

The global threat from the irreversible accumulation of trifluoroacetic acid (TFA)

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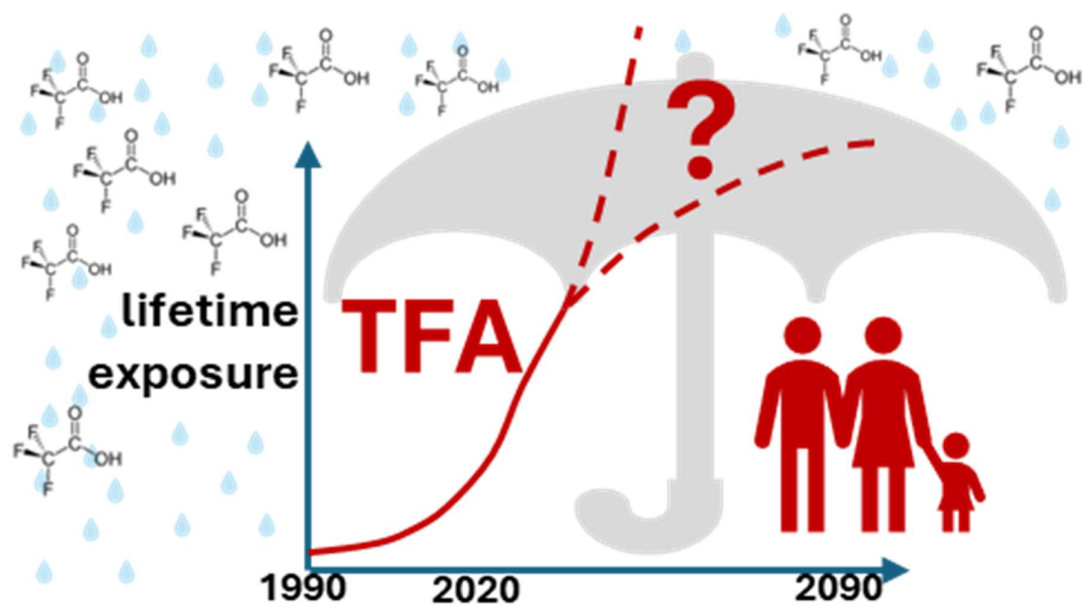
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27 **GRAPHIC ABSTRACT**

28



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Abstract

Trifluoroacetic acid (TFA) is a hydrophilic, non-degradable substance that has been increasing in concentrations within diverse environmental media, including rain, soils, human serum, plants, plant-based foods, and drinking water. Currently, TFA concentrations are orders of magnitude higher than those of other per- and polyfluoroalkyl substances (PFAS). This accumulation is due to many PFAS that have TFA as a transformation byproduct, including several fluorinated gases (F-gases), high-volume pesticides, pharmaceuticals and industrial chemicals, in addition to direct industrial release. Due to TFA's extreme persistence and mobility, these concentrations are increasing irreversibly. What remains less clear is the thresholds where irreversible effects on local or global scales occur. There are indications from mammalian toxicity studies that TFA is toxic to reproduction and that it exhibits liver toxicity. Ecotoxicity data are scarce, with most data for aquatic systems; fewer data are available for terrestrial plants, where TFA bioaccumulates most readily. Collectively, these trends imply that TFA meets the criteria of a planetary boundary threat for novel entities because of increasing planetary-scale exposure, where potential, irreversible disruptive impacts on vital earth system processes could occur. The rational response to this is to instigate binding actions to reduce emissions of TFA and its many precursors.

Keywords: trifluoroacetic acid, intergenerational exposure, market transition, PMT, vPvM, exposome

Synopsis: (~20 words)

Rapidly increasing TFA concentrations, coupled with TFA's extreme persistence, mobility and the possibility of irreversible impacts, should prompt action to reduce TFA emissions.

Introduction

Trifluoroacetic acid (TFA) belongs to the subclass of per- and polyfluoroalkyl substances (PFAS) known as ultra-short chain perfluoroalkyl acids (PFAAs). TFA is by far the most abundant PFAS in the environment^{1–6}. For example, Neuwald et al. demonstrated that TFA accounted for more than 90% of the total PFAS concentration (of 46 individual PFAS analyzed) in various drinking water sources in Germany². Tian et al. observed TFA and perfluoropropionic acid (PFPrA) concentrations of similar proportion in air, dry deposition particles and plant leaves surrounding two landfills in China, and these concentrations were an order of magnitude higher than those of the 21 other PFAS analyzed⁴. Chen et al. measured 25 PFAS in total around two fluorochemical manufacturing plants in China, covering 8 different media (air, various water, soil, dust, plant leaves, sediment), with TFA concentrations being consistently 1-2 orders of magnitude higher than other PFAS⁵.

An initial wave of scientific interest in the environmental fate and effects of TFA started around the mid-1990s, due to novel fluorinated refrigerants (hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs)) being introduced to the market after the ozone-depleting chlorofluorocarbons (CFCs) were phased out under the Montreal Protocol^{7–12}. When fluorinated gases (F-gases, encompassing gases with R-CF₃ moiety, R-CF₂-R moiety or inorganic fluorides), or other fluorinated organic substances, contain a C-CF₃ moiety that is resistant to biochemical or photochemical degradation, TFA will commonly show up as a terminal degradation product. In recent years, interest in TFA has been re-established due to rapidly increasing concentrations observed in remote locations, drinking water sources and human blood^{2,13–15}.

There has been increasing debate since the 1990s about the hazard-related concerns of TFA and other short-chain PFAAs, which have been considered comparatively less bioaccumulative and toxic than PFAAs with longer perfluoroalkyl chains^{8,9,16–23}. However, these early reports did not consider TFA's ubiquitous accumulation in the exposome, in

82 particular its observed accumulation in water resources and bioaccumulation in plants and
83 crops. Although there are fewer toxicological data compared to long-chain PFAAs, we will
84 present in this study that there are more than sufficient data to conclude that TFA poses a risk
85 to humans and the environment, and meets the criteria of a planetary boundary threat for
86 novel entities^{24–27}. Here we will present evidence for this because of TFA's 1) increasing
87 planetary exposure, which is 2) an irreversible burden from many sources that can cause 3)
88 disruptive effects on human health and earth system processes. Our analysis leads to the
89 conclusion that policy, industry, and innovation actions to reduce TFA emissions should be
90 enacted globally as soon as possible to protect future generations from the subsequent effects
91 of TFA accumulation.

92

93 **Increasing planetary exposure**

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95 A review of the scientific literature was conducted to obtain an overview of average and
96 maximum concentrations in diverse environmental media (see Supplementary Information for
97 a full methodology and collected data). In brief, 43 studies reporting on TFA concentrations
98 spanning from the late 1990s to the 2020s were selected and monitoring data were analyzed.
99 Collectively, these data indicate that TFA exposure is widespread and increasing.

100 Recent median concentrations of TFA in precipitation were measured at 0.29 µg/L in the
101 USA²⁸, 0.34 µg/L in Germany²⁹ and 0.70 µg/L in Fuxin, China⁵. These median concentrations
102 are similar to the proposed limits of total PFAS in drinking water in the EU draft recast Drinking
103 Water Directive³⁰, which places a threshold of total PFAS of 0.5 µg/L. In surface water and
104 groundwater studies, median levels of TFA are commonly above 0.5 µg/L. A recent report
105 measuring TFA in European surface water (median 1.2 µg/L) and groundwater (median ~1
106 µg/L), recorded exceedance of this total PFAS threshold in 79% of samples, with more than
107 98% of detected PFAS being TFA³¹.

In crops and other plants, short and ultrashort PFAAs undergo rapid uptake and bioaccumulation, particularly in aerial plant compartments^{35–38}. Chen et al.⁵ detected concentrations of up to 3800 µg/g_{dw} of TFA in plants in the vicinity of the fluorochemical industrial site in China with an average field bioaccumulation factor of 13000. TFA has been in general found to be enriched in conifers³⁹, wheat, maize⁵, various tree species^{4,5} and some wetland species⁴⁰. Consequently, high concentrations of TFA in plant-based foods⁴¹ and plant-based beverages such as beer and tea⁴² were reported, indicating that the ingestion of plant-based foods and beverages could be a significant route for human (and animal) exposure in addition to drinking water.

TFA was detected in human blood from China³² with median concentrations of 8.46 µg/L, similar to the levels of long-chain PFAAs, despite TFA not being considered bioaccumulative according to regulatory criteria³³. A similar study in the USA reported a median of 6 µg/L and a maximum of 77 µg/L¹⁸, where TFA alone had a 57% contribution to the sum of a total of 39 PFAS measured. Thus, the concentrations of TFA in non-occupationally exposed US populations are similar to the concentrations of bioaccumulative legacy long-chain PFAAs (e.g. PFOS, PFHxS, PFNA, PFDA) measured in the serum of the occupationally exposed population³⁴. Because of high uptake, TFA reaches levels in human serum that are much higher than what its low bioaccumulation potential would indicate.

To demonstrate the change in concentrations and trends over the years, **Figure 1** presents a comparison of pre-2010 and post-2010 data (by the reported year of sampling, not the year of publication). This cut-off year was chosen because the 1st of January 2010 was the final deadline for stopping the last remaining production of CFCs⁴³; therefore, it is a key date regarding the phase-in of replacement F-gases. This date is also coincident with a slump in interest in TFA, which attracted some initial attention during the introduction of F-gases around the late 1990s, as opposed to the more recent interest in the past few years due to its increasing detection during PFAS monitoring.

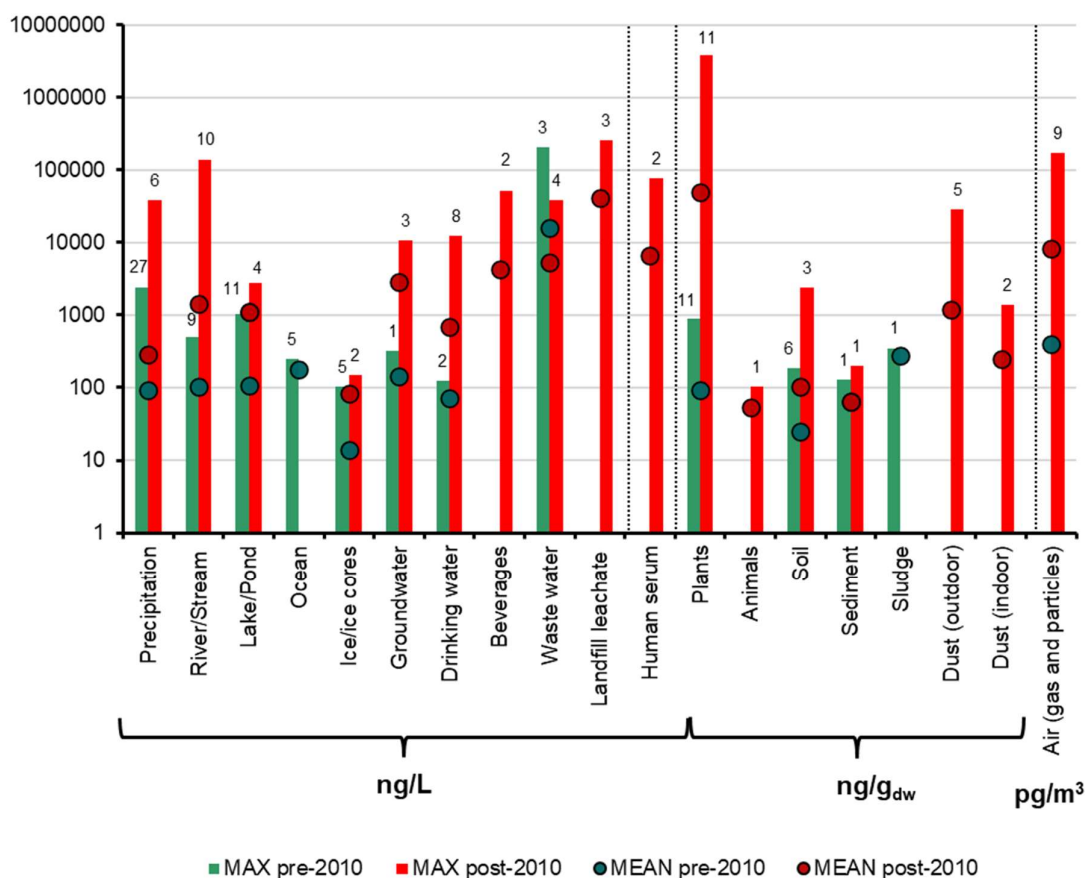


Figure 1. Comparison of detected TFA concentrations in different media summarized as before 2010 (in green) and after 2010 (in red). Maximum reported values of maximum concentrations found in the literature review are shown as vertical bars and mean values of reported monitoring means and medians are shown with overlapping dots. Numbers indicating the number of summarized individual data points are shown above the corresponding bars.

When pre- and post-2010 concentration data are available in a specific medium (**Figure 1**) an increase in TFA by orders of magnitude in both maximum and mean concentrations in several environmental compartments is evident, including for precipitation, rivers and streams, groundwater and drinking water, soil and plants. While atmospheric media were the main focus of monitoring studies dated pre-2010 (especially precipitation), more data from other media became available after this cut-off year – with new media relevant to human exposure (e.g.

plant-based beverages, crops, indoor and outdoor dust, human serum) and ecosystem exposures (e.g. animals such as locusts, autochthonous tree species) that were not available pre-2010 or were rarely measured (e.g. drinking water).

More detailed time trends are available in certain areas. Urban surface waters around Beijing were sampled in 2002⁴⁴, and resampled in 2012⁴⁵, showing up to a 17-fold increase in TFA concentrations over 10 years, while tap water detections went from non-detection to 0.16 ng/L in 2012⁴⁵. Freeling et al. reported an increase in wet deposition in Germany from 22 to 30 t/year during 1995–1996 to 68 to 98 t/year in 2019²⁹. Pickard et al. used dated Arctic ice cores to show a rapid increase in deposited TFA after the entry-into-force of the Montreal Protocol, in 1989, from non-detection or a few ng/L to 129 and 148 ng/L¹⁵. In 2021, Cahill et al. reported a 6-fold increase in TFA in a stream transect in California since 1998⁴⁶. Freeling et al. analyzed archived leaf samples of different tree species for TFA and observed increases by factors of up to 12.5 in TFA concentrations in some species from 1989 to 2020²⁹. A study in indoor and outdoor dust found an increase in TFA by a factor of 4 between 2013 and 2017⁴⁷.

An irreversible burden from multiple sources.

TFA has no known environmental degradation pathway^{48,49}. This means that the mass of TFA that exists on the planet is approximately proportional to the amount emitted. Based on its persistence and high mobility, due to lack of sorption^{13,50}, the ultimate recipient is the Earth's hydrosphere. As TFA is omnipresent in all water bodies, from groundwater, deep and surface oceanic water, ice cores, drinking water, bottled water^{1,2,15,42,45,51–53}, dilution in many ways has already occurred, and will not be a way of substantially reducing exposure. Similarly, enrichment in plants will follow constantly increasing TFA concentrations in water and soil. With limited TFA loss processes for elimination from plant tissues because of TFA's persistence (no biotransformation) and presence in fully ionic form (strong acid, no volatilization), constant passive uptake from soil pore water via the transpiration stream can be expected for the lifetime of the plant as long as there is an input of TFA available. This

theory is supported by findings for other short- and ultrashort-chain PFAAs³⁷ and is in agreement with the results by Zhang et al.⁵⁴, who did not observe a steady-state concentration being reached for TFA in their plant uptake experiments. The global average of TFA concentrations in humans (serum), animals and plants can only increase.

Methods to remove TFA from water are expensive and often inefficient due to TFA's persistence and mobility^{51,55,56}. In some cases, water purification methods as common as ozonation and chlorination are also a source of TFA, depending on the presence of its precursors⁵¹. The most effective solution would be reverse osmosis (RO) to up-concentrate TFA, followed by some expensive destruction technique. However, RO treatment of water, particularly wastewater, compared to other forms of water treatment is both more expensive^{57,58}, and requires a substantial amount of energy⁵⁹. Further, destructive techniques for concentrated TFA may lead to harmful byproducts. At high temperatures (> 170°C) and certain conditions, TFA can be converted to the potent greenhouse gas fluoroform (CF₃H)⁶⁰, which may be relevant in the context of heating or burning organic matter or RO brine concentrates containing TFA.

TFA accumulation is expected to increase for the foreseeable future due to emissions from multiple sources. One of the most discussed is F-gases used as refrigerant chemicals. Refrigerant chemicals have a history of being problematic. CFCs were originally introduced as “safer”, alternative refrigerants to ammonia, sulfur dioxide and methyl chloride, until it was discovered that highly persistent CFCs were decomposing stratospheric ozone, particularly over Antarctica^{61–63}, indicating that CFCs were a planetary boundary threat⁶⁴. To protect the ozone layer from poorly reversible depletion, the Montreal Protocol⁶⁵ required CFCs used in refrigeration and air conditioning systems to be substituted with HCFCs and HFCs⁶⁶. HCFCs have lower ozone depletion potential than CFCs, and HFCs have no depletion potential; however, HFCs have a high global warming potential (GWP)⁶⁶. Further amendments to the Montreal Protocol and the European F-gas Regulation aimed to replace the high-GWP F-

gases with low-GWP alternatives⁶⁷. Nevertheless, the substances proposed as replacements – hydrofluoroolefins (HFOs) and even currently applied HFCs – add to the problem that many of the HFOs and HFCs can in part (e.g. HFC-134a, HFC-143a, HFC-1234ze, HCFO-1233zd) or completely be converted to TFA, with one known HFO, tetrafluoropropene (TFP, HFO-1234yf), having a 100% TFA yield^{68,69}. TFA formed in this way is readily scavenged from the atmosphere by wet (and to a lower extent, dry) deposition^{12,45,70}. Hence, a dramatic increase in atmospheric TFA could arise from the use of new HFO refrigerants. The use of HFO-1234yf alone was predicted to be responsible for 6900 t/year emissions of TFA in 2020 in the EU alone, with a potential increase of up to 47650 t/year by 2050. This shift in F-gases alone could cause emissions of TFA to increase by orders of magnitude in the coming years⁶⁸.

TFA is registered under REACH as manufactured and/or imported into the EU in volumes ranging from 100 to 1000 tons per year.⁵⁰ Additionally, there is usage as an intermediate, but this usage does not require registration, so the volume remains unknown. TFA is therefore emitted directly from industrial production in Europe, and there is further evidence of emissions from global manufacturers. Xie et al. measured TFA in the surrounding environment (surface water, groundwater, air, dust, soil) of three fluorochemical plants near Jinan, China, having TFA and related inorganic fluoride intermediates as their main products⁷¹. Though surface water concentrations measured by Xie et al. had a maximum of ~2.6 µg/L, in Southern France a TFA-producing plant's discharge recipient recently recorded concentrations up to 7600 µg/L.⁷²

In addition to F-gases and direct TFA production^{71,72}, there are several other precursors contributing to the accumulation of TFA in the environment, including a variety of groups of chemicals containing the C-CF₃ moiety, such as agrochemicals^{51,73–75}, pharmaceuticals⁵¹, (fluoro)polymers^{76–78} and other PFAS^{13,51,79}. For this reason, TFA has been dubbed a “Substance from Multiple Sources” by Nödler and Scheurer⁸⁰, highlighting the difficulty in ascertaining the main sources of TFA in monitoring studies of water resources^{14,19}. TFA and its precursors can be emitted from point sources such as the (fluoro)chemical industry^{5,51},

wastewater treatment plants and landfills^{4,81,82}, and sites with a history of the use of aqueous film-forming foams (AFFFs)^{81,83}. Another source of TFA that is of increasing attention, but has already been discussed since the late 1990s, is transformation products from the thermal destruction of fluoropolymers⁴⁸ as well as treatment of PFAS by destruction methods^{51,84,85}. The yields of TFA from diverse PFAS destruction methods are often unknown and this should be taken into consideration when developing new remediation methods for PFAS¹⁶.

The German Environment Agency (Umweltbundesamt, UBA) published estimates for TFA emissions from sources in Germany⁸⁶. The available data indicate that refrigerants and blowing agents were the largest quantifiable source of TFA with emissions at ~ 2000 t/year in Germany, followed by pesticides at ~ 457 t/year (mainly flufenacet, diflufenican and fluazinam), and human pharmaceuticals at ~ 29 t/year. Emissions from other sources, such as direct production of TFA, biocides, veterinary pharmaceuticals, and fluorochemicals in products could not be quantified⁸⁶. There have been speculations about natural sources of TFA, but these have recently been discredited by Joudan et al.⁸⁷, who presented that only increasing anthropogenic sources of TFA can explain its exponential increase in recent decades.

Disruptive Effects on Human Health and Earth System Processes

There may be a disruptive effect of TFA on human health or to Earth system processes that is currently unknown, similar to how the effects of longer-chain PFAAs on human health, and of CFCs on the ozone layer, were initially unknown by the broader scientific and regulatory community. Overcoming this ignorance is the hardest part of understanding that a certain novel entity that is irreversibly increasing in concentrations globally may pose a planetary boundary threat²⁵. Such effects cannot be fully described or anticipated by known paradigms of hazard assessment. However, as standard hazard categories are commonly used in

defining regulatory human health and environmental thresholds for chemicals, this is where we start our analysis of TFA potentially causing a disruptive impact.

Known health and environmental thresholds.

A recent review by Dekant & Dekant (2023) summarized mammalian toxicity of TFA, referring specifically to human toxicity. Most toxicity tests on which human health risk assessments were based are rat studies, which found mild liver hypertrophy (increased size of the liver) as the lead effect (at high concentrations). More human-relevant tests directed towards a mechanistic understanding and not only towards filling regulatory apical endpoints should be conducted in the future. Currently, there is an intention to change the CLP classification of TFA and its salts to Category 1B: Presumed human reproductive toxicant, based on new evidence of embryo-fetal developmental toxicity in rabbits, submitted to ECHA by The German Federal Office for Chemicals^{50,88}. If TFA were to be classified as toxic for reproduction, this would indicate that increasing concentrations in drinking water and food could lead to decreased fertility rates. In 2020, Germany has established a TFA human-health guideline concentration for drinking water at 60 µg/L, which is based on a chronic rat toxicity (feeding) study, but emphasized that the concentration in drinking water should be kept as low as reasonably possible and a value of 10 µg/L should be targeted⁸⁹.

Under the EU's regulation on classification and labelling (CLP), TFA is classified as causing severe skin burns and eye damage (H314), harmful if inhaled (H332), and harmful to aquatic life with long-lasting effects (H412)⁹⁰. Under REACH, the toxicological threshold for the general population (Derived No Effect Level, DNEL) is derived only for the oral route and set to 0.042 mg/kg_{bw}/day, while for other routes of exposure, no hazard has been assumed and concluded. The threshold for the oral route was derived based on the observed effects from a 90-day rat feeding study⁵⁰. Human toxicokinetic evaluation of TFA showed rapid oral absorption, submission to enterohepatic circulation, and body distribution via blood which included passing through the placenta barrier. The main excretion routes are considered to be via urine and bile. TFA did not exceed the regulatory bioaccumulation criteria in humans and is

considered non-bioaccumulative⁵⁰. However, this latter conclusion should be considered in the context of continuously accumulation in exposure media, such as drinking water and plant-based food and beverages, implying that internal concentrations will increase despite TFA being non-bioaccumulative.

Contrary to the most recent human toxicological review¹⁷, a similar and recent review was not available for (eco)toxicity data. We conducted a search of the USEPA ECOTOX database⁹¹ and ECHA registration dossiers (where currently TFA falls under the hazard classification “chronic 3” (H412), which indicates long-term harmful effects for water-dwelling organisms)⁵⁰ and found that most efforts towards the determination of (eco)toxicity of TFA are from the 1990s. Algae are considered the most sensitive trophic level, with *S. capricornutum* the most sensitive species and 0.12 mg/L the lowest determined No-Observed Effect Concentration (NOEC), which was determined for the TFA sodium salt (Solvay data, ECOTOX database extracted for TFA/NaTFA and reported in Berends et al.^{8,91}). Selected ecotoxicity endpoints (acute and chronic) for other organisms are reported in Table S2 of the Supplementary Information, with listed ecotoxicological thresholds and their abbreviations. Overall, most of the testing was performed for acute toxicity, with only a few studies investigating the chronic toxicity of TFA.

Predicted No-Effect Concentrations (PNECs) are concentration thresholds commonly derived in environmental risk assessment that should be protective of the whole ecosystem. They are based on ecotoxicity data and extrapolation factors based on data abundance, test duration (acute/chronic), and data quality/uncertainty⁹². For TFA, the lowest PNEC of 0.12 µg/L was derived by Xie et al.⁷¹ and was based on algae that were previously shown as the most sensitive trophic level, including a high uncertainty factor due to the scarcity of (eco)toxicity data. The ECHA REACH dossier reports a freshwater PNEC of 0.56 mg/L and a marine water PNEC of 0.056 mg/L, both based on the algal study reporting the 72h ErC50 (EC50 based on growth rate) of 56 mg/L⁵⁰. More than half of the surface water median and/or mean

concentrations from peer-review studies reported as post-2010 already exceed both of those freshwater PNECs (Table S1, Figure S2).

Among terrestrial organisms (ecotoxicity studies), only plants were tested for TFA toxicity. The final short-term EC50 was 4.7 mg/kg soil dry weight and a long-term NOEC was 0.83 mg/kg soil dry weight. It was mostly the plant shoot growth that was affected⁵⁰. However, considering TFA's high affinity for plant uptake, further testing of TFA plant toxicity is needed¹³. This NOEC is already similar to soil TFA background concentrations and is several orders of magnitude lower than TFA soil concentrations in contamination hotspots (Figure 1, SI)^{5,93}.

Given the persistence of TFA, exposure to TFA should be considered chronic and life-long for all species. However, chronic studies are still relatively scarce, with chronic data from standardized tests being limited in time of exposure to, for example, 35 days in fish, 21 days in *Daphnia*, 90 days in rat, or 36 days in crop plants⁵⁰ (Table S2, SI), which are insufficient in their extrapolation to potential impacts from lifetime exposure to TFA. Hence, none of the current studies considered actual long-term exposure to TFA, which would be more relevant given its ubiquitous and increasing presence over long time scales.

Unknown environmental and health impacts

As TFA is accumulating in diverse ecosystems, researchers should focus on non-traditional exposure and impact pathways that effect biogeochemical processes. Despite the extremely high plant uptake of TFA and its implications, controlled uptake experiments were rarely performed and reported for TFA. Zhang et al.⁵⁴ performed a set of hydroponic experiments with TFA and other ultra-short and short PFCAs. Here, the root uptake was exceptionally high for TFA (e.g. TFA concentration in roots was > 100 times higher than that of PFHxA)⁵⁴, indicating that the interface partitioning of TFA and specific interactions with organic solids need to be researched further and accounted for in assessing its environmental fate and behavior properties, particularly (bio)accumulation potential.

Direct effects of TFA on soil quality were only recently investigated;⁹⁴ here effects on the soil pH, microbial respiration, bacterial abundance and litter decomposition were reported, the latter being affected at concentrations similar to current TFA concentrations in soil for contamination hotspots as described in Chen et al⁵ (13 - 2400 ng/g_{dw}). Bott and Standley observed the incorporation of TFA into cells by microbial communities in freshwater surface sediments⁹⁵ after also demonstrating TFA incorporation in biomolecules such as proteins in aquatic organisms spanning a range of trophic levels¹¹. Concentrations that were used in these ~1.5 to 2.5 year experiments overlap with those currently observed in waters worldwide, from a few 2.2 to 43 µg/L, (Table S1, Figure S2, SI), and resulted in significant cell incorporation of TFA⁹⁵. It was also demonstrated that at elevated concentrations, the presence of TFA in the atmosphere may influence aerosols and cloud formation, boosting the formation of atmospheric clusters involved in new aerosol particle formation^{96,97}. As concentrations of TFA will likely increase by at least an order of magnitude in the coming decade, further investigations of TFA on biogeochemical processes is warranted.

CONCLUSIONS

Based on the data presented above, the increasing accumulation of TFA can be considered to meet the conditions of a planetary boundary threat,^{98,99} as it fulfils the following three conditions defined by Persson et al.²⁵ “*Condition 1 (C1) – the pollution has a disruptive effect on a vital earth system process of which we are ignorant; Condition 2 (C2) – the disruptive effect is not discovered until the associated impacts are, or inevitably will be, manifested at a global scale; and Condition 3 (C3) the impacts are poorly reversible because the level of pollution in the global environment cannot be readily reduced...*” Condition 1 (C1) is fulfilled based on the many surface water samples that exceed the lowest established PNEC (0.12 µg/L)⁷¹, as well as some soil concentrations that have exceeded the lowest established NOEC (0.83 mg/kg soil)⁵⁰. Further, there are some indications of toxicity that have caused the first drinking water advisories to be established based on concerns to human toxicity⁸⁹. The existence of such health advisory and regulatory values has been used as the basis for

361 establishing C1 in relation to four PFAAs previously.²⁷ Furthermore, the possibility of
362 unknown, long-term disruptive effects, which may be already occurring, but which we are
363 ignorant of, cannot be excluded. Condition 2 (C2) is fulfilled as TFA is manifested globally in
364 all environmental media, such as its ongoing bioaccumulation in crops. TFA hotspots can be
365 found around the globe, such as around industrial sites, and are spreading. Condition 3 (C3)
366 is fulfilled as when effects are realized globally, they will be irreversible for the foreseeable
367 future, due to TFA's extreme persistence and mobility, coupled with emissions from multiple
368 sources.

369 Though currently TFA does not have as well-established health advisories or regulatory limits
370 as the four PFAAs in a previous planetary boundary study²⁷, it is likely that new
371 advisories/limits will be introduced in the coming years as more research on the impacts of
372 TFA emerges. With the projected exponential increase in TFA concentrations in human tissue,
373 human diet and the environment, the question is not if TFA can exceed a planetary boundary,
374 but which irreversible health or Earth system impacts would be first observed at a planetary
375 scale, and where thresholds should be set to limit the severity of such impacts.

376 The potential long-term, irreversible impacts from the rapidly increasing emissions of TFA from
377 anthropogenic sources should be used as a rationale to start immediately discussing policy,
378 industry and innovation actions towards the phase-out of high-volume substances that lead to
379 increasing TFA accumulation. Obvious places to start would be to limit the use of HFOs, as
380 well as high-volume pesticides such as flufenacet, diflufenican and fluazinam, which are well
381 known to form large volumes of TFA^{86,89}. Other pharmaceuticals, veterinary products and
382 industrial chemicals that release TFA via transformation processes should also be considered
383 for phase-out or substitutions. As discussions and policy mechanisms to phase out the sources
384 of TFA could take some time, the rational response to the global threat posed by accumulating
385 TFA is to act swiftly before the irreversible impacts are realized to humans and the
386 environment. Transitioning away from TFA precursors is the most effective way of
387 safeguarding future generations from this planetary boundary threat.

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391 **SUPPORTING INFORMATION**

392 The Supporting Information is available free of charge at <https://xxxx>

393 The monitoring data collection and methodology, full set of collected monitoring data and an
394 overview of selected ecotoxicity values referred to in this study is available in a docx and xlsx
395 file.

396

397 **ACKNOWLEDGMENT**

398 Funding is acknowledged under the European Union's Horizon 2020 research and innovation
399 program project ZeroPM, under grant agreement No 101036756, and the Horizon Europe
400 project ARAGORN under grant agreement 101112723.

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