of 1000. Our argument is provided below.

As correctly identified by EFSA, a concern for developmental neurotoxicity of TFA cannot be dismissed as its DNT potentially has not been assessed. This is of concern, particularly considering that TFA causes developmental toxicity in rabbits (eye and skeletal malformations), and endocrine disruption in rat offspring (T4 and THS alterations, changes in thyroid and parathyroid weight). Moreover, immunotoxicity has not been sufficiently investigated. It's an important data gap as based on the scientific literature[7], a common characteristic of PFAS is their potential to cause adverse effects on the immune system. In addition, here the EOGRTS indicates the potential of TFA to be immunotoxic.

According to the Pesticide Regulation Annex II 3.6 when values such as of ADI and ARfD are established "*an appropriate safety margin of at least 100 shall be ensured, taking into account the type and severity of effects and the vulnerability of specific groups of the population*" Moreover, when there are critical effects of particular significance "*such as developmental neurotoxic or immunotoxic effects, an increased margin of safety shall be considered*".

[7] Ehrlich, V., Bil, W., Vandebriel, R. et al. Consideration of pathways for immunotoxicity of per- and polyfluoroalkyl substances (PFAS). Environ Health 22, 19 (2023). https://doi.org/10.1186/s12940-022-00958-5

The NOAEL from the toxicity studies is 1.8 mg/kg bw per day from the 52-week toxicity study in rats.

Considering that the study was done on adult rats and not on offspring, as well as that TFA causes developmental toxicity, is immunotoxic, an endocrine disruptor and potentially neurotoxic during early life, an additional safety factor of 10 on the top of the safety margin of 100 is the minimum expected, if not higher. This is also supported by the fact that TFA is very persistent and therefore the exposure will be chronic (long-term). In addition, it's important to note that there are several PFAS pesticides and other PFAS substances that are TFA emitters, and therefore not only there are multiple sources of TFA but the background exposure levels are already above zero.

Therefore, the ADI should be set at least at 1.8 µg/kg bw per day.

Our comment on ADI is also relevant for ARfD.

Additional studies

Considering that TFA is a common breakdown product of approximately 30 PFAS active substances currently on the market, and that it is widespread in the environment, present in certain food products, and highly persistent, the human population -including vulnerable groups such as children and pregnant women- is widely and chronically exposed to this substance. Based on indications from existing toxicity studies and the identified data gaps, it is important to conduct a chronic toxicity assessment for the following endpoints: developmental neurotoxicity, immunotoxicity, and carcinogenicity.

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Pesticide Action Network (PAN Europe) is a network of NGOs working to reduce the use of hazardous pesticides and have them replaced with ecologically sound alternatives. We work to eliminate dependency on chemical pesticides and to support safe sustainable pest control methods. Our network brings together over 45 consumer, public health and environmental organisations and women's groups from across Europe.