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Environmental Risk Assessment of Trifluoroacetic Acid

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Environmental Risk Assessment of Trifluoroacetic Acid

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ABSTRACT

The Montreal Protocol was developed in 1987 in response to concerns that the chlorofluorocarbons (CFCs) were releasing chlorine into the stratosphere and that this chlorine was causing a depletion of stratospheric ozone over Antarctica. This international agreement called for a phase out of these CFCs. Industry initiated a major effort to find replacements that are safe when properly

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used and safe to the environment. The toxicology and environmental fate of these first generation replacements has been studied extensively.

It was determined that the new substances break down in the environment to give predominantly carbon dioxide, water and inorganic salts of chlorine and fluorine. The only exception is that some substances also break down to yield trifluoroacetic acid (HTFA), a substance resistant to further degradation. Recognizing this, industry embarked on a research and assessment program to study the potential effects of trifluoroacetate (TFA) on the environment and to investigate possible degradation pathways. The results of these recently completed studies are summarized below and described in further detail in this paper.

Trifluoroacetic acid is a strong organic acid with a pK_a of 0.23. It is miscible with water and its low octanol/water partition coefficient ($\log P_{ow} = -2.1$) indicates no potential to bioaccumulate.

Industrial use is limited and environmental releases are very low. Some additional TFA will be formed from the breakdown of a few halogenated hydrocarbons, most notably HFC-134a (CF_3CH_2F), HCFC-124 (CF_3CH_2Cl), and HCFC-123 (CF_3CHCl_2). As these substances have only been produced in limited commercial quantities, their contribution to environmental levels has been minimal. Surprisingly, environmental measurements in many of diverse locations show existing levels of 100 to 300 $ng \cdot l^{-1}$ in water with one site (Dead Sea) having a level of 6400 $ng \cdot l^{-1}$. These levels cannot be accounted for based on current atmospheric sources and imply a long-term, possibly pre-industrial source. Generally, soil retention of TFA is poor although soils with high levels of organic matter have been shown to have a greater affinity for TFA when contrasted to soils with low levels of organic matter. This appears to be an adsorption phenomenon, not irreversible binding. Therefore, TFA will not be retained in soil, but will ultimately enter the aqueous compartment.

Modeling of emission rates and subsequent conversion rates for precursors has led to estimates of maximum levels of TFA in rain water in the region of 0.1 $\mu g \cdot l^{-1}$ in the year 2020.

TFA is resistant to both oxidative and reductive degradation. While there had been speculation regarding the possibility of TFA being degraded into monofluoroacetic acid (MFA), the rate of breakdown of MFA is so much higher than for TFA that any MFA formed would rapidly degrade. Therefore, there would be no buildup of MFA regardless of the levels of TFA present in the environment.

Although highly resistant to microbial degradation, there have been two reports of TFA degradation under anaerobic conditions. In the first study, natural sediments reduced TFA. However, even though this work was done in replicate, the investigators and others were unable to reproduce it in subsequent studies. In the second study, radiolabeled TFA was removed from a mixed anaerobic *in vitro* microcosm. Limited evidence of decarboxylation has also been reported for two strains of bacteria grown under highly specific conditions. TFA was not biodegraded in a semi-continuous activated sludge test even with prolonged incubation (up to 84 days).

TFA does not accumulate significantly in lower aquatic life forms such as bacteria, small invertebrates, oligochaete worms and some aquatic plants including *Lemna gibba* (duckweed). Some bioaccumulation was observed in terrestrial higher plants, such as sunflower and wheat. This result appeared to be related to uptake with water and then concentration due to transpiration water loss. When transferred to clean hydroponic media, some elimination of TFA was seen. Also, more than 80% of the TFA in leaves was found to be water extractable, suggesting that no significant metabolism of TFA had occurred.

At an exposure level of $1200 \text{ mg}\cdot\text{l}^{-1}$ of sodium trifluoroacetate (NaTFA) — corresponding to $1000 \text{ mg}\cdot\text{l}^{-1}$ HTFA — no effects were seen on either *Brachydanio rerio* (a fish) or *Daphnia magna* (a water flea). With duckweed, mild effects were seen on frond increase and weight increase at the same exposure level. At a concentration of $300 \text{ mg}\cdot\text{l}^{-1}$ no effects were observed. Toxicity tests were conducted with 11 species of algae. For ten of these species the EC_{50} was greater than $100 \text{ mg}\cdot\text{l}^{-1}$. In *Selenastrum capricornutum* the no-effect level was $0.12 \text{ mg}\cdot\text{l}^{-1}$. At higher levels the effect was reversible. The reason for the unique sensitivity of this strain is unknown, but a recovery of the growth rate was seen when citric acid was added. This could imply a competitive inhibition of the citric acid cycle.

The effect of TFA on seed germination and plant growth has been evaluated with a wide variety of plants. Application of NaTFA at $1000 \text{ mg}\cdot\text{l}^{-1}$ to seeds of sunflower, cabbage, lettuce, tomato, mung bean, soy bean, wheat, corn, oats and rice did not affect germination. Foliar application of a solution of $100 \text{ mg}\cdot\text{l}^{-1}$ of NaTFA to field grown plants did not affect growth of sunflower, soya, wheat, maize, oilseed rape, rice and plantain. When plantain, wheat (varieties Katepwa and Hanno) and soya were grown in hydroponic systems containing NaTFA, no effects were seen on plantain at $32 \text{ mg}\cdot\text{l}^{-1}$, on wheat (Katepwa) and soya at $1 \text{ mg}\cdot\text{l}^{-1}$, or on wheat (Hanno) at $10 \text{ mg}\cdot\text{l}^{-1}$; some effects on growth were seen at, respectively, $100 \text{ mg}\cdot\text{l}^{-1}$, $5 \text{ mg}\cdot\text{l}^{-1}$, $5 \text{ mg}\cdot\text{l}^{-1}$, and $10 \text{ mg}\cdot\text{l}^{-1}$ and above.

TFA is not metabolized in mammalian systems to any great extent. It is the major final metabolite of halothane, HCFC-123 and HCFC-124. The half-life of TFA in humans is 16 hours. As expected, the acute oral toxicity of the free acid is higher than the one of the sodium salt. The inhalation LC_{50} (2 hour exposure) for mice was $13.5 \text{ mg}\cdot\text{l}^{-1}$ (2900 ppm) and for rats it was $10 \text{ mg}\cdot\text{l}^{-1}$ (2140 ppm). Thus, TFA is considered to have low inhalation toxicity. The irritation threshold for humans was 54 ppm.

As one would expect of a strong acid, it is a severe irritant to the skin and eye. When conjugated with protein, it has been shown to elicit an immunological reaction; however, it is unlikely that TFA itself would elicit a sensitization response. Repeat administration of aqueous solutions have shown that TFA can cause increased liver weight and induction of peroxisomes. Relative to the doses (0.5% in diet or $150 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ by gavage) the effects are mild.

In a series of Ames assays, TFA was reported to be non-mutagenic. Its carcinogenic potential has not been evaluated. Although TFA was shown to accumulate in amniotic fluid following exposure of pregnant animals to high levels of halothane (1200 ppm), no fetal effects were seen. Likewise, a reproduction

study that involved exposure of animals to halothane at levels up to 4000 ppm for 4 hours per day, 7 days per week, resulted in no adverse effects. Given the high levels of halothane exposure, it is unlikely that environmental TFA is a reproductive or developmental hazard.

Overall the toxicity of TFA has been evaluated in stream mesocosms, algae, higher plants, fish, animals and humans. It has been found to be of very low toxicity in all of these systems. The lowest threshold for any effects was the reversible effect on growth of one strain of algae, *Selenastrum capricornutum*, which was seen at $0.12 \text{ mg}\cdot\text{l}^{-1}$. There is a 1000-fold difference between the no-effect concentration and the projected environmental levels of TFA from HFCs and HCFCs ($0.0001 \text{ mg}\cdot\text{l}^{-1}$). Based on available data, one can conclude that environmental levels of TFA resulting from the breakdown of alternative fluorocarbons do not pose a threat to the environment.

Key Words: hydrochlorofluorocarbons (HCFCs), hydrofluorocarbons (HFCs), CFC alternatives, trifluoroacetate (TFA), environmental fate, ecotoxicity.

INTRODUCTION AND PERSPECTIVE

The Montreal Protocol was developed in 1987 in response to concerns that the chlorofluorocarbons (CFCs) were releasing chlorine into the stratosphere and that this chlorine was causing a depletion of stratospheric ozone over Antarctica. This international agreement called for a phase out of these CFCs. Industry initiated a major effort to find safe replacements. The Alternative Fluorocarbons Environmental Acceptability Study (AFEAS) was formed in 1989 by several chemical companies from Europe, Japan, and the United States with the aim of assessing the environmental acceptability of a range of hydrochlorofluorocarbons (HCFCs) and hydrofluorocarbons (HFCs). Studies by independent researchers over the next six years were coordinated with work supported by U.S. and European government agencies. The results showed that, unlike CFCs, alternative fluorocarbons will break down readily in the lower atmosphere to form simple inorganic species already present in the environment (NASA, NOAA and AFEAS, 1995 and references cited therein). However, a few of the HCFCs and HFCs can be expected to form trifluoroacetyl halides that will dissolve in environmental water to give trifluoroacetate (TFA) salts.

In 1991, in response to concerns that this would introduce a new and potentially hazardous material into the environment, AFEAS initiated a research program to determine the environmental fate of TFA and to provide a timely and accurate forecast of potential ecological impact. The initial concern had been that HFC-134a (1,1,1,2-tetrafluoroethane, an alternative to CFC-12) would form TFA, which has relatively low mammalian toxicity, and that the TFA would subsequently react in the environment to give monofluoroacetic acid (MFA), which is acutely poisonous at low doses. Theoretical and experimental data (Emptage, 1994) quickly removed these concerns about MFA ac-

cumulation in the environment, but there was still a clear need to examine the ecological impact of TFA.

A panel of advisors was convened in 1992 to outline research that would provide a valid and systematic approach to assessing the impact of TFA. The experts suggested a strategy to identify key “pressure” points in the major biogeochemical cycles — carbon fixation, mineralization, nitrogen fixation and bioaccumulation in plants — where TFA could conceivably exert a major influence. Furthermore, plans were devised for assessing whether TFA can be biodegraded in the environment. This approach was then used to guide an evolutionary research program that was executed over the last 4 years through collaborative efforts between academic and industrial laboratories. The minimum levels of quality control were compliance with “Good Laboratory Practice” guidelines or publication of the results in peer-reviewed journals.

A number of physico-chemical and biodegradation studies have been completed, in addition to biological investigations. During the course of the work it became clear that TFA is not a new environmental contaminant. It is present in contemporary air, precipitation and surface waters from around the world, and before significant amounts of HFC or HCFC precursors have been produced and released.

The program described here represents one of the most comprehensive efforts to assess the environmental impact of a chemical ever undertaken by industry. The risk assessment is a synthesis of the research results and an assessment based on best available data. It consists of a comparison of the anticipated future levels of TFA, arising from decomposition of HFCs and HCFCs, with concentrations that would exert environmental effects. More specifically, the risk assessment covers: general substance information, sources, distribution and releases into the environment, exposure measurements, degradation, accumulation, effects assessment, and risk characterization.

In this article, the following abbreviations will be used:

TFA: trifluoroacetate

HTFA: trifluoroacetic acid

NaTFA: sodium trifluoroacetate

GENERAL SUBSTANCE INFORMATION

Identification of the Substance

Name:	Trifluoroacetic acid
CAS number:	76-05-1
Synonym:	HTFA
Formula:	$\text{CF}_3\text{CO}_2\text{H}$
Molecular weight:	114

Name:	Sodium trifluoroacetate
CAS number:	2923–18–4
Synonym:	NaTFA
Formula:	$\text{CF}_3\text{CO}_2\text{Na}$
Molecular weight:	136

Physico-Chemical Properties

HTFA

Physical state:	Colorless fuming (hygroscopic) liquid
Specific gravity:	$1484 \text{ kg}\cdot\text{m}^{-3}$ at 25°C
Melting point:	-15.3°C
Boiling point:	72°C
Vapor pressure:	105.7 hPa at 20°C
Water solubility:	Miscible in all proportions (Feenstra-Bieders and Olthof, 1992)

Partition coefficient

n-Octanol/water (log):

–2.1 (Feenstra-Bieders and Olthof, 1992;

Thus, 1997)

–0.2 (calculated according to Rekker)

0.325 (ClogP for Windows V 1.0.0)

0.5 (SRC's KOWWIN v1.52)

pKa: 0.23

pH (1% solution): 1

pH (100 $\text{mg}\cdot\text{l}^{-1}$ distilled water): 3.1

pH (10 $\text{mg}\cdot\text{l}^{-1}$ distilled water): 7.4 – 7.75

pH (100 $\text{mg}\cdot\text{l}^{-1}$ buffered
ISO water): 4

pH (10 $\text{mg}\cdot\text{l}^{-1}$ buffered
ISO water): 7.4 (Thus and van Dijk, 1996)

Henry's Law Constant $K_{\text{H}} = 1.1 \times 10^{-2} \text{ Pa}\cdot\text{m}^{-3}\cdot\text{mol}^{-1}$ at 25°C
(Bowden *et al.*, 1996)

UV/vis absorption: No absorption at $\lambda > 250 \text{ nm}$
(van Dijk, 1992a)

Conversion Factors

(air, 1 atm, 25°C): $1 \text{ mg}\cdot\text{l}^{-1} = 214 \text{ ppm}$; $1 \text{ ppm} = 4.66 \text{ mg}\cdot\text{m}^{-3}$

NaTFA

Physical state: White (hygroscopic) powder

Melting point: 207°C (decomposition)

Water solubility: $625 \text{ g}\cdot\text{l}^{-1}$ (25°C)

pH (2% solution): 7

Partition coefficient

n-Octanol/water (log): –3.31 (SRC's KOWWIN v1.52)

SOURCES

Production and Known Sources

According to Elliott (1994), trifluoroacetic acid is manufactured by only three companies: Halocarbon Products Corporation in the United States, and Rhône-Poulenc and Solvay in Europe. The quantities involved are relatively small — of the order of 1000 metric tons per year (J. Franklin, personal communication), an estimate that is consistent with the quoted revenue of the major U.S. producer (McConville, 1996). The processes are enclosed, with effluent being subject to local requirements for disposal of chemical waste. Similar chemical waste streams can also arise from processes in which trifluoroacetate is produced as a byproduct. From one such plant (DuPont – Fayetteville, North Carolina), the site effluent contained about 3 ppm of trifluoroacetate (Chumley, 1992).

Environmental trifluoroacetate can also be produced during the oxidation of several organofluorine compounds released to the atmosphere by human activities. Halothane and isoflurane anaesthetics, which have been in use since the 1970s, yield trifluoroacetate (R. Atkinson, personal communication). Also, some of the fluorocarbon alternatives to CFCs decompose in the atmosphere to form trifluoroacetate (NASA, NOAA, and AFEAS, 1995) and, while these sources are currently small, they could become significant in the future and merit the closer scrutiny given below.

Uses

Trifluoroacetic acid is widely used in the fine chemicals industry and as a laboratory reagent: for derivatizing carbohydrates, amino acids and peptides; as a catalyst in esterification reactions and the Beckmann rearrangement of oximes to amides, and for protein synthesis (Elliott, 1994). In all cases, the material is either consumed or becomes part of a chemical waste stream. The quantities released into the atmosphere are very small indeed.

Emission Pattern

The known sources can be expected to yield fluxes of trifluoroacetate into the environment that differ significantly in both geographical distribution and the first compartment into which they are released. For example, only if there are fugitive emissions of vapor will material that is used as a chemical intermediate give rise to a point source of atmospheric contamination, otherwise releases can be expected to be to the aqueous compartment.

The Henry's Law constant (K_H) for trifluoroacetic acid estimated from measurements by Bowden *et al.* (1996) is $8.95 \pm 0.1 \times 10^{-3} \text{ mol} \cdot \text{kg}^{-1} \cdot \text{atm}^{-1}$, which translates into a value for K_H of $1.1 \times 10^{-2} \text{ Pa} \cdot \text{m}^{-3} \cdot \text{mol}^{-1}$. With such a value, and because trifluoroacetic acid is totally miscible with water and has a log K_{OW} value of -0.2 , the preferred environmental compartment will be water, rather than air, ground, or biota. The rules set out by Ballschmiter (1992) state that, if K_H is less than $2 \text{ Pa} \cdot \text{m}^{-3} \cdot \text{mol}^{-1}$ and log K_{OW} is less than 4, the material should preferentially distribute into the aqueous compartment of the environment.

Thus, trifluoroacetic acid that is emitted from processes as vapor, or trifluoroacetate that is formed from other materials by reaction in the atmosphere will partition rapidly into cloud, rain, or surface water.

Substances that decompose in the atmosphere by oxidation or photolysis will give rise to diffuse fluxes of decomposition products into the atmosphere as the first compartment. These substances have atmospheric lifetimes ranging from about 1 to 40 years (WMO, 1994) so that most decomposition occurs at or near the background concentration of the substance after it has become well mixed in the atmosphere. The decomposition mechanisms depend on physical and chemical properties and processes that are relatively well understood (NASA, NOAA, and AFEAS, 1995) so that it is possible to calculate accurately the future atmospheric concentrations of precursors to trifluoroacetate, given a particular set of scenarios for emissions. Furthermore, the flux of trifluoroacetic acid, into the atmosphere and thence into rain and surface water, can be estimated from the precursor concentrations with confidence and provides the possibility of verifying the magnitude of known fluxes against environmental observations.

Concentrations of trifluoroacetate observed in the air, in precipitation and in surface waters in Europe are several orders of magnitude larger than the known source fluxes would allow (Frank *et al.*, 1996). Similar concentrations have been observed in contemporary water and air samples from Nevada, USA; Canada; Australia and South Africa (Zehavi and Seiber, 1996; Frank and Klein, 1997; Grimvall *et al.*, 1997), suggesting that there is one or more large unknown source of environmental trifluoroacetate. The sizes of the fluxes of the known source gases are not in doubt; their concentrations calculated from estimated emissions are consistent with observations, and additional contemporary sources, substantially larger than those known, must be invoked to explain the observed environmental concentrations of trifluoroacetate.

The current environmental burden from the decomposition of man-made fluorocarbons, and the anticipated future burden resulting from future emissions of such precursors, should be evaluated in the context of the background concentrations that have been observed.

DISTRIBUTION AND RELEASES INTO ENVIRONMENT

From Trifluoroacetic Acid Production and Use

With a pKa of 0.23, the strength of trifluoroacetic acid approaches that of mineral acids. Unlike the mineral acids, it is miscible not just with water but with fluorocarbons and most common organic solvents including methanol, benzene, carbon tetrachloride, acetone, ether, and hexane. It is a good solvent for proteins, leading to its use in protein synthesis. It is useful for making derivatives of carbohydrates, amino acids and peptides from which the trifluoroacetyl protective group can be removed relatively easily (Elliott, 1994). Trifluoroacetic acid is a useful catalyst for esterifications of alcohols, acylations of aromatics (Halocarbon, 1967) and in the Beckmann rearrangement of

oximes to amides (Huber, 1955). These uses are typical of the fine chemicals industry and of laboratories, and the total global production of trifluoroacetic acid is expected to reflect the small scale of the uses. Although there are no audited data for production and use, informal estimates suggest that the quantities involved are of the order of 1000 metric tons per year.

Trifluoroacetic acid is stable to oxidation and so can be prepared by a number of routes that involve the oxidation of compounds that have α -trifluoromethyl groups. Thus, alkaline permanganate oxidation of 2,3-dichlorohexafluorobut-2-ene gives an 87% yield of the acid (Henne and Trott, 1947) and, in a manner similar to atmospheric degradation processes, photochemical oxidation of 1-chloro-2,2,2-trifluoroethane or 1,1-dichloro-2,2,2-trifluoroethane with oxygen gives high yields of trifluoroacetyl chloride that can be hydrolyzed to trifluoroacetic acid (Haszeldine and Nyman, 1959; Dittmann, 1975).

Like the use processes, the production processes involve reactions in contained and/or aqueous systems from which fugitive losses of trifluoroacetic acid to the atmosphere are small. In many cases the use is as a raw material so that most of it is wholly converted and cannot be released as trifluoroacetic acid or its salts. From both production and use, any persistent loss is likely to be in the form of solution in chemical waste streams, the disposal and treatment of which will be subject to local controls.

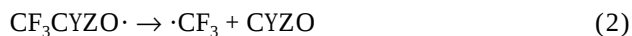
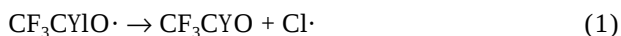
Deliberate production and use of trifluoroacetic acid does not appear to be a significant contributor to current global environmental levels.

By-Product from Chemical Syntheses

Production of hexafluoropropylene oxide can result in an aqueous waste stream containing trifluoroacetate. The concentration of trifluoroacetate measured in one plant outfall was 3 ppm or less (Chumley, 1992) and, while this may or may not be typical of such processes, the compartment and the concentration are consistent with the properties discussed in a previous section.

Atmospheric Oxidation of Fluorinated Hydrocarbons

In recent years the atmospheric decomposition of halocarbons, particularly those fluorocarbons that could replace CFCs, has been the subject of intensive study. It is now agreed that the mechanism involves an initial abstraction of the hydrogen atom in the molecule by atmospheric hydroxyl radicals to yield water and a haloalkyl radical. The latter reacts rapidly with oxygen to give a haloalkylperoxy radical that undergoes further reactions, generally with nitric oxide or hydroperoxyradicals. The product in both cases is a haloalkoxy radical, which can react further in one of three ways, depending on its molecular composition: C-Cl bond cleavage, C-C bond cleavage or hydrogen abstraction (Cox *et al.*, 1995; McCulloch and Sidebottom, 1993; Midgley, 1995). Thus, the general reactions of those haloalkoxy radicals that could form precursors to trifluoroacetate are:



where Y and Z can be Br, Cl, F, or H.

The ultimate products of many of these reactions are fluoride and chloride ions and carbon dioxide. These are neither new to the environment nor expected to be introduced at rates that would significantly enhance the background levels (WMO, 1989). However, if Y is either Br, Cl, CF_3 , or F then the products of reactions (1) and (3) are trifluoroacetyl halides that can, on hydrolysis with atmospheric or surface water, form trifluoroacetic acid. Thus, trifluoroacetic acid is by no means a universal product of the degradation of fluorinated hydrocarbons; the parent compound requires a CF_3 group and a halogen atom on the α carbon adjacent to it. Substances that fulfill these criteria are:

CF_3CHClBr	1-bromo-1-chloro-2,2,2-trifluoroethane	'Halothane'
$\text{CF}_3\text{CHClOCHF}_2$	1-chloro-2,2,2-trifluoroethyl difluoromethyl ether	'Isoflurane'
CF_3CHCl_2	1,1-dichloro-2,2,2-trifluoroethane	HCFC-123
CF_3CHFCl	1-chloro-1,2,2,2-tetrafluoroethane	HCFC-124
$\text{CF}_3\text{CH}_2\text{F}$	1,1,1,2-tetrafluoroethane	HFC-134a
$\text{CF}_3\text{CHFCF}_3$	1,1,1,2,3,3,3-heptafluoropropane	HFC-227ea

HFC-125 (1,1,1,2,2-pentafluoroethane) matches the criteria but undergoes solely C-C bond cleavage according to reaction (2); reaction (1) would require the cleavage of a C-F bond which is not possible under atmospheric conditions. Halothane and isoflurane anaesthetics are expected to form totally trifluoroacetyl chloride or bromide (probably the former) (R. Atkinson, personal communication). HCFC-123 is converted 98% to trifluoroacetyl chloride, HCFC-124 100% to trifluoroacetyl fluoride and HFC-227ea yields equal amounts of carbonyl difluoride and trifluoroacetyl fluoride (Zellner *et al.*, 1994). HFC-134a, however, can undergo both reactions (2) and (3) so that it forms a mixture of trifluoroacetyl fluoride, formyl fluoride and carbonyl difluoride (Tuaizon and Atkinson, 1995; Cox *et al.*, 1995). The extent to which each reaction will proceed in the atmosphere depends on the local temperature where decomposition is occurring and the local pressure, particularly partial pressure of oxygen for reaction (3). At sea-level, only some 18% of the HFC-134a de-

composing is converted to trifluoroacetyl fluoride but, with increasing altitude (and consequently reducing temperature and pressure), the yield of trifluoroacetyl fluoride increases and it becomes the major product at the tropopause. An average yield for the troposphere is calculated to be in the region of 40% (Cox *et al.*, 1995; Franklin, 1993; Midgley, 1995). Recently, it has been suggested that these conversions to trifluoroacetyl fluoride might be overestimates and that the true value could be as little as 12% or one third of the value now accepted. This view is based on work done in a laboratory system that contained NO (Wallington *et al.*, 1996), which is thought to enhance the scission reaction via a relatively stable $\text{CF}_3\text{CFHOONO}$ intermediate. If this is truly representative of the atmospheric behavior of HFC-134a, it would reduce the expected flux of TFA from this source by a factor of about three. A yield of 40% is, however, used throughout the calculations of source strengths in this assessment on the grounds that this is the value used in most of the atmospheric modeling studies and that it represents a maximum from the HFC-134a source.

Trifluoroacetyl fluoride is stable towards photolysis in the troposphere but trifluoroacetyl chloride (and bromide) will photolyze there, reducing the apparent yields of these acid halides from the parent compounds to about 60% of stoichiometry in the case of the acid chloride (Cox *et al.*, 1995).

The acid halides will be taken up by atmospheric or surface water relatively rapidly; the rates are governed by the rate constants of the hydrolysis reactions forming trifluoroacetic acid and their Henry's constants for aqueous solution. In all cases, the maximum lifetime for the acid halide would be of the order of 30 days and the minimum lifetime, which is governed more by cloud formation probabilities, is about 10 days (Kolb *et al.*, 1995a,b).

These lifetimes are long compared with regional mixing times so that, having been formed in the atmosphere, the trifluoroacetyl halide would be dispersed on a continental scale before being deposited as trifluoroacetic acid. Nevertheless, the lifetimes are short compared to those of the parent compounds which are governed by the rates of reaction with hydroxyl radicals. The atmospheric lifetimes of the parent compounds range from about 1 year, in the case of the anaesthetics, halothane and isoflurane (Brown *et al.*, 1990), through 1.4 years for HCFC-123 (WMO, 1994), 6.1 years for HCFC-124, and 14.6 years for HFC-134a (IPCC, 1996a). In all cases, such lifetimes mean that the compounds will be hemispherically, if not globally, dispersed and so they will react at concentrations that are relatively constant geographically. Local variations in hydroxyl radical concentrations are liable to have more profound effects on the rates and extent of reactions (Madronich and Dentener, 1995; Kanakidou *et al.*, 1995).

Current Releases

The atmospheric concentrations of the HCFCs and HFC-134a are determined. On the contrary, there are no concentration measurements and only informal estimates for releases of the anaesthetics (halothane and isoflurane)

to the atmosphere. It has been assumed that halothane remains the most used of the fluorocarbon anaesthetics at a maximum of 1500 metric tons per year globally, and that all the material used is emitted to atmosphere (McCulloch, 1995b). The figure is consistent with the productive capacity and market share of the major manufacturer (C&P News, 1995 and 1996). The same references suggest that production has been at or near this level for several years so that the fluxes of these anaesthetics and their atmospheric decomposition can be assumed to be in equilibrium. If the use of isoflurane were half as much as that of halothane, the total quantity of trifluoroacetyl chloride formed by the anaesthetics would be in the region of 1540 metric tons per year; given that this material photolyzes, the effective flux would be 930 metric tons per year, equivalent to a global deposition rate of 800 metric tons per year of trifluoroacetic acid.

The potential HCFC precursors to trifluoroacetic acid are at the point of their limits of detection in the atmosphere (P.G. Simmonds, personal communication), inferring that their concentrations are, at most, 0.1 parts per trillion by volume (pptv). The upper limits for the atmospheric burdens of these compounds are 2500 metric tons of HCFC-123 and 2300 metric tons of HCFC-124, consistent with the values given in McCulloch (1995b) for lower limits of detection. The value for HCFC-123, coupled with its atmospheric lifetime of 1.5 years, equates to a decomposition rate of 1690 metric tons per year which, after allowing for the photolysis of the trifluoroacetyl chloride product, gives a deposition rate for trifluoroacetic acid of 760 metric tons per year. Similarly, the deposition rate for trifluoroacetic acid from HCFC-124 is calculated to be 320 metric tons per year.

Contemporary concentrations of HFC-134a in the atmosphere are 2.5 pptv in the Northern Hemisphere and 1.2 pptv in the Southern Hemisphere (Montzka *et al.*, 1996; Oram *et al.*, 1996). This corresponds to an atmospheric burden of approximately 31,000 metric tons. Using the atmospheric lifetime of 14.6 years, the decomposition rate is calculated to be 2140 metric tons per year. At a 40% yield, this would amount to 960 metric tons per year of trifluoroacetic acid deposited globally from this source.

HFC-227ea has yet to be detected in the atmosphere and so the potential contribution from it has been assumed to be zero now. Therefore, the maximum estimate for the total contemporary deposition rate of trifluoroacetate from fluorinated hydrocarbons is $800 + 760 + 320 + 960$, or a total of 2800 metric tons per year.

Scenarios for Future Releases of Precursors

Alternative Scenarios

With the exception of the anaesthetics, demand for which is static or even falling, the fluorocarbon precursors to trifluoroacetic acid are expected to be released in progressively larger amounts throughout the coming decades. Production and use of HCFCs is controlled under the Montreal Protocol, so that the emissions of HCFC-123 and HCFC-124 will become limited within the next

25 years and will eventually fall to zero. There is no specific regulatory limit on HFCs and so, theoretically, growth of HFC-134a emissions could continue unabated. In order to judge the potential future effects of these materials on the environment, various scenarios have been proposed, based on several methodologies.

1. For the Enquete Commission of the German Parliament (DB, 1994) on life cycle analysis applied to HFC-134a and other substitute refrigerants, emissions of HFC-134a were calculated to reach $160 \text{ kT}\cdot\text{yr}^{-1}$ by 2020, with production in that year running at $310 \text{ kT}\cdot\text{yr}^{-1}$. The calculations were based on projection of underlying demand, using projected regional GDPs, and views on the extent of substitution and integrity of containment.
2. The demand for alternative fluorocarbons over the period to 2020 was estimated by McCulloch (1994, 1995a) from a detailed analysis of the historical market for CFCs and estimates for their replacement by HCFCs and HFCs. The values for HFC-134a production and emissions in 2020 were almost identical to those in DB (1994). No data for HCFCs 123 and 124 were provided by this work.
3. In order to gauge the potential climate change effect from future emissions of fluorocarbons, the Intergovernmental Panel on Climate Change (IPCC) has provided scenarios for HCFCs and HFCs. These were developed by projecting CFC demand and proposing almost total substitution of that demand using HCFCs and HFCs. The scenarios, which cover all greenhouse gases, were originally proposed in 1992 to replace the 1990 scenarios that were considered unacceptable by the parties to the Rio Convention. They have been updated in the light of changing regulations and the latest version is contained in the "Second Assessment Report" (IPCC, 1996b). Only for HCFC-123 is the emission specified in mass units; it is proposed that it reaches a maximum of $130 \text{ kT}\cdot\text{yr}^{-1}$ at the end of this century, falling to $13 \text{ kT}\cdot\text{yr}^{-1}$ by 2020. Emissions of HCFC-124 are not mentioned; presumably they are expected to be very low. For HFC-134a, the scenario output is in terms of atmospheric concentrations and values of 200–230 pptv are proposed for the year 2020, the variability arising from different assumptions about overall economic growth. The equivalent emissions can be back-calculated from these concentrations and, for HFC-134a, amount to 400–470 $\text{kT}\cdot\text{yr}^{-1}$. HFC-227ea is not included specifically in this scenario.

The much larger values proposed in the IPCC scenarios reflect the underlying assumption that the materials are used to substitute in all historic markets for CFCs, including immediately dispersive uses such as aerosol propellants. They may be unrealistically high. For example, the IPCC scenarios anticipated that the current atmospheric concentration of HFC-134a would be 13 to 14 pptv. The actual measurements, as described above, show a global average

of about 2 pptv (Montzka *et al.*, 1996; Oram *et al.*, 1996). For reasons such as this the IPCC scenarios are not used in this assessment.

Development of a Standard Concentration of TFA

The possible future deposition rate of trifluoroacetic acid has been calculated using mathematical models of the lower atmosphere. In addition to the chemical reactions themselves, these models take account of the geographical distributions of:

- The concentration of hydroxyl radicals with which the parent compounds react first of all
- The emissions of the parent compounds
- The rainfall that scavenges trifluoroacetic acid from the atmosphere (Kanakidou *et al.*, 1995; Rodriguez *et al.*, 1994).

Because most of the rainfall and the highest regional concentrations of hydroxyl occur in the tropics, the mass deposition rate of trifluoroacetic acid is highest in this region. Starting from the scenario described in McCulloch (1994), Kanakidou *et al.* (1995) calculate that the tropical concentration would be up to $2 \text{ mol} \cdot \text{m}^{-2} \cdot \text{yr}^{-1}$ and that this would be equivalent to $1 \text{ nmol} \cdot \text{l}^{-1}$ of rainwater. The latter value would correspond to $100 \text{ ng} \cdot \text{l}^{-1}$. Over Europe the deposition rate in 2020 would be about $0.5 \text{ } \mu\text{mol} \cdot \text{m}^{-2} \cdot \text{yr}^{-1}$ and, over the United States, levels would be up to double this.

These values are of the same order of magnitude as those calculated by Rodriguez *et al.* (1994), on the basis of a scenario from the U.S. Environmental Protection Agency; the latitudinal variation (up to a factor of 40) and longitudinal variation (a factor of 3) are also similar. In the year 2020, the modeled decomposition flux of HFC-134a was calculated to be $115 \text{ kT} \cdot \text{yr}^{-1}$, with a further $20 \text{ kT} \cdot \text{yr}^{-1}$ each of HCFCs 123 and 124. The implied global deposition of trifluoroacetic acid then would be $155 \text{ kT} \cdot \text{yr}^{-1}$.

With such close agreement on potential future deposition rates, this quantity (rounded to 160,000 metric tons per year), and a corresponding rainwater concentration of $0.1 \text{ } \mu\text{g} \cdot \text{l}^{-1}$ ($0.0001 \text{ mg} \cdot \text{l}^{-1}$) are adopted as standards for this risk characterization.

Accumulation of TFA in Aquatic Ecosystems

The objective of this section is to review whether conditions could occur in the environment which could lead to a significant accumulation of TFA in natural water bodies. It appears to be possible to accumulate a riverborne flux of TFA from "Normal" concentrations of a few hundreds of nanograms per liter to several thousands of nanograms per liter in receiving waters from which there is no outflow, only evaporation. In the case of the River Jordan / Dead Sea system (Table 3), consideration of the volumes and flows indicates accumulation over many hundreds of years.

Recently, the assumption has been made by Tromp *et al.* (1995) that TFA can accumulate to very high concentrations in seasonal wetlands, which are special aquatic ecosystems that dry out periodically and are replenished only by rainfall. It is necessary to examine if the hypothesis developed in that work could occur in real conditions.

Tromp *et al.* (1995) conducted a sensitivity study of the potential for enhancement of TFA concentrations in such ecosystems. In the study, several assumptions were used concerning both the conditions that might lead to higher concentrations of TFA in rainwater (in comparison with expected average concentrations calculated by mathematical models; see previous sections) and the characteristics of the seasonal wetlands that would favor accumulation. A calculation presented in the paper shows that a seasonal wetland, receiving rainfall for a total period of 30 years at a local (enhanced) TFA concentration of $1 \text{ mg}\cdot\text{l}^{-1}$, with an evaporative loss rate of 5 yr^{-1} , and a loss of TFA out of the wetland by seepage (or other physical or biological process) at a rate of 0.1 yr^{-1} , would reach a concentration of $100 \text{ mg}\cdot\text{l}^{-1}$ at the end of that period. However, this is simply a mathematical calculation that has been conducted by adding together the consequences of extreme conditions without regard for the probability that they could occur simultaneously. In the real environment it is highly improbable that all of the necessary conditions for accumulation will happen together and be maintained for decades. The step-by-step review of those conditions carried out below indicates that the probability that such accumulation will take place over decades is close to zero.

First, the seasonal wetland would need to be located near a large urban area, where the assumption is made that local conditions could lead to enhanced TFA concentration in rainwater. These local conditions would have to meet several criteria.

1. The concentrations of precursors to TFA should be higher than average, due to local emissions. A factor of 10 to 20 is suggested in Tromp *et al.* (1995), but observations in the Los Angeles area (notorious for local pollution) show an historic factor of about 3 for CFC-11 (Bastable *et al.*, 1990). CFC-11 was used in the blowing of polyurethane foams and in whole building air conditioning. The most significant TFA precursor is expected to be HFC-134a, which is used in refrigeration and air conditioning applications where smaller emissions factors are expected and further improvements in containment are likely in the coming decades. The appropriate enhancement factor therefore is less than 3.
2. The oxidizing capacity of the local atmosphere (including the OH radical concentrations) would be higher due to local pollution, thus increasing the rate of conversion of the precursors. A possible factor of 10 is quoted in Tromp *et al.* (1995), but calculations based on actual observations of tropospheric ozone, NO_x, water vapor, carbon monoxide, methane and non-methane hydrocarbons at Riverside, California in June

suggest that the OH field enhancement in that portion of the Los Angeles Basin does not exceed a factor of 2 (Ko *et al.*, 1995).

3. It would be necessary to have an appropriate combination of pollution event and rainfall, the most effective rainout of TFA occurring when rain immediately followed a pollution event. The implicit assumption in Tromp *et al.* (1995) is that only the most effective rainout occurs and that it is repeated systematically throughout the year for decades. The real situation, for example, in the Los Angeles Basin, is that rainfall happens preferentially in the winter months, when photochemical activity in the atmosphere is lowest (Ko *et al.*, 1995). The same authors pointed out that no rainfall event was observed during June 1990 and, in that case, TFA would be dispersed (on a continental scale) before being rained out. It is expected that pollution events would last more than one day, allowing precursor concentrations to increase; this would be possible under an inversion layer that trapped the gases within the "boundary" layer. Observations show that such highly polluted conditions are associated with low wind speed. On the other hand, rainout of the TFA formed within the pollution event needs a change in meteorological conditions bringing in a new air mass, with clouds and rain. For effective rainout of the TFA, this change in meteorology must not affect the stability of the boundary layer and must not disperse the TFA before rainout. It is not clear that such a mechanism could exist in the real atmosphere and, even if it did, it would be an exceptional event. An attempt to calculate the resulting increase of the average TFA concentration from uncorrelated rain and pollution events gives a value of the order 15% increase at most (Ko *et al.*, 1995). The probability of maintaining conditions that give total local rainout over a period of decades is therefore not far from zero.

Secondly, the long-term accumulation in seasonal wetlands requires:

4. A closed system, maintained for decades, where seepage or loss by other physical processes such as aeolian transport would be small. Vernal pools, examples of seasonal wetlands suggested to be most at risk, have been shown to have significant seepage (Sefchick *et al.*, 1994).
5. An evaporation rate high enough to have a severalfold increase in TFA concentration each year.

Tromp *et al.* (1995) chose a value of 5 yr^{-1} for this parameter, but the largest evapoconcentration factor for vernal pools is 2.2 as reported by Sefchick *et al.* (1994) and inferred from chloride ion concentration that is indicated as the best conservative solute with sodium ion. It is also important to point out that such evapoconcentration factors reflect concentrations variations but not accumulation from year to year. Evapoconcentration factors vary with the type and location of the wetland and with the ion concentrated and this observation yields the most appropriate value.

Each condition listed above, even taken alone, has little probability of occurring. For accumulation to take place, not only do the conditions have to occur together but this combination of conditions has to be maintained for decades. In conclusion, although some accumulation of TFA may take place in aquatic ecosystems like vernal pools, accumulation to high concentrations as described in Tromp *et al.* (1995) appears to be highly improbable.

Soil Adsorption

The degree to which TFA adsorbs to soils may affect its bioavailability to plants and bacteria, the general mobility of this compound through soils and aquifers, and, of course, the concentration to which TFA could accumulate in the soil. The soil-water milieu may vary greatly in terms of mineral and organic compositions, as will the flux of cations and anions through these matrices. Therefore, if there is an interaction of TFA with specific components of the soil, this interaction may be site-specific and non-uniform in occurrence. Clearly, the problem of assessing soil adsorption in a controlled manner and in a way that is useful for developing a global perspective is very difficult.

Two laboratory studies were conducted to directly assess the partitioning of TFA between water and a variety of soil types under controlled laboratory conditions. The first study by van Dijk (1992b) showed that TFA did not adsorb to soil. The second study by Richey *et al.* (1997) showed that TFA generally interacted only weakly with most soils but was strongly adsorbed by some soils which contained high levels of organic matter. The data are not necessarily contradictory but may reflect the heterogeneity of soils tested. The studies are discussed in more detail below.

The first study examined the interaction of sodium TFA with three different soil types, obtained from locations in Northern Europe. The salient properties of the soils from van Dijk (1992b) follow.

	<i>Sand</i>	<i>Sandy Loam</i>	<i>Loam</i>
% Clay	2.7	8.3	16.5
% Silt	6.4	27.8	46.8
% Sand	90.9	64.1	36.7
pH	5.5	6.5	7.5
% Organic Carbon	4.3	1.3	2.6

These soils represent a relatively narrow range in terms of organic carbon and clay content; pH varied from mildly acidic to slightly alkaline. The researchers tested a soil/water mixture comprising 2 g soil and 10 ml of 10 µM calcium acetate in mixture with 40 µM sodium TFA. The supernatants were assayed for TFA after 16 hours of incubation. The results of the analyses indicated that <3% of the added TFA had been retained by the soil. This was equivalent to partition coefficients (K_d , soil concn./aqueous concn.) of <0.2 l·kg⁻¹.

A second study was performed on 54 different soils from disperse environments located predominantly in North America and Europe (Richey *et al.*, 1997). Rather than list the 54 soils individually, the ranges of important parameters are summarized here.

pH	2.76 – 5.85
% Clay	1% – 27%
% Organic Matter	1.4% – 93.3%

In these experiments adsorption isotherms were determined for 1:5 or 1:20 soil:solution ratios (for high organic or high mineral soils, respectively) over a range of TFA concentrations: 0, 2, 4, 7, 10, 20, 30, 40 μM NaTFA. TFA adsorption was determined by the difference in supernatant TFA concentrations after an equilibration period of 24 hours. Of the 54 soils tested, 20 soils showed no significant retention of TFA. Of the remainder, 23 gave K_d values <2 (high to intermediate mobility) and 8 soils exhibited low mobility of TFA ($K_d = 2$ to 10). Only three soils gave K_d values >10 ; the maximum K_d reported was 20 (60% retention) for a peat core containing 93% organic matter. At all sites where TFA retention was determined for both organic and mineral soils, greater retention was observed for the organic soil.

TFA adsorption was compared to that of other ions: bromide, chloride, fluoride, nitrate, and sulfate. The results indicated that TFA was not the most strongly retained of the common ions with the relative order for a high (82.5%) organic soil as follows: fluoride (most strongly retained) $\gg$ sulfate $>$ chloride $>$ TFA $>$ bromide $>$ nitrate. For intermediate (24.8%) organic matter soil: fluoride = sulfate $>$ chloride = TFA $>$ bromide $>$ nitrate. Anions were also shown to competitively inhibit TFA adsorption. For example, 150 μM sulfate — not an excessive environmental sulfate concentration — caused 50% reduction in TFA adsorption.

In comparing the two studies it is clear that a much larger representation of soil types was investigated in the work by Richey *et al.* (1997) and that the organic content of many of the soils in that work was strikingly higher. Organic content was determined by Richey *et al.* to be in positive correlation with TFA adsorption. The relatively low organic content of the soils in the van Dijk study may have led to the accurate conclusion for that study that TFA did not adsorb. One disturbing aspect of the van Dijk study was the use of 10 mM calcium acetate in the TFA equilibration mixture, use of such high concentration of a TFA analogue might have suppressed TFA binding. It should be noted that the TFA concentration used in both studies was 3 to 4 orders of magnitude higher than that anticipated in the environment in the year 2020.

Field manipulation experiments were conducted at two sites at the Hubbard Brook Experimental Forest (New Hampshire, USA). Field results generally agreed with laboratory studies, indicating that there is considerable variability in soil retention of TFA. TFA adsorption occurred mainly in the surface soil, where organic content was highest, and diminished with soil depth. Additions of TFA to an upland forest soil were largely transported with drain-

age water (>70%). In contrast, additions of TFA were strongly retained in a wetland with <5% of the added TFA exiting the system in water. The remainder of the TFA in the wetland was found in soil and plant tissues (Likens *et al.*, 1997). As in the laboratory studies of Richey *et al.* (1997), TFA mobility in field plots (Berger *et al.*, 1997) was found to be comparable with that of bromide, which is widely used as a conservative hydrologic tracer.

It can be concluded that typical soils do not exhibit significant retention of TFA, but that some partitioning to organic-rich soils is observed. Although none of the investigators examined the reversibility of TFA binding, based on the maximum observed partition coefficient (K_d) of 20 (Richey *et al.*, 1997), the maximum concentration bound to soil — in equilibrium with the projected rainfall concentration from CFC alternatives of $0.0001 \text{ mg} \cdot \text{l}^{-1}$ — would be $0.002 \text{ mg} \cdot \text{kg}^{-1}$.

EXPOSURE MEASUREMENTS

Aquatic Compartment

A number of groups have determined TFA in the aquatic environment at concentrations ranging upwards of a few nanograms per liter. Air, rain, and surface waters in Europe were extensively sampled and analyzed for trifluoroacetate during 1995 by Frank *et al.* (1996) and Frank and Klein (1997). This built on previous work by the same authors. The analytical methods were standardized and measurements made in air and rainwater samples during 1993 and 1994 (Frank *et al.*, 1995). The results of their determinations of the TFA concentrations in the Roter Main river in 1995 are given in Table 1; Figure 1 shows the analyses for both 1995 and 1996. There is no discernible seasonal trend.

Table 2 shows the results of TFA determinations in river and lake waters in Europe and the approximate locations of the sample points. The locations of European seawater, air, and precipitation sample points are shown in Figure 2.

Table 1. TFA content of the Roter Main River at Bayreuth, Germany (Frank *et al.*, 1996).

Date of Sample	TFA ($\text{ng} \cdot \text{l}^{-1}$)
March 1995	160 ± 27
April 1995	80
May 1995	140
June 1995	110
October 1995	280
November 1995	110
December 1995	60
Average	140

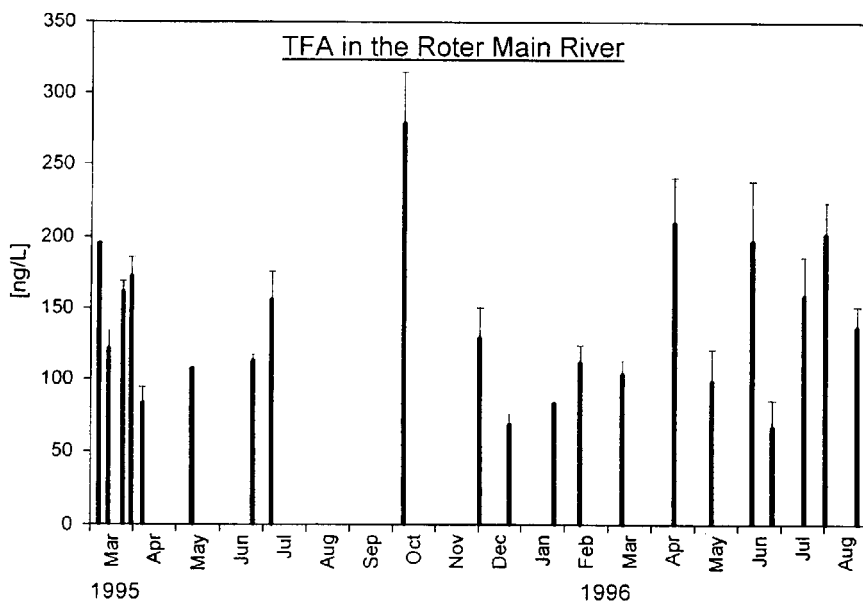


Figure 1. TFA in the river Roter Main at Bayreuth.

Surface water in and around Reno, Nevada, showed far higher concentrations of trifluoroacetate using a comparable, but different, analytical method (Zehavi and Seiber, 1996). The highest concentration that was recorded exceeded that in the Dead Sea (Frank *et al.*, 1996) by a factor of 6. In both cases, if the samples of the receiving waters and the rivers feeding them are representative, accumulation over many hundreds of years would be necessary to account for the observations.

Table 3 shows the concentrations reported for surface waters in Israel, Russia, Brazil, South Africa, and the United States. Table 4 shows the seawater concentrations recorded by Frank and co-workers for samples from the Baltic and North Seas and the Atlantic and Pacific Oceans. Figure 3 shows the sampling locations for all of the non-European surface water determinations, together with the locations of precipitation samples. Table 5 lists the results of determinations of trifluoroacetate in contemporary and ancient spring, mineral, and tap waters.

Table 2. Present TFA concentration in lakes and rivers in Europe (Frank *et al.*, 1996; Frank and Klein, 1997)

Location	Sample date	TFA determination		
		ng.l ⁻¹	n	S.D. ^a
R. Elbe (Wittenberg, Germany)	24 Feb 95	200	3	10
R. Danube (Regensburg, Germany)	25 Mar 95	200	3	2
R. Pegnitz (Nürnberg, Germany)	26 Mar 95	150	3	3
R. Mistelbach (Bayreuth, Germany)	24 Mar 95	215	3	9
R. Main (Mainleus, Germany)	3 Apr 95	40	3	16
R. Neckar (Tübingen, Germany)	23 Apr 95	260	3	5
R. Elbe (Hamburg-Altona, Germany)	7 Jul 95	100	5	14
R. Weiser (Bremerhaven, Germany)	6 Jul 95	100	4	7
R. Rhine (Duisburg-Ruhort, Germany)	6 Jul 95	630	4	15
R. Warnow (Rostock, Germany)	9 Jul 95	60	4	25
R. Nabb (Schwandorf, Germany)	9 Jul 95	130	3	14
R. Seine (Paris, France)	Jul 95	40		
R. Loire (Nantes, France)	Jul 95	330		
R. Rhine (Bregenz, Austria)	14 Sep 95	55	3	9
R. Kemiojki (Tärytie, Finland)	15 Jul 96	210	5	20
Lake Fichtel (Fichtelberg, Germany)	17 May 95	70	3	25
Lake Weißenstadt (Weißenstadt, Germany)	17 May 95	115	2	100
Lake Constance (Constance, Germany)	14 Sep 95	60	3	8
Lough Skannive (Ireland)	1 Nov 95	20	3	21
Lough Ahalia (Conemara, Ireland)	1 Nov 95	<10	3	—

^a S.D. is the Standard Deviation of n analyses.

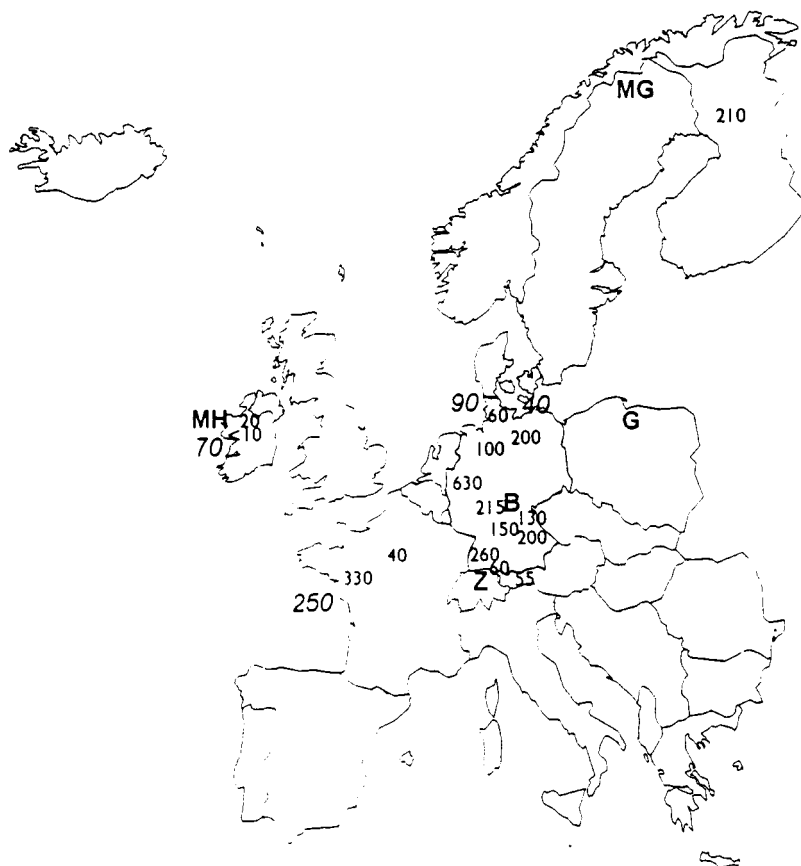


Figure 2. Approximate locations and concentrations of environment TFA measured in Europe Air and precipitation samples: B, Bayreuth; G, Gdansk; MG, Mårmo Glacier; and MH, Mace Head. Seawater determination are shown in *italic*; rivers and lakes are in normal print.

While the whole of the world has not been covered by the sampling program, it is apparent that trifluoroacetic acid is a ubiquitous contaminant of surface waters over a large part of the earth's surface. It is also present in air and rain samples (see subsequent section) and in samples of old ice. The determinations in enclosed lakes in Nevada and Israel that could indicate long-term accumulation, over several hundred years, would point to a source that is not just a present day industrial activity.

Table 3. TFA in surface waters others than European.

Location	Sample date	TFA determination			Ref.
		ng·l ⁻¹	n	S.D. ^a	
Lake Kinneret (Capernaum, Israel ⁺)	11 Nov 95	200	3	4	1
R. Jordan (Israel)	11 Nov 95	250	3	8	1
Dead Sea (En Bokek, Israel)	10 Nov 95	6400	3	9	1
R. Jennessesj (Krasnoyarsk, Russia)	28 Jul 96	35		25	2
R. Tocantins (Cotijuba, Brazil)	31 Aug 96	<15		—	2
R. Apies (South Africa)	31 May 96	500		7	2
Vaal River (South Africa)	30 Aug 96	100		5	2
Golden Gate Pond (South Africa)	26 Oct 96	40		14	2
Oudtshoorn (South Africa)	23 Oct 96	<15		—	2
Tweede Tol (South Africa)	22 Oct 96	<15		—	2
Manzanita Lake (Nevada, USA)	27 May 94	3600		—	3
Manzanita Lake (Nevada, USA)	27 May 94	3300		—	3
Manzanita Lake (Nevada, USA)	27 May 94	3000		—	3
Manzanita Lake (Nevada, USA)	5 Jun 94	3100		—	3
Truckee River (Nevada, USA ⁺⁺)	27 Jun 94	≥370		—	3
Virginia Lake (Nevada, USA)	27 Jun 94	≥180		—	3
Irrigation ditch (Landover, CA, USA)	12 Jul 94	140		—	3
Pyramid Lake (Nevada, USA ⁺⁺)	14 Jul 94	40,000		—	3
Pyramid Lake (Nevada, USA ⁺⁺)	14 Jul 94	40,900		—	3
Stonegate Lake (Nevada, USA)	21 Jul 94	7490		—	3

Note: + and ++ indicate locations at different parts of the same hydrological systems. References: 1, Frank *et al.* (1996); 2, Frank and Klein (1997); 3, Zehavi and Seiber (1996).

^a S.D. is the Standard Deviation of n analyses.

Table 4. Seawater analyses (Frank *et al.*, 1996; Frank and Klein, 1997).

Location	Sample date	TFA determination		
		ng-l ⁻¹	n	S.D. ^a
North Sea (Husum, Germany)	7 Jul 95	90	4	17
Baltic Sea (Warnemünde, Germany)	8 Jul 95	40	3	26
N. Atlantic (Ile d'Yeu, France)	7 Sep 95	250	3	70
N. Atlantic (Mace Head, Ireland)	7 Sep 95	70	4	26
S. Atlantic (Cape Pt., South Africa)	18 Oct 95	160	3	3
S. Pacific (Noosa Heads, Australia)	22 April 96	200	3	26

^aS.D. is the Standard Deviation of n analyses.



Figure 3. Approximate locations and concentrations of environment TFA other than in Europe. Air and precipitation samples: D, Davis, California; MC, Mount Cook, New Zealand; QML, Queen Maud Land, Antarctica; R, Rensselaer, Canada; and Reno, Nevada. Seawater measurements are shown in *italic*; rivers and lakes are in normal print.

Terrestrial Compartment

There are no data on background concentrations of TFA in soil or on soil surfaces.

Table 5. Springs, mineral water wells, and potable water.

Location	Sample date	TFA determination			Age yrs. ^a	Ref.
		ng·l ⁻¹	n	S.D.		
Saale Spring (Germany)	17 May 95	130	3	13	c	1
Eger Spring (Germany)	17 May 95	110	3	23	c	1
Naab Spring (Germany)	17 May 95	80	3	8	c	1
Weißer Main Spring (Germany)	17 May 95	70	3	12	c	1
Friesen Spring (Germany)	17 May 95	320	3	5	c	1
Antonien Well (Kondrau, Germany)	28 Oct 95	<10		—	>700	2
Dippold Well (Kondrau, Germany)	28 Oct 95	<10		—	—	2
Bavarn Well (Kondrau, Germany)	28 Oct 95	23	3	15	~200	2
Gerwig Well (Kondrau, Germany)	28 Oct 95	10	3	34	—	2
Thüringer Wald (Schmalkalden, Germany)	5 Nov 95	<10		—	400 ± 60	2
Rennsteig Well (Schmalkalden, Germany)	5 Nov 95	13	3	26	185	2
Tapwater (U. Nevada, Reno, NV USA)	8 Jun 94	150		—	c	3
Tapwater (Riverside, CA, USA)	19 Jul 95	41		—	c	3
Tapwater (U. California, Davis, CA USA)	28 June 94	55		—	c	3

Note: References: 1, Frank *et al.* (1996); 2, Frank and Klein (1997); 3, Zehavi and Seiber (1996).

^a c signifies contemporary.

Atmosphere

Over the same period of time that they were determining trifluoroacetate concentrations in surface waters, Frank and co-workers conducted an extended campaign to sample and analyze air and precipitation in Bayreuth, Germany. The results are shown in Table 6 for 1995. Figures 4 and 5 show the air and precipitation analyses for both 1995 and 1996.

Table 6. TFA concentrations in air and precipitation at Bayreuth during 1995 (Frank *et al.*, 1996).

Month	Air (pg·m ⁻³)	Rain (ng·l ⁻¹)
March	55 ± 20	100 ± 50
April	70 ± 40	40 ± 4
May	50 ± 15	130 ± 65
June	50	190; 240
July	25; 25	70 ± 20
August		120 ± 110
September	70; 120	100
October	30	75
November	20	60 ± 55
December	20	30
Average	50	100

Note: The variability reported here is between samples and does not represent uncertainty of analyses of the same sample.

Values determined during the earlier campaign, in 1993 and 1994 when the method was being developed, were of a similar order, ranging from 18 to 620 pg·m⁻³ for air (with one outlier at 3230 pg·m⁻³) and <3 to 120 pg·g⁻¹ (ng·l⁻¹) for rainwater (Frank *et al.*, 1995). The determinations are consistent with the levels observed in surface waters (see previous section).

The observation that concentrations in air under the tree canopy in a forest are consistently greater than concentrations in a clearing (reproduced in Figure 6) was interpreted by Frank and Klein (1997) to indicate that the forest canopy was involved in the deposition mechanism.

Analyses have also been performed on air and precipitation samples from the western USA (Zehavi and Seiber, 1996) and on samples of precipitation from a wide range of remote locations in the Northern and Southern Hemispheres (Grimvall *et al.*, 1997). The data are recorded in Table 7.

Similarly to their surface water determinations, Zehavi and Seiber (1996) reported levels of TFA in rain and fog that were high but consistent with the measurements of Frank *et al.* (1996). Grimvall and co-workers have shown not only that TFA is widely distributed — from Arctic to Antarctic — at low concentrations, but that it was present in precipitation in the Swedish Arctic some 400 years ago. The levels in old ice from the Mårmo Glacier are similar to present day concentrations. Given the lower limit of detection of Grimvall's method, the results in Table 7 are consistent with those in Table 5.

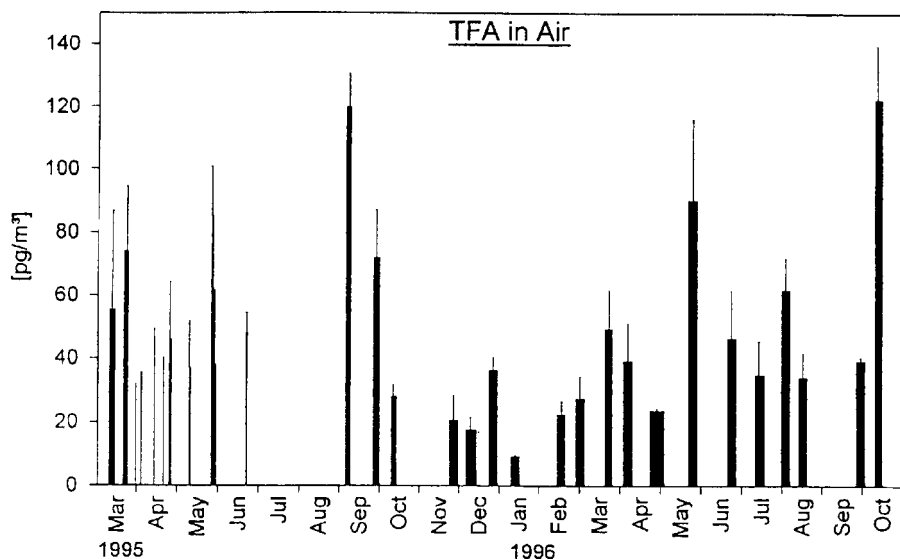


Figure 4. TFA in air near Bayreuth from March 1995 to October 1996. The width of each column represents the duration of the sampling; from November 1996 the length of a typical sampling period was 5 to 7 days.

The significance of the discovery of low concentrations of TFA in precipitation in remote areas is that it indicates a geographically dispersed source. With an atmospheric lifetime (towards rainout) of a few weeks, it would not be possible for TFA that is generated in the northern hemisphere to be present in southern hemispherical precipitation.

There are too few results to map the deposition of TFA definitively, so that a global mass balance is not possible. It is, however, instructive to examine the actual deposition in a well characterized location, such as Bayreuth, and compare it with the deposition from known sources predicted by atmospheric models.

Global Measurements and Their Significance for Future Emissions

As described in a previous section, the current potential sources of trifluoroacetic acid would provide, at most, 2800 metric tons per year distributed throughout the world. It is also apparent, from the atmospheric modelling that has been carried out to assess the possible future deposition of trifluoroacetic acid, that this quantity will not be deposited evenly over the globe but will fall preferentially on tropical regions. Models of future deposition can be used to geographically distribute the current contribution. Kanakidou *et al.* (1995) calculated that, from a global flux of 160,000 metric tons per year of tri-

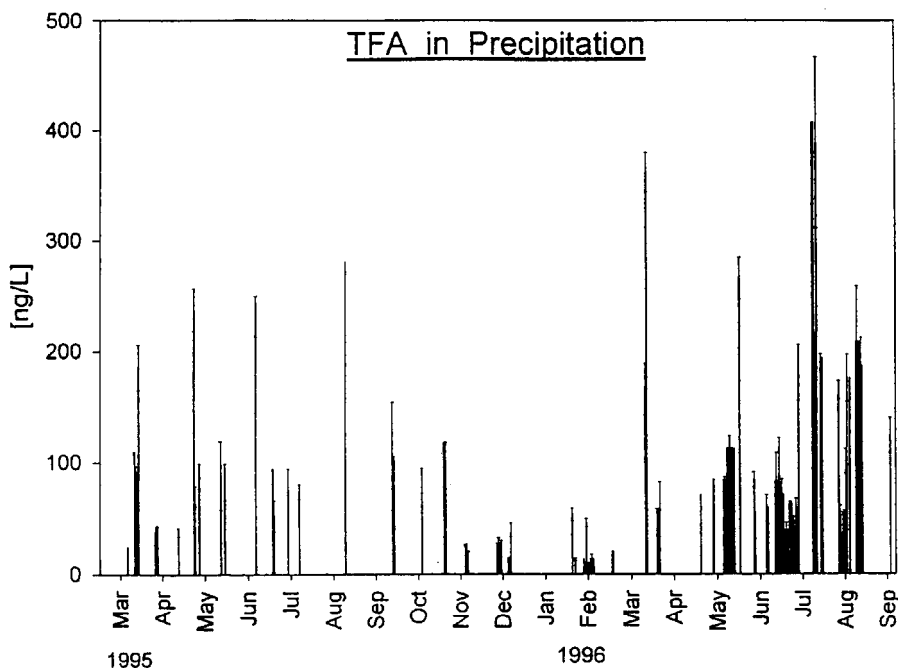


Figure 5. TFA in precipitation near Bayreuth from March 1995 to October 1996. Expanded scale from May to September 1996.

fluoroacetic acid, the deposition rate in Europe would be $0.5 \mu\text{mol} \cdot \text{m}^{-2} \cdot \text{yr}^{-1}$; scaling the current contribution to this would imply a deposition rate of $0.5 \times 2800/160,000$ or $8.8 \text{ nmol} \cdot \text{m}^{-2} \cdot \text{yr}^{-1}$, equivalent to $1 \mu\text{g} \cdot \text{m}^{-2} \cdot \text{yr}^{-1}$. The annual rainfall at Nurnberg, near Bayreuth, is $620 \text{ mm} \cdot \text{yr}^{-1}$ (van der Leeden, 1975) so that the expected concentration in rainwater there from current sources is $1/0.62 \mu\text{g} \cdot \text{m}^{-3}$ or $1.6 \mu\text{g} \cdot \text{m}^{-3}$, which equates to $1.6 \text{ ng} \cdot \text{l}^{-1}$.

The measured concentration at Bayreuth averages $100 \text{ ng} \cdot \text{l}^{-1}$ so the expected concentration of trifluoroacetic acid in rain from known sources is less than $1/60^{\text{th}}$ of that observed.

DEGRADATION

Overview

The ionic character of TFA precludes simple partitioning of the molecule into fatty tissues of animals. As mentioned previously, it is expected that the compound will be found in aqueous compartments such as lakes, rivers, oceans, estuaries, and associated sediments. The steady state levels of TFA within these compartments will depend on the ambient input concentrations of

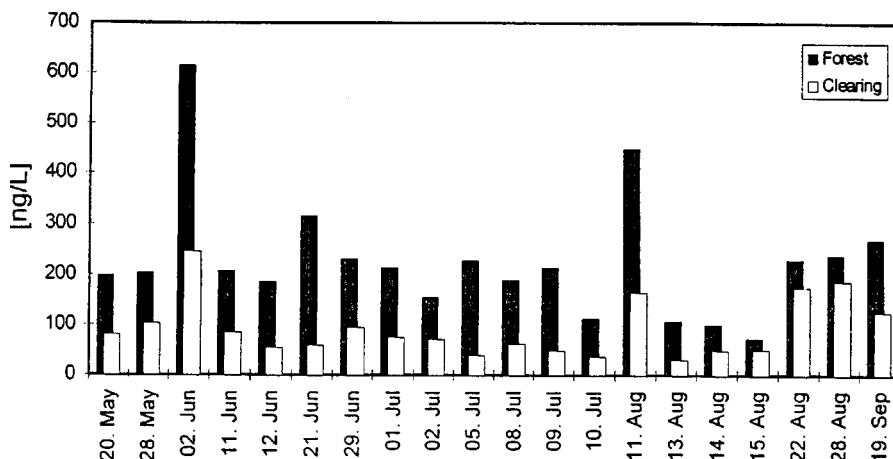


Figure 6. TFA in precipitation at a forest site and nearby clearing (1-km south of the University of Bayreuth). The higher column of each pair always represents the TFA contents in the precipitation collected under the spruce tree canopy, including tree canopy runoff.

TFA in precipitation and TFA removal processes. The ultimate fate of TFA will largely depend on four processes:

- A. Biodegradation
- B. Abiotic mineralization
- C. Accumulation or uptake of TFA by organisms (see Accumulation Section)
- D. Adsorption (see earlier section)

Processes A and B are truly degradative and contribute to a net loss of TFA from the system; they will be the focus of discussion in this section. Process C may result in transformation of TFA into a biological constituent molecule, a fluorinated metabolite of TFA, or simply temporary sequestration. Process D is not true removal of the TFA from the environment but rather sequestration of the compound onto, for example, soil particles, resulting in less mobility or bioavailability.

Biodegradation

Reductive dehalogenation is well known to be an effective natural mechanism for destruction of chlorinated hydrocarbons. However, defluorination by this mechanism is thought to be much more difficult due to the lower reduc-

Table 7. TFA in precipitation at other locations.

Location	Precipitation	Sample date	TFA	
			ng·l ⁻¹	Ref.
Kantonales Labour Building Roof, Zürich, Switzerland	Rain	Sept 95	50	2
Alpthal, Switzerland	Rain	Sept 95	80	2
Mace Head, Ireland	Rain	Oct 26–29, 95	<15	2
Mace Haed, Ireland	Rain	Feb 6–8, 96	62	4
Mace Head, Ireland	Rain	Feb 9, 96	58	4
Mace Head, Ireland	Rain	Feb 27, 96	4	4
Mace Head, Ireland	Rain	Mar 12, 96	17	4
Mace Head, Ireland	Rain	Mar 12–13, 96	93	4
Mace Head, Ireland	Rain	Mar 12–13, 96	8	4
Mace Head, Ireland	Rain	Mar 13, 96	14	4
Mace Head, Ireland	Rain	Mar 14–17, 96	2	4
Resolute, Canada	Snow	Apr 96	33	4
Resolute, Canada	Snow	Apr 96	3	4
Resolute, Canada	Snow	Apr 96	7	4
Resolute, Canada	Snow	Apr 96	2	4
Queen Maud Land, Anarctica	Snow	1996	2	4
Queen Maud Land, Anarctica	Snow	1996	9	4
Mount Cook, New Zealand	Snow	1996	3	4
Gdansk, Poland	Rain	1996	~100	4
Mårmo Glacier, Sweden	Old ice	1996	6.2	4
Mårmo Glacier, Sweden	Old ice	1996	5	4
Mårmo Glacier, Sweden	Old ice	1996	3	4
Davis, California, USA	Fog	Jan 14, 94	≥208	3
Davis, California, USA	Fog	Jan 14, 94	≥80	3
Reno, Nevada, USA	Rain	Sept 28, 94	34–37	3
Reno, Nevada, USA	Rain	Sept 28, 94	31	3
Santa Rosa, California, USA	Rain	Dec 28, 94	48	3
Santa Rosa, California, USA	Fog	Dec 28, 94	279	3
Reno, Nevada, USA	Rain	July 17, 95	90	3

Note: References: 2, Frank and Klein (1997); 3, Zehavi and Seiber (1996); 4, Grimvall *et al.* (1997).

tion potential of the C-F bond (−2 volts). Monofluoroacetate (MFA) is known to be degraded hydrolytically by enzymes generically known as fluoroacetate dehalogenases. In fact, microorganisms containing these enzymes have been isolated and shown to hydrolyze MFA with release of fluoride. However, these organisms do not degrade difluoroacetate (DFA) or trifluoroacetate. This is consistent with the relative stability of these compounds (TFA>>DFA>MFA) (Emptage, 1994).

TFA may be considered to be an analogue of a central biological metabolite — acetate. Transformation of TFA by enzymatic systems specialized for acetate metabolisms might be another route for TFA transformation resulting either in mineralization or incorporation into cellular material. However, rates for TFA transformation by this route have been estimated using purified enzyme systems and found to be less than 0.5% of the rate of acetate (Peijnenburg *et al.*, 1994), which suggests that TFA will not compete effectively with acetate in biological systems.

Demonstration of TFA Biodegradation

The studies summarized below represent a variety of empirical approaches to demonstrate TFA biodegradation in field- or laboratory-derived microbial cultures.

Measurements

Determination of the biodegradative potential of microorganisms for a specific compound is typically carried out using one transformation, or lack of transformation (of TFA), which can be inferred from one or more of the following analyses: TFA-dependent microbial growth, TFA-dependent oxygen consumption, appearance of defluorination or decarboxylation products such as methane or carbon dioxide using [1-¹⁴C]-labeled TFA, fluoride anion, and direct demonstration of TFA loss.

Microbiological Approaches

1. Enrichment for degradative bacteria using the compound in question (TFA) as the sole carbon and energy source in the presence of added nutrients such as ammonium or phosphate. In this case bacteria, which can utilize the compound, will grow preferentially.
2. Microbial growth on standard carbon and energy sources is independent of the test compound; however, biodegradation of the test compound is dependent on growth and metabolism of the bacteria on natural or standard carbon sources. Standard biodegradation tests employing organic-rich inocula such as digester sludge is one example of this approach. This is a co-metabolic mechanism where transformation of the test compound does not result in any specific advantage for the organism or does it result in any enrichment of bacteria that specifically degrade the test compound.

3. Intrinsic metabolic capability of a naturally occurring sample. Transformation of the test compound is assessed in a naturally occurring sample without any additional nutrient or carbon source.

Anaerobic Degradation of TFA: Reductive Defluorination

Reductive processes are expected to be operative under anaerobic or highly reducing conditions such as those referred to as “methanogenic” or “sulfate-reducing.” Anticipated products from the reductive defluorination of TFA are ultimately methane, fluoride, and carbon dioxide.

Early studies using unamended marine sediment (San Francisco Bay) or freshwater sediments incubated with ^{14}C -labeled TFA clearly demonstrated a reductive defluorination process resulting in sequential formation of DFA, MFA, acetate and methane (Visscher *et al.*, 1994). This sequence was observed under methanogenic and to a lesser degree sulfate-reducing conditions. Other respiratory acceptors such as nitrate, ferric iron or oxygen failed to produce defluorination although some fluoroform was reported under aerobic conditions. This phenomenon has only been observed in certain field samples by the one laboratory. The results also showed that TFA inhibited methanogenesis at low concentrations (10 μM) and that at higher concentrations of TFA, the compound could inhibit its own biodegradation.

Reinvestigation of samples from the same field sites (by the same laboratory) failed to confirm the initial results (Matheson *et al.*, 1996). Another laboratory reported that marine sediments from the sites that had previously been shown to be active by Visscher *et al.* (San Francisco Bay) for methanogenic TFA biodegradation were unable to degrade TFA (Emptage *et al.*, 1997). The initial results of Visscher *et al.* have not been replicated despite numerous attempts by the original investigators as well as others.

Chauhan *et al.* (1995) carried out anaerobic closed microcosm bottle incubations inoculated with soils obtained from globally diverse sites as well as anaerobic digester sludge. These were assessed for transformation of $[2-^{14}\text{C}]$ -labeled TFA to $^{14}\text{CO}_2$. These tests showed no evidence for biotransformation with either nutritionally amended or unamended bottles.

An assessment of anaerobic biodegradation by using the “sequential column microcosm” was also conducted by the same group. This approach involves a succession of compartmentalized but interdependent microbial communities that are distinguished on the basis of mode of respiration. The sequence starts with the most reducing conditions (*i.e.*, methanogenic) and progresses toward more oxidizing physiologies by separate additions of sulfate, iron, nitrate, and ultimately oxygen into the sequence of chambers downstream of the initial methanogenic chamber. In this way a broad cross-section of microbial metabolism may be individually assessed in one experiment. $[1-]$ or $[2-^{14}\text{C}]$ -labeled TFA input and ^{14}C -labeled TFA output as well as total radioactive counts were monitored for each chamber and inferred from the loss in steady-state levels of TFA. In addition, fluoroform and $^{14}\text{CO}_2$ were assayed in the methanogenic chamber. Results from these experiments showed sustained

and long-term loss of 25 to 30% of the incoming TFA in the methanogenic chamber. Only very minor amounts of $^{14}\text{CO}_2$ were detected in the headspace of the culture vessel. However, total counts of radioactivity exiting the chamber were only slightly diminished. The results suggest that either the TFA was complexed such that it did not migrate on the HPLC column and was thus invisible by this method, or that it was transformed to another soluble aqueous phase metabolite that was not recovered in the HPLC analysis. No losses were noted for subsequent chambers involving sulfate reduction, iron reduction, nitrate respiration, photosynthetic sulfide respiration, or aerobic dark respirations. No definite product was ever identified from the putative methanogenic transformation; however, a conversion of TFA to a nonvolatile product was hypothesized to account for the losses. The inference that some biotransformation occurred based on loss alone must be viewed cautiously until direct evidence for the "nonvolatile product" can be obtained.

Aerobic Degradation of TFA: Decarboxylation

Compelling evidence for decarboxylation of TFA was obtained using pure cultures of *Azoarcus tolulyticus* tol-4, or *Pseudomonas putida* strain KZ6R. The researchers demonstrated release of labeled carbon dioxide from TFA labeled in the 1-position (Chauhan *et al.*, 1995). Decarboxylation activity was strictly dependent on the substrates on which the cells were grown. *A. tolulyticus* had to be pre-grown on toluene as the carbon source with nitrate as the electron acceptor, whereas *P. putida* had to be aerobically pre-grown on 4-chlorobenzoate. Neither organism exhibited the activity during its normal growth on these substrates but rather only after harvesting the cells, concentrating them and resuspending them in fresh medium. The TFA decarboxylation activity of the cells was dependent on the age of the culture and the metabolic state of the cells. The resting cells rapidly lost the ability to decarboxylate TFA. However, the cells were capable of transforming up to 16% of millimolar levels of TFA during the optimal period of activity. The exacting nutritional requirements, and the instability of the activity argue against extrapolating this observation to the natural environment outside the laboratory. It is not known at this time how effective the transformation is at very low levels of TFA anticipated in the environment. It is also unclear as to what the biochemical mechanism is other than the correlation with aromatic catabolism.

Aerobic Closed Bottle Tests using Diverse Inocula

The transformation of [$1\text{-}^{14}\text{C}$] TFA was assessed in aerobic microcosms inoculated with composite samples consisting of a blend of soils from geographically diverse regions of the globe, digester sludges, or organic rich soil fractions from sites in Michigan (Chauhan *et al.*, 1995). No evidence for aerobic mineralization was obtained from analysis for $^{14}\text{CO}_2$ in these incubations.

A semicontinuous activated sludge test was conducted by van Ginkel and Kroon (1992a,b) according to EEC, OECD, and ISO test guidelines. The pro-

cedures assessed fluoride release from aerobic digester sludge incubations that included co-metabolic substrates yeast extract, acetate or peptone and vitamin B₁₂. The semi-continuous sludge test demonstrated that TFA had no effect on the efficacy of the sludge as a biodegradation agent. No fluoride was detected in the effluent from the SCAS units even though there was an approximately 20% reduction of TFA in the effluent (van Ginkel and Kroon, 1992a). Closed bottle tests were also performed. These incubations typically lasted for periods of up to 84 days after which fluoride was measured. No detectable fluoride was observed in the bottle tests. The tests were considered negative for TFA biodegradation (van Ginkel and Kroon, 1992b).

Aerobic Biodegradation of TFA by Monooxygenase-Containing Bacteria

Certain bacteria contain enzymes (monooxygenases) that are capable of inserting oxygen into aliphatic and aromatic hydrocarbons. By virtue of this, these bacteria are capable of aerobic degradation of a wide variety of chlorinated hydrocarbons such as trichloroethylene (TCE), dichloroethylene and vinyl chloride. To test for the ability of monooxygenases to degrade TFA, a set of methylotrophic and propanotrophic bacteria were grown and tested against compounds known to be degradable (*i.e.*, TCE) as well as TFA. DeFlaun (1996) tested nine strains comprising *Pseudomonas mendocino* KR1, *Pseudomonas putida* F1, *Methylosinus trichosporium*, *Mycobacterium vaccae*, as well as five isolates (designated ENV2C, ENV2D, ENV2R, ENV2W, and ENVOB) that were known to degrade HFCs or HCFCs. These strains were tested against [1-¹⁴C] TFA with TCE as a positive control (DeFlaun, 1996). Assays were performed for ¹⁴CO₂, fluoride, MFA, and TFA. The results showed that even with cultures which vigorously degraded TCE within 24 hours there was no detectable decarboxylation or dehalogenation of TFA after 13 days. No MFA or fluoride was detected in any incubation.

Abiotic Mineralization

Irradiation of natural waters by sunlight can produce reactive species such as HO·, RO₂·, and O₂·H and solvated electrons. The only ones capable of oxidizing or reducing TFA are HO and solvated electrons (eAq⁻). However, the concentrations of these species in natural waters are likely to be very low and their rates of reaction with TFA, together, do not support a role for these agents in the destruction of TFA (Maruthamuthu *et al.*, 1995; Maruthamuthu and Huie, 1995).

One possible photocatalytic mechanism involving ferric- or manganese-assisted photodecarboxylation (photo-Kolbe) reactions was shown to be effective for degradation of chloroacetates and mono- or difluoroacetates but not for trifluoroacetate (Maruthamuthu and Huie, 1994).

Trifluoroacetic acid has been shown to undergo photooxidation on a variety of iron oxyhydroxide surfaces (Pehkonen *et al.*, 1995). Similarly with the

other fully halogenated acetic acids, this reaction proceeds by a photo-Kolbe mechanism to yield HF and CO₂, but the rate is so low that it is unlikely to have much environmental relevance.

TFA was shown to be inert to photocatalytically generated oxidizing species on semiconductor surfaces. TFA was also shown to be inert to redox- and radical-induced degradation except at pHs above 10.5 (Asmus *et al.*, 1994).

In a study of the rates of reductive dehalogenation versus structure, $t_{1/2}$ times for reductive transformation of a series of chlorocarbons as well as TFA (based on structure-activity relationships) were obtained under anaerobic conditions in the presence of sediment. The reductive dehalogenation reactions were presumably microbial in origin, but this was not directly demonstrated in the study. In contrast to the fully chlorinated ethanes and ethenes, which are readily dehalogenated, the $t_{1/2}$ for TFA — obtained by extrapolation — was found to be over 200 years in these biologically active sediments (Peijnenburg *et al.*, 1994). These results are consistent with those obtained in other laboratories investigating the reductive dehalogenation of TFA but contrast with the report by Visscher *et al.* (1994).

Due to the recycling of TFA between water and air and the rapid rainout of TFA from clouds (10 days), it is unlikely that there will be any aqueous phase degradative process that could compete with rainout kinetically. Oxidation of TFA by NO₃⁻, SO₄⁻, Cl₂⁻, OH[·] followed by decarboxylation may occur with a $t_{1/2}$ on the order of 80 years. Ferric-assisted photodecarboxylation was shown to be ineffective for TFA (Wine, 1994).

Conclusion

TFA is a highly stable molecule to known abiotic or biological degradation mechanisms. The microbiological studies summarized here involved both empirical screens of naturally occurring soils as well as focused tests of known degradative mechanisms. TFA biodegradation was investigated in aerobic and anaerobic bacterial cultures with pure isolates as well as crude environmental samples. These studies have not identified evidence for a widespread, environmentally significant, biological mechanism for defluorination of TFA. Therefore, the assessment is that TFA will be very long-lived in the environment. This prediction suggests that renewed emphasis be placed on identifying the background levels of TFA in the environment as well as how this TFA may compartmentalize.

Despite published data claiming rapid reductive defluorination of TFA (Visscher *et al.*, 1994), the evidence for this mechanism of TFA removal must be considered hypothetical until the original result can be further confirmed or supported. The weight of theoretical considerations as well as the combined experience of the five laboratories involved in these projects suggests that confirmation is unlikely. This does not rule out the possibility that the result was correct but due to a rare concatenation of physical and biological factors.

The result reported by Chauhan *et al.* (1995) that clearly demonstrated decarboxylation, but not defluorination, of TFA may be of limited environmental

significance as a mechanism for destruction of TFA in the environment. Experience with a wide variety of real environmental samples by that laboratory, as well as other laboratories, suggest that decarboxylation of TFA is not widespread in nature or is it easily induced where it is present. Indeed, even the laboratory strains only produce the activity under very controlled conditions. The fate of the CF_3^- moiety in the decarboxylation reaction is unknown.

Therefore, for the purpose of this risk assessment, we will assume, as a reasonable worst case, that no degradation of TFA is likely to occur in the environment.

ACCUMULATION

The physico-chemical properties of TFA (high solubility and low K_{ow}) indicate that the molecule would not partition significantly to the lipid phase of cells and therefore significant bioconcentration by this mechanism would not be expected. However, other mechanisms that might lead to a bioaccumulation of TFA have been investigated.

Due to the structural similarity of TFA to acetate, a major biosynthetic precursor molecule, studies were performed to assess the level of cellular incorporation of TFA into biomass. Bott and Standley (1994) investigated the incorporation of $[2-^{14}\text{C}]$ TFA into microbial cell mass, small invertebrates, and plants. The cellular components were assayed and comprised the lipid, carbohydrate, and proteinaceous fractions.

Aquatic communities, including bacteria, aquatic invertebrates, and plants, were set up in flowing water mesocosms to provide a source of biological samples for experimentation. One of these communities was exposed to NaTFA ($30 \mu\text{g}\cdot\text{l}^{-1}$) for nearly 2.5 years; the other was an unexposed control run for a comparable period of time. Results showed that sediment microbial communities exposed to TFA in mesocosms for approximately 2.5 years incorporated more radiolabeled TFA than communities exposed for <1 year, with rates increasing from -1×10^{-13} to $22 \times 10^{-13} \mu\text{g TFA}\cdot\text{cell}^{-1}\cdot\text{day}^{-1}$ (Bott and Standley, in review). The cause of the change, whether due to a microbial adaptation to the TFA exposure or a change in some other environmental variable(s) is unclear. Incorporation was correlated positively with the amount of TFA added to samples and exposure time.

Microbial incorporation of radiolabeled TFA by cells cultured from those sediments (at a test concentration of $10 \mu\text{g}\cdot\text{l}^{-1}$) demonstrated incorporation into biomolecule fractions such as lipids, proteins and residual (e.g., cell wall) materials. Incorporation into these fractions in bacteria increased from 0.005% of total counts to 0.024% over this 2.5 year period (Bott and Standley, 1994; Standley and Bott, in review). Oligochaete worms exposed to $40 \mu\text{g NaTFA}\cdot\text{l}^{-1}$ also showed low uptake of TFA into biomolecules. The oligochaetes contained radiolabel that was not extractable as TFA; it was primarily associated with the protein fraction. The presumptive incorporation product from TFA has not been identified. Jewelweed also contained radiolabel that was not extractable as TFA, but the levels of label incorporated ranged from

0.0069% of the total exposure for roots to 0.012% of the total for leaves after a 32-day exposure. Apparent incorporation factors were low for other macro-invertebrates and plants. These studies suggest that microbial biomass is not a major sink for TFA, but that there is an association of TFA with biomass that could be due to biochemical incorporation.

As part of a study to determine the possible defluorination of TFA by the freshwater green alga, *Selenastrum capricornutum*, van Dijk (1996) reported a bioaccumulation factor (BCF) of approximately 10, based on radiolabeled residues in cells filtered from the medium. However, the study did not correct for any radioactivity from the medium that may have been retained on the filter due to evaporation or adsorption and therefore may have overestimated the radioactivity associated with the cells.

In a toxicity study with *Lemna gibba* (duckweed, a floating aquatic higher plant) described in another section, ^{14}C -labeled residues of TFA were determined after 7 days exposure to a range of concentrations in the culture medium (Smyth *et al.*, 1993). The bioconcentration factors were low, ranging from 1.0 to 1.6, reflecting the hydrophilic properties of the substance and the lack, in this species, of a differentiated water transport (transpiration) system.

In terrestrial higher plants, the uptake and transpiration of water, to replace that lost by the leaves as a consequence of photosynthetic gas exchange, provides a mechanism for the bioaccumulation of TFA. Prior to the AFEAS program, root uptake and transport of TFA in the xylem tissues had been demonstrated in tomato seedlings (Rollins *et al.*, 1989), using nuclear magnetic resonance imaging. However, the exposure concentration was very high (approximately $51,000 \text{ mg HTFA} \cdot \text{l}^{-1}$ as a buffered solution) and the exposure duration was too short (17 hours) to evaluate the bioaccumulation potential. Subsequently, sunflower (*Helianthus annuus*) seedlings were exposed to a single concentration ($2 \mu\text{g HTFA} \cdot \text{l}^{-1}$) of ^{14}C -radiolabeled trifluoroacetic acid in the aqueous (hydroponic) medium surrounding the roots (Thompson *et al.*, 1994). Plants were removed at intervals and the concentration of ^{14}C residues determined in root, stem, and leaf tissue. After 12 days the remaining plants were transferred to clean medium and sampled for a further 4 days. ^{14}C residues in the leaf tissues increased continuously over the period of exposure, with a BCF of approximately 22 after 12 days. The stem tissue behaved similarly but with a lower rate of accumulation (12-day BCF of approximately 5). Root tissue reached apparent equilibrium after 5 days exposure with a BCF of approximately 3. The accumulation rate was somewhat less than would be expected from passive influx in the transpiration stream without efflux. The concentrations measured in the root medium also suggested either a concurrent efflux or some partial barrier to influx.

All tissues showed a decline in ^{14}C -residue concentrations on transfer to clean medium. Although this can be attributed largely to dilution by growth, a significant quantity of radiolabel was lost to the medium surrounding the roots and it was concluded that the plants showed some excretion (deposition) of accumulated radiolabel to the root medium. More than 80% of the ^{14}C residues in the leaves were found to be extractable in water after tissue maceration

(Thompson and Gillings, 1996). Fractionation of the extract using ion chromatography showed the residues co-eluted with a trifluoroacetate standard spiked into leaf extract, suggesting that no significant metabolism of TFA had occurred.

As part of a 5-week hydroponic toxicity study with wheat (Thompson *et al.*, 1995) (described in a subsequent section), the accumulation of ^{14}C residues of trifluoroacetate was also monitored. At $1\text{ mg NaTFA}\cdot\text{l}^{-1}$, the bioconcentration factor in the total aerial tissue (shoots), based on fresh weight, increased continuously over the exposure period, to a final value of 27. The concentrations in the tips of the shoots were approximately four times greater than in the remaining shoot tissues. This factor was used to estimate a tissue concentration of approximately $1000\text{ mg}\cdot\text{kg}^{-1}$ (fresh weight) corresponding with tissue necrosis observed in the shoot tips at $10\text{ mg NaTFA}\cdot\text{l}^{-1}$, after 28 days. After 35 days, a BCF of 43 was determined for the whole shoots.

Davison and Pearson (1997) analyzed tissues of soya and wheat exposed to NaTFA by determination of inorganic fluoride, after fusion with sodium carbonate to cleave any C-F bonds. Concentrations were expressed as NaTFA in dry tissue, after background fluoride subtraction. For soya exposed to $5\text{ mg}\cdot\text{l}^{-1}$ under hydroponic conditions for 44 days, the concentration in the tissue of the oldest (first trifoliate) leaves reached a plateau after approximately 20 days. Each successive set of leaves attained higher tissue concentrations, except for the fifth trifoliate that were still expanding at final harvest but already contained a higher concentration than had been reached by the older, second trifoliate. As symptoms first appeared on the third trifoliate leaves, the tissue concentration was approximately $150\text{ mg NaTFA}\cdot\text{kg}^{-1}$ dry weight. It was concluded that the stage of development of the leaf is important and that TFA is most toxic to young, expanding leaves and has little effect on mature leaves with a similar tissue concentration.

In a further study with soya at $1\text{ mg NaTFA}\cdot\text{l}^{-1}$, Davison and Pearson (1997) found that the slight symptoms observed were associated with tissue concentrations of $160\text{ to }190\text{ mg NaTFA}\cdot\text{kg}^{-1}$ dry weight. Tissue concentration in the whole shoots of wheat exposed to the same concentration (which caused no effects) reached a plateau at approximately $55\text{ mg NaTFA}\cdot\text{kg}^{-1}$ dry weight after 25 days and had decreased slightly after 43 days. At $5\text{ mg NaTFA}\cdot\text{l}^{-1}$, the tissue concentration was approximately $190\text{ mg TFA}\cdot\text{kg}^{-1}$ dry weight when growth was beginning to be inhibited.

The final leaf/shoot tissue concentrations (on a dry weight basis) for the different hydroponic studies are summarized in Table 8. For comparison, these are also expressed as bioconcentration factors based on tissue fresh weights, although it should be noted that fresh weights were not determined (and are therefore estimated) for some of the studies. Different analytical methods were also employed (see above). At concentrations at or below the no effect level of $1\text{ mg}\cdot\text{l}^{-1}$, bioconcentration factors ranged from 5.4 to 27. Frank (1994) reported concentrations of TFA in spruce needles sampled from Tübingen, Germany, of $98\text{ to }195\text{ ng}\cdot\text{g}^{-1}$ (presumed to be based on fresh weight). Recent measurements (Frank *et al.*, 1996) suggest an average concentration of approx-

Table 8. Summary of bioconcentration of TFA by hydroponic exposure of terrestrial plants.

Species and tissue	Duration (days)	Tissue		Bioconcentration factor (BCF) ^a
		Exposure concentration (mg·l ⁻¹)	concentration (mg·kg ⁻¹ dry weight)	
Sunflower leaf ¹	12	0.002	0.424	22
Wheat	35	1.0	190	27
Shoot/leaf ²	35	10.0	2300	43
Wheat	43	1.0	43	(5.4)
Shoot/leaf ³	43	5.0	195	(4.9)
	43	10.0	770	(9.6)
Soya leaf ³	33	1.0	191 ^b	(24)
	43	5.0	620 ^c	(16)

Note: ¹Thompson *et al.* (1994).

²Thompson *et al.* (1995).

³Davison and Pearson (1997).

^a BCF based on fresh weight of tissue. Values in parenthesis are from studies in which fresh weight was not determined and BCFs have been calculated using an approximate, estimated fresh/dry ratio of 8.0.

^b Only the fifth set of trifoliate leaves were measured.

^c Fourth trifoliate leaves, which contained the highest concentration.

imately 100 ng·l⁻¹ in rainwater, suggesting a bioconcentration factor of 1 to 2. Although conifer needles are relatively long lived, this may indicate that the relatively low water usage of such leaves may enable excretory translocation to become more significant.

There is good evidence to suggest that the toxicity of TFA to plants is related to the tissue concentration of the accumulated material that is dependent on the transpiration flow from the roots. However, because the mode of action appears to involve specific processes in the leaf, possibly related to leaf expansion, it is not possible to specify precisely the critical tissue concentrations in terms of the whole leaf. However, the lowest tissue concentration associated with adverse effects was 150 mg·kg⁻¹ dry weight, in expanding soya leaves (Davison and Pearson, 1997). It would appear that when exposure is at or below the

threshold for effects, the tissue concentrations tend to plateau and accumulated TFA is reduced by growth and by excretion via the roots. Leaf-fall represents an ultimate removal mechanism for any residual TFA in mature leaves.

EFFECTS ASSESSMENT

Microorganisms

Effect of TFA on Methanogenic Communities

A vital part of the carbon cycle involves the formation and degradation of acetate during anaerobic methanogenesis. This process occurs globally but can be differentiated in terms of specific environments. Commercially or environmentally important methanogenic populations are found in anaerobic digestors, sediments, and rumen of ruminant animals. The principal microorganisms are generically referred to as methanogens, many species of which specialize in the transformation of acetate to methane and carbon dioxide. Methanogenesis was assessed for any toxic effects of TFA by measuring the rates of methane formation from anaerobic digester samples, sediment samples, and rumen samples in the presence of increasing concentrations of TFA up to 10 mM (1114 ppm) according to Emptage *et al.* (1997). The results indicated that there was no significant effect of TFA, even at the 10 mM concentration, on any incubation. Monofluoroacetate did however exert toxicity, as expected, at levels as low as 10 mM. These results contrast with those reported by Visscher *et al.* (1994), which suggested inhibition of methanogenesis at low concentrations (0.1 mM TFA). The discrepancy in the results cannot be accounted for at this time except to note that the toxicity was observed in the same sediments which exhibited rapid TFA biodegradation (see a previous section). TFA biodegradation was not observed in the study by Emptage *et al.* (1997). Overall, the results suggest that TFA is inert in these systems and that endogenous methanogenesis was neither stimulated nor inhibited.

Effect of TFA on Activated Sludge

A semicontinuous activated sludge test was conducted by van Ginkel and Kroon (1992a) according to EEC, OECD, and ISO test guidelines. This test also indicated that TFA had no discernible effect on the performance of the sludge for catalyzing biodegradation of organic carbon.

Effect of TFA on Acetate Metabolism by Microbial Communities

Acetate is a key intermediate in most living organisms. Ecologically, the mineralization of acetate to carbon dioxide is a key link in the biogeochemical carbon cycle. Therefore, it is essential to know whether TFA, which is structurally close to acetate, could interfere with acetate metabolism.

Experiments were conducted to assess the interaction of TFA with the metabolism of [$1\text{-}^{14}\text{C}$] acetate by freshwater microbial communities which had not been previously exposed to TFA (Bott and Standley, in review). The approach comprised additions of non-labeled TFA or non-labeled acetate to parallel in-

cubations containing [$1\text{-}^{14}\text{C}$] acetate. Evidence for interaction with metabolism of acetate would then be inferred from the effects observed on incorporation of radiolabel into biomass or evolution of ^{14}C carbon dioxide. According to Bott and Standley (1994), none of the differences in ^{14}C acetate metabolism between the unamended control and any of the TFA or acetate treatments were statistically significant (Dunnett's test, $p > 0.05$). Between 85 and 90% of the [$1\text{-}^{14}\text{C}$] acetate radioactivity was found in the biomass and there was no significant difference between controls and TFA-treated incubations. These results suggest that TFA at concentrations several orders of magnitude higher than those anticipated in the environment did not impact acetate mineralization to carbon dioxide or did it affect incorporation of acetate into cellular material.

Similar experiments were performed using samples derived from TFA-treated ($30\text{ }\mu\text{g}\cdot\text{l}^{-1}$ 3-months exposure) or control mesocosms. Experimental TFA additions were 200, 20, and $2.4\text{ }\mu\text{g}\cdot\text{l}^{-1}$. Cell-specific rates of acetate mineralization rates were similar for samples from the TFA-treated and control mesocosms. With samples from each mesocosm there were never statistically significant differences in [$1\text{-}^{14}\text{C}$] acetate metabolism over the range of TFA concentrations tested. The percentage of radioactivity in the biomass ranged between 80 and 90% and there were no significant differences between unamended controls and TFA-treated samples.

At extraordinarily high nonradioactive acetate additions of 4 to $450\text{ mg}\cdot\text{l}^{-1}$, there was suppression of ^{14}C acetate metabolism, as would be anticipated from expected isotopic dilution of ^{14}C acetate. At $440\text{ mg}\cdot\text{l}^{-1}$, TFA also suppressed ^{14}C acetate metabolism, although to a lesser extent than did cold acetate suggesting some weak interaction of TFA with acetate metabolism at these concentrations.

These competition experiments using benthic microbial communities also clearly demonstrated that TFA and acetate were not strongly competitive compounds in terms of mineralization or incorporation into biomass.

The effect of TFA has been investigated in three species of free-living nitrogen-fixing bacteria (Nagel and Odom, 1997). The species were selected on the basis of phylogenetic diversity and because they have been used in many laboratory studies on the biochemistry of nitrogen fixation. A common aerobic soil microorganism (*Azotobacter vinelandii*), a freshwater photosynthetic bacterium (*Rhodobacter capsulatus*), and a common anaerobe (*Clostridium pasteurianum*) were the test species. The effect of TFA on these species was determined during nitrogen-dependent growth, growth on fixed nitrogen (ammonium ion), and on nitrogenase activity itself. The experiments were designed to determine whether TFA was specifically toxic to nitrogen fixation versus a more general physiological aspect. No effect of TFA on growth either by N_2 fixation or with ammonium ion as nitrogen source was noted even at concentrations as high as 1 mM ($\sim 100\text{ ppm}$) TFA with either the *R. capsulatus* or *A. vinelandii* strain. *C. pasteurianum* was only tested for TFA toxicity during growth on fixed nitrogen due to difficulties in obtaining significant rates of N_2 fixation with this strain. Increases in production of molecular hydrogen were noted at very high

TFA concentration (>50 ppm) in *Rhodobacter capsulatus*. This effect could be due to either stimulation of nitrogenase activity or inhibition of hydrogen reutilization at these very high TFA concentrations.

Aquatic Organisms

Only acute toxicity studies are available; unless otherwise stated these were carried out with NaTFA. A number of studies employed radiochemical analysis of the test solutions, which confirmed the nominal concentrations and demonstrated no significant decline during the test period. In view of this and the known stability of the compound and low potential for adsorption, the remaining studies were carried out without analysis of water concentrations. All endpoints reported here are based on nominal concentrations.

Acute toxicity in fish, determined in *Brachydanio rerio*, did not reveal any effect at $1200 \text{ mg}\cdot\text{l}^{-1}$ during 96 hours of exposure. For water flea *Daphnia magna*, the same result was obtained after 48 hours of exposure. The acute NOEC for these two species, representing primary and secondary consumers, is $1200 \text{ mg}\cdot\text{l}^{-1}$ NaTFA (corresponds to $1000 \text{ mg}\cdot\text{l}^{-1}$ of TFA).

A study using HTFA with *Daphnia magna* showed a 24-hour EC_{50} of $55 \text{ mg}\cdot\text{l}^{-1}$ (Rhône-Poulenc, 1995); this was attributed to a pH effect.

A toxicity study on duckweed (*Lemna gibba*) showed EC_{50} values for frond increase and weight increase of respectively: 1100 and $1200 \text{ mg}\cdot\text{l}^{-1}$. For both endpoints, a NOEC of $300 \text{ mg}\cdot\text{l}^{-1}$ has been recorded (Smyth *et al.*, 1993).

Toxicity tests with sodium trifluoroacetate in algae were conducted on 11 different species: *Selenastrum capricornutum*, *Chlorella vulgaris*, *Scenedesmus subspicatus*, *Chlamydomonas reinhardtii*, *Dunaliella tertiolecta*, *Euglena gracilis*, *Phaeodactylum tricornutum*, *Navicula pelliculosa* (Smyth *et al.*, 1994a), *Skeletonema costatum* (Smyth *et al.*, 1994b), *Anabaena flos-aquae* (Smyth *et al.*, 1994c) and *Microcystis aeruginosa*. These 11 species belong to 4 different classes: Chlorophyceae (4 freshwater and 1 marine species), Euglenophyceae (1 freshwater species), Cyanophyceae (2 freshwater species) and Bacillariophyceae (1 freshwater and 2 marine species).

Selenastrum capricornutum (alternative names: *Raphidocelis subcapitata* or *Pseudokirchneriella subcapitata*) was the most sensitive species for sodium trifluoroacetate. This unicellular alga is the most frequently used for ecotoxicity determination under laboratory conditions. Based on the results of five toxicity tests with *Selenastrum capricornutum*, a concentration of $0.12 \text{ mg}\cdot\text{l}^{-1}$ ($120 \text{ }\mu\text{g}\cdot\text{l}^{-1}$) can be considered a toxicity threshold concentration. Adverse effects on the growth of this species were not found at this concentration. For the remaining 10 algal species the EC_{50} values were all higher than $100 \text{ mg}\cdot\text{l}^{-1}$ (see Table 9).

Algal studies were also conducted with potential metabolites of trifluoroacetate, like difluoroacetate and monofluoroacetate. Monofluoroacetate is a toxic substance which mode of action is the inhibition of the citric acid cycle. Studies with *Selenastrum capricornutum* and *Scenedesmus subspicatus* revealed ef-

Table 9. Endpoints (mg·l⁻¹) of the toxicity tests with algae and sodium trifluoroacetate.

Species	EC ₅₀		NOEC ^a		LOEC ^a	
	Biomass integral	Growth rate	Biomass integral	Growth rate	Biomass integral	Growth rate
<i>Chlorophyceae</i>						
<i>S. capricornutum</i>	4.8	160	<0.36		0.36 (11)	
<i>S. capricornutum</i>			0.12 (0.34)		0.36 (12)	
<i>S. capricornutum</i>	0.7 ^b	14 ^b				
<i>S. capricornutum</i>	1.5	27	0.30 (11)		1.0 (11)	
<i>S. capricornutum</i>	1.5	7.7	0.15 ^c (10)	1.2 ^c (10)		
<i>C. vulgaris</i>	>1200	>1200	1200 (1.6)			
<i>S. subspicatus</i>	>120	>120				
<i>C. reinhardtii</i>	>120	>120	120 (−2.4)			
<i>D. tertiolecta</i>	>124	>124	124 (5.1) ^d			
<i>Euglenophyceae</i>						
<i>E. gracilis</i>	>112	>112	112 (0.0)			
<i>Bacillariophyceae</i>						
<i>P. tricornutum</i>	>117	>117	117 (1.4)			
<i>N. pelliculosa</i>	1200	2400	600 (16)	600 (5)	1200 (53)	
<i>S. costatum</i>	>2400	>2400	2400 (10)	2400 (−1)	1200 (17)	
<i>Cyanophyceae</i>						
<i>A. flos-aquae</i>	2400	>2400	600 (13)	600 (0)	1200 (29)	1200 (3)
<i>M. aeruginosa</i>	>117	>117	117 (6.8)			

Note: The endpoints were determined at test termination (biomass integral) or were based on the whole test period (growth rate).

^a Between brackets the inhibition percentage of the biomass integral or growth rate is given.

^b Due to the large ratio between test concentrations (10) and the low number of replicates (only 2 erlenmeyers per concentration) the value is only a rough estimate.

^c EC₁₀ value (determined with log/probit method).

^d The inhibition of the biomass integral was statistically significant (p = 0.018).

fects on growth at sodium monofluoroacetate concentrations which were several orders of magnitude lower than effect concentrations of sodium trifluoroacetate (see Table 10).

Table 10. EC_{50} ·72 h values ($mg \cdot l^{-1}$) based on growth rate.

Species	Test compound		
	Sodium trifluoroacetate	Sodium difluoroacetate	Sodium monofluoroacetate
<i>Selenastrum capricornutum</i>	± 12	> 12	0.012–0.12
<i>Scenedesmus subspicatus</i>	> 120	> 120	0.012–0.12
<i>Chlorella vulgaris</i>	> 1200	12–120 ^a	> 120

^a Based on only one erlenmeyer per concentrate.

There is some evidence that exposure to trifluoroacetate results also in the inhibition of the citric acid cycle. *Selenastrum capricornutum* exposed to sodium trifluoroacetate showed a recovery of the growth when citric acid was added. Furthermore, there seems to be a correlation between the sensitivity of an algal species for trifluoroacetate and monofluoroacetate. Both compounds are not toxic for *Chlorella vulgaris* (see Table 10).

One semi-field study with mesocosm streams has been conducted with sodium trifluoroacetate (Bott and Standley, 1995) to study the potential effects of trifluoroacetate on freshwater algal communities and primary productivity. The long-term exposure to a mean sodium trifluoroacetate concentration of 31 to 32 $\mu g \cdot l^{-1}$ had no effect on the primary productivity of the diatom dominated algal flora. Effects on organic carbon excretion which were related to high levels of TFA were noted in some experiments. TFA did not alter the algal species composition in the stream mesocosm.

In conclusion, based on the results of laboratory toxicity tests in fish, *Daphnia*, duckweed, and in a large number of algal and based on the results of the semi-field study with stream mesocosms, an exposure of an aquatic ecosystem to a sodium trifluoroacetate concentration of 0.12 $mg \cdot l^{-1}$ did not show adverse effect.

Terrestrial Organisms

Terrestrial Plants

Inputs of TFA to the terrestrial environment will be exclusively via wet and dry deposition from the atmosphere. Due to the high water solubility of TFA and its salts, the assessment of terrestrial effects should be based primarily on precipitation and soil-water concentrations.

Prior to 1993, there was little information available on the toxicity of TFA to higher plants. Poignant (1957) had observed phytotoxicity to *Triticum vulgare*,

by pre-emergence application, at and above 1500 mg NaTFA·l⁻¹. He also reported the same level of activity to maize (*Zea mays*), meadow grass (*Poa annua*), and sweetcorn (*Alopecurus agrestis*). Ingle (1968) reported significant inhibition of shoot growth of germinating wheat seeds and root growth of germinating tomato seeds at 114 and 285 mg HTFA·l⁻¹ (buffered solutions), respectively; TFA showed the weakest phytotoxicity of the seven halogenated aliphatic acids tested. Atmospheric exposure of a conifer, *Taxus baccata* var. *Repandens*, to HTFA had been investigated by gradually increasing the vapor concentration from 100 to 2100 ppm over a period of 21 days (Freist, 1986). No effects were observed after 19 days (up to 1900 ppm). Slight necrosis of the tips of the young needles was observed at 2100 ppm, which was attributed to the acidity of condensation water which formed on the needles.

Because of these indications of phytotoxic potential, the effect of TFA has been investigated for a large number of terrestrial higher plant species. Unless otherwise stated, the experiments employed sodium trifluoroacetate and the concentrations are expressed as the sodium salt.

In preliminary studies with sunflower, wheat, and mung bean, using OECD protocols, the exposure concentrations (1, 10, 100, and 1000 mg·kg⁻¹) were expressed by dry weight of soil (Windeatt and Thompson, 1993a,b). As explained above, the results from such tests are of limited value since the soil moisture levels, and thus the soil water concentrations of TFA, fluctuate widely between plant watering occasions. However, they provided evidence that further studies on higher plants were necessary. Significant effects on germination and emergence (14 days from seed sowing) were observed at 1000 mg·kg⁻¹ dry soil for wheat and mung bean and at 10 mg·kg⁻¹ dry soil for sunflower. Subsequent vegetative growth was more sensitive; after a further 14 days, a significant reduction in the weight of aerial tissue was observed at 10 mg·kg⁻¹ dry soil for wheat and mung bean and at 1 mg·kg⁻¹ dry soil for sunflower.

The effects of aqueous exposure to TFA on seed germination was investigated (Thompson and Windeatt, 1994) for 10 species of terrestrial plant, including dicotyledons (sunflower, cabbage, lettuce, tomato), leguminous dicotyledons (mung bean, soybean), and monocotyledons (wheat, corn, oats, rice). The seeds were added to filter papers soaked with solutions of TFA; except for small seed species, the seeds were also presoaked in the same solutions. No effects were observed for any species at the maximum concentration tested that was 1000 mg·l⁻¹.

Seedlings of plantain (*Plantago major*) and wheat (*Triticum aestivum* variety Katepwa) were exposed to a range of TFA concentrations in the aqueous (hydroponic) medium surrounding the roots. After 14 days, growth of plantain was affected at 100 mg·l⁻¹ of sodium trifluoroacetate, but there was no effect at 32 or 10 mg·l⁻¹ (Thompson, 1995). Growth of wheat was affected at the lowest concentration tested (32 mg·l⁻¹) in the preliminary 14-day study and this species was tested again in a longer study at lower concentrations (Thompson *et al.*, 1995). After 5 weeks, wheat growth was inhibited at 10 mg·l⁻¹ with tissue necrosis evident first in the shoot and leaf tips; there was no effect at 1 mg·l⁻¹ of TFA.

In a similar hydroponic study (Davison and Pearson, 1997), growth of the same variety of wheat was inhibited at a concentration of $5 \text{ mg}\cdot\text{l}^{-1}$; the effects became apparent after 30 to 35 days, with more severe effects at 10 and $100 \text{ mg}\cdot\text{l}^{-1}$. As in the earlier study, there was no significant effect at $1 \text{ mg}\cdot\text{l}^{-1}$ at the end of the exposure (43 days). Using the same system, another variety of wheat (Hanno) showed lower sensitivity; no effects were found at $5 \text{ mg}\cdot\text{l}^{-1}$ and only slight growth inhibition at $10 \text{ mg}\cdot\text{l}^{-1}$ after 52 days exposure.

Under these hydroponic conditions, soya bean plants, which had proven more sensitive than several other species to foliar application of TFA (see below), gave results essentially similar to those of the sensitive wheat variety. In a preliminary experiment, symptoms of toxicity were observed at 5 and $10 \text{ mg}\cdot\text{l}^{-1}$ but were more severe at the higher concentration, becoming apparent after 20 days. Subsequently, exposure concentrations of $5 \text{ mg}\cdot\text{l}^{-1}$ and $1 \text{ mg}\cdot\text{l}^{-1}$ were tested, in separate experiments, for 43 and 33 days, respectively. At $5 \text{ mg}\cdot\text{l}^{-1}$, effects on growth (dry weight) were observed after approximately 30 days, with symptoms appearing more severe in the younger, expanding leaves. At $1 \text{ mg}\cdot\text{l}^{-1}$, there was no significant effect on final weight (33 days). However, in some plants approximately 25% of the 4th and 5th trifoliate leaves (the youngest) appeared to show slight symptoms (slight rounding of the tip and barely discernible necrosis of the margin), but this was variable between plants.

Other studies (Davison and Pearson, 1997) have investigated the effects of foliar application of solutions of NaTFA. Seedlings (7 days old) of seven species of terrestrial plant (sunflower, soya, wheat, maize, oilseed rape, rice, and plantain) were field-grown, to ensure that the leaves were fully hardened, sprayed (60 microns droplet size) with solutions of NaTFA for 7.5 hours and kept wet with the mist for a further 16.5 hours. The soil and plant roots were protected from the application. After 3 weeks, there was no effect of NaTFA on the height, leaf number, stomatal conductance, final harvest weight or chlorophyll and carotenoid concentrations of any of the species at the maximum concentration tested which was $100 \text{ mg}\cdot\text{l}^{-1}$. There was a significant decrease in specific leaf area only for wheat at $100 \text{ mg}\cdot\text{l}^{-1}$.

A subsequent study, at only $100 \text{ mg}\cdot\text{l}^{-1}$, used a similar system but with laboratory grown plants (wheat, maize, sunflower and soya), both with and without protection of the soil and roots from the spray (Davison and Pearson, 1997). Only soya showed any symptoms of toxicity. These were apparent by both routes of exposure, suggesting that laboratory grown plants were more sensitive to foliar application than those field-hardened; however, the symptoms were much more severe when the NaTFA solution was able to reach the roots.

In a further experiment, soya seedlings were exposed to a range of concentrations of NaTFA applied to the soil surface in a volume equivalent to 10 mm of rainfall every 3 days for 44 days. There was no effect at 1, 5, and $10 \text{ mg}\cdot\text{l}^{-1}$ on dry weight, leaf size, or stomatal conductance (transpiration) and no visible injury. At $100 \text{ mg}\cdot\text{l}^{-1}$, symptoms of toxicity were apparent and leaf size (but not dry weight) was reduced, suggesting TFA affected leaf expansion. Although this regime simulated relatively high rainfall (100 mm per month), the effec-

tive concentration was more than one order of magnitude higher than by hydroponic exposure. This suggests that the hydroponic exposures represent the worst case situation, possibly because transpiration rates are maximized.

Studies by Emerich (1997) have shown that TFA at a concentration of $1 \text{ mg} \cdot \text{kg}^{-1}$ of soil had no effect on the germination or growth of soybean seedlings. Also, $1 \text{ mg TFA} \cdot \text{kg}^{-1}$ had no discernible effect on the nitrogen-fixing capacity of these soybean plants as determined by plant nodule development or by direct assay of nitrogenase activity of these soybean nodules. Toxic effects were, however, observed in the development of the plants and in the nodulation patterns at 10 and $100 \text{ mg TFA} \cdot \text{kg}^{-1}$. Comparable results were obtained when the studies were carried out under hydroponic conditions, at concentrations of 1, 10, and $100 \text{ mg TFA} \cdot \text{l}^{-1}$. There were no significant effects on any parameter at $1 \text{ mg} \cdot \text{l}^{-1}$, with pronounced effects on plant development at 10 and $100 \text{ mg} \cdot \text{l}^{-1}$.

It can be concluded that the most significant route of exposure for terrestrial plants is uptake from soil-water via the roots. TFA enters the transpiration stream and is taken to the shoots and leaves where there is a tendency for TFA to bioaccumulate as the water evaporates. For the most sensitive species, with long-term, continuous exposure under conditions allowing high transpiration rates, no effect on the growth of plants occurs at $1 \text{ mg} \cdot \text{l}^{-1}$ (see Table 11). This concentration is four orders of magnitude higher than the projected rainwater concentration of TFA derived from CFC alternatives.

Terrestrial Invertebrates

Because of the low toxicity of TFA to aquatic invertebrates (see a previous section) and other higher organisms, it was not considered necessary to test terrestrial, soil-dwelling organisms.

Mammals

Distribution, Toxicokinetics, and Metabolism

The distribution half-life of TFA in rabbits was about 20 minutes (Kinoshita, 1989). After intravenous administration in rats, approximately 58% of the TFA was distributed in the total body water, whereas plasma proteins were binding 10% (Holaday and Cunnah, 1976).

In human blood, TFA binds mainly to albumin (44 to 54%) and only little (4 to 14%) to erythrocytes (Dallmeier and Henschler, 1981; Holaday and Cunnah, 1976).

After NaTFA administration via drinking water to male Wistar rats the amount of organically bound fluorine in the plasma and the liver reached a steady level within 3 days of treatment with a 1:1 ratio of liver to plasma concentrations (Stier *et al.*, 1972).

In pregnant mice, the TFA concentration ratio between amniotic fluid/maternal plasma became >1 at 24 hours after an intravenous infusion. Approximately 20 to 30% of the TFA was bound to amniotic fluid and plasma macromolecules (Ghantous *et al.*, 1986).

Table 11. Summary of the ecotoxicity of sodium trifluoroacetate.

Aquatic organisms	EC₅₀/LC₅₀	LOEC	NOEC
<i>Selenastrum capricornutum</i> (freshwater green alga)	4.8 mg/l	0.36 mg/l	0.12 mg/l
(new name: <i>Raphidocelis</i> <i>subcapitata</i>)	1.5 mg/l		0.15 mg/l
<i>Anabaena flos-aquae</i> (blue-green alga)	2400 mg/l	1200 mg/l	600 mg/l
<i>Navicula pelliculosa</i> (freshwater diatom)	1200 mg/l	1200 mg/l	600 mg/l
<i>Skeletonema subspicatus</i> (marine diatom)	>2400 mg/l	—	2400 mg/l
<i>Chlorella vulgaris</i> (freshwater green alga)	>1200 mg/l	—	1200 mg/l
<i>Scenedesmus subspicatus</i> (freshwater green alga)	>120 mg/l	—	—
<i>Chlamydomonas reinhardtii</i>	>120 mg/l		>120 mg/l
<i>Microcystis aeruginosa</i>	>117 mg/l		>117 mg/l
<i>Phaeodactylum tricornutum</i> (marine alga)	>117 mg/l		>117 mg/l
<i>Dunaliella tertiolecta</i>	>124 mg/l		>124 mg/l
<i>Euglena gracilis</i> (freshwater alga)	>112 mg/l		>112 mg/l
<i>Daphnia magna</i> (crustacea)	>1200 mg/l	—	1200 mg/l
<i>Brachydanio rerio</i> (Zebra fish)	>1200 mg/l	—	1200 mg/l
<i>Lemna gibba</i> (duckweed) vegetative growth	1100 mg/l	600 mg/l	300 mg/l

Table 11. Summary of the ecotoxicity of sodium trifluoroacetate. (continued)

Terrestrial plants		EC ₅₀ /LC ₅₀	LOEC	NOEC
Multiple species (monocotyledons and dicotyledons)	Seed germination	> 1000 mg/l	—	1000 mg/l
Mung bean	Soil application	5.7 mg/kg	10 mg/kg	1 mg/kg
Sunflower (<i>Helianthus annuus</i>)	Soil application	12 mg/kg	1 mg/kg	< 1 mg/kg
	Foliar application	—	—	100 mg/l
Wheat (<i>Triticum aestivum</i>)	Soil application	12 mg/kg	10 mg/kg	1 mg/kg
	Root exposure	—	10 mg/l	1 mg/l
	(var. Katepwa)	—	5 mg/l	1 mg/l
	(var. Hanno)	—	10 mg/l	5 mg/l
	Foliar application	—	100 mg/l	50 mg/l
Plantain (<i>Plantago major</i>)	Root exposure	—	100 mg/l	32 mg/l
Maize, rice, plantain, sunflower, oilseed rape	Foliar application	—	—	100 mg/l
Soya	Root exposure	—	10 mg/l	1 mg/l
	Foliar application	—	100 mg/l	10 mg/l

Note: For comparison, the anticipated environmental concentration is in the region of 0.0001 mg/l.

Units: mg/kg (dry weight of soil): for tests with NaFTA applied to soil.
mg/l: for tests with NaFTA in aqueous solution.

Key: EC₅₀ = test concentration resulting in a 50% effect; the table lists EC₅₀ for biomass.

LC₅₀ = concentration at which 50% of the organisms show an effect (mortality).

LOEC = lowest observed effect concentration.

NOEC = no observed effect concentration.

TFA has been shown to be the ultimate biotransformation product of HCFC-123 (2,2-chloro-1,1,1-trifluoroethane) (Harris *et al.*, 1991; Olson *et al.*, 1991). In a study with HCFC-123 in lactating Sprague-Dawley rats, TFA was determined in milk. The measured concentration in milk increased 5 to 23% after saponi-

fication, indicating that a part of the TFA was covalently bound to peptides or proteins (Buschmann, 1996).

TFA was also identified as a major metabolite of halothane. A study (Kinoshita, 1989) using rabbits exposed to halothane demonstrated that the biliary route is the most important excretory pathway for biotransformed TFA. A large quantity of the acid is excreted into the bile, reabsorbed in the gastrointestinal tract, and appears in the circulating blood. The elimination half-life after intravenous injection or oral administration of TFA was 34 and 48 hours, respectively. Enterohepatic circulation is one of the probable mechanisms of the long lasting excretion of TFA.

Kawahara *et al.* (1988) have reported salivary excretion of TFA in surgical patients and Mirkov *et al.* (1988) have reported excretion of TFA in the digestive juice after halothane inhalation in guinea pigs.

The majority of metabolized HCFC-123 is excreted as TFA in the urine (Vinegar *et al.*, 1994). Following a 6-hour exposure of lactating Sprague-Dawley rats to 1000 ppm HCFC-123 and after 1 hour of nursing (15 ml milk per litter containing $50 \mu\text{g}\cdot\text{ml}^{-1}$ TFA), each litter excreted over 16 hours an average quantity of $79 \mu\text{g}$ TFA in 9.1 ml urine. This study illustrates the relative high concentration in the mothers milk and the prolonged retention of TFA by the rat pup (Buschmann, 1996). In adult rats the plasma half-life after intravenous injection was 30 hours (Holaday and Cunnah, 1976).

Intravenous-injected TFA in two human volunteers was completely (95 to 100%) excreted via the urine over 63 to 72 hours (plasma half-life 25 to 32 hours) (Holaday and Cunnah, 1976).

In a 2-week (5-day week) exposure study with 22 ppm halothane the TFA concentration in the blood in the second week was only slightly higher compared to that of the first week. TFA level in human blood and urine are correlated linearly with levels in blood (0.2 to $9 \text{ mg}\cdot\text{l}^{-1}$) being approximately three times higher (Dallmeier and Henschler, 1981).

TFA has not been found to be metabolized to any appreciable extent in rats (Fraser and Kaminsky, 1988).

Acute Toxicity

Acutely, trifluoroacetic acid would be categorized as being moderately toxic by the oral route of administration having a LD_{50} of a 2 to 5% solution in the range of 200 to $400 \text{ mg}\cdot\text{kg}^{-1}$ body weight in rats and mice (Patty, 1963). Oral LD_{100} , LD_{10} , and LD_0 values were reported by another laboratory to be 1000 , 500 , and $250 \text{ mg}\cdot\text{kg}^{-1}$ body weight, respectively (Kheilo and Kremneva, 1966).

The sodium salt of trifluoroacetic acid is much less toxic than the free acid. No deaths were observed when mice were administered intraperitoneally up to $5000 \text{ mg}\cdot\text{kg}^{-1}$ of NaTFA; whereas, a dose of $150 \text{ mg}\cdot\text{kg}^{-1}$ HTFA caused death in 2 out of 5 mice, a result which is comparable to that obtained with an equimolar dose of hydrochloric acid (Blake *et al.*, 1969).

Other reported LD_{50} values obtained with the sodium salt using the intraperitoneal route of administration include: $>4000 \text{ mg}\cdot\text{kg}^{-1}$ (Rosenberg, 1971)

and $>2000 \text{ mg}\cdot\text{kg}^{-1}$ (Airaksinen and Tammisto, 1968; Airaksinen *et al.*, 1970). An intravenous LD_{50} for NaTFA was reported to be $1200 \text{ mg}\cdot\text{kg}^{-1}$ for mice (Airaksinen and Tammisto, 1968).

Information on the acute inhalation toxicity of HTFA is limited to a single Russian report (Kheilo and Kremneva, 1966). Values were reported for LC_{50} for both mice and rats. The LC_{50} for a 2-hour exposure in mice was reported to be $13.5 \text{ mg}\cdot\text{l}^{-1}$ ($\sim 2900 \text{ ppm}$); additional values for LC_{100} and LC_{10} (2 hour) were $20.4 \text{ mg}\cdot\text{l}^{-1}$ (4366 ppm) and $9.2 \text{ mg}\cdot\text{l}^{-1}$ (1968 ppm), respectively. The 2-hour LC_{50} for the rat was reported to be $10 \text{ mg}\cdot\text{l}^{-1}$ (2140 ppm) with additional values for LC_{100} and LC_{10} (2 hour) of $11.5 \text{ mg}\cdot\text{l}^{-1}$ (2461 ppm) and $8.3 \text{ mg}\cdot\text{l}^{-1}$ (1776 ppm). According to these investigators, for rats the threshold concentrations are $4 \text{ mg}\cdot\text{l}^{-1}$ (856 ppm) based on "the temperature reaction of the body" and $1.5 \text{ mg}\cdot\text{l}^{-1}$ (321 ppm) based on "neuromuscular excitability." The threshold concentration for irritation in humans exposed for one minute is $0.25 \text{ mg}\cdot\text{l}^{-1}$ ($\sim 54 \text{ ppm}$).

Following treatment of Swiss male mice with either a single intraperitoneal dose of $1000 \text{ mg}\cdot\text{kg}^{-1}$ or $2000 \text{ mg}\cdot\text{kg}^{-1}$ NaTFA, hepatocytes were observed to have a cloudy swelling with slight accumulation of fat accompanied by an increase in liver glycogen at the lower dose. At the higher dose, vacuolization was also noted (Rosenberg and Wahlstrom, 1971).

At $2000 \text{ mg}\cdot\text{kg}^{-1}$ NaTFA given to mice intraperitoneally, the glucose-6-phosphate dehydrogenase activity in livers and erythrocytes was slightly increased and a transient decrease in glutathione and NADPH content was observed in the liver at 12 hours after administration. This decrease was also observed in erythrocytes at 24 hours (Rosenberg, 1971).

The relative low toxicity of TFA is demonstrated by comparison with two closely related chemicals: trifluoroethanol (TFE) and trifluoroacetaldehyde (TFAlD). The intraperitoneal LD_{50} s of TFE, TFAlD and NaTFA were 158 to 195, 650 and $>2000 \text{ mg}\cdot\text{kg}^{-1}$, respectively, in male Swiss mice (Airaksinen and Tammisto, 1968; Airaksinen *et al.*, 1990). When these three chemicals were each administered to 10-week old, male AlpK/AP strain (Wistar-derived) rats with single intraperitoneal (Lloyd *et al.*, 1986) or single oral (Lloyd *et al.*, 1988) doses of 10 and $25 \text{ mg}\cdot\text{kg}^{-1}$ body weight, TFE and TFAlD caused a dose-related reduction in testis weight within 3 days, which was accompanied by morphological changes. In marked contrast, TFA did not cause any observable testicular effects on weight or morphology.

Using an *in vitro* Sertoli/germ cell co-culture system obtained from the rat, at concentrations of 0.1 to 1 mM, TFAlD produced dose-related effects including increased germ cell loss of pachytene and dividing spermatocytes. The germ cell losses were accompanied by leakage of the pachytene spermatocyte marker enzyme lactic acid dehydrogenase-X (LDHX) and decreased lactate and pyruvate production. With TFA increased cell loss and increased LDHX leakage became only apparent at 10 mM. No response was observed with 10 mM TFE (Lloyd *et al.*, 1986). In a similar study (Williams, 1997) in isolated Leydig cell cultures, Sertoli cell only cultures and Sertoli/germ cell co-cultures obtained from the Sprague-Dawley rat TFAlD had also the most wide ranging

and severe effects on the function of isolated testicular cells, affecting all three cell systems. TFA and TFE show only a small effect on Leydig cell function and essentially no effect on the Sertoli/germ cell cultures. The apparent difference of activity of TFE between *in vitro* and *in vivo* is explained by the metabolism of TFE *in vivo* to TFAlD.

TFE, especially when muscular fibrillations were induced by atropine-neostigmine, caused a drop in the lactate and pyruvate pool in muscle and liver of mice and guinea pigs, probably by inhibition of glycolysis. In guinea pig muscle a decrease of ATP was also seen. NaTFA had little, if any, effect on ATP, lactate and pyruvate. Both NaTFA and TFE had no effect on citrate values, showing that they do not block the Krebs' cycle (Airaksinen and Tammisto, 1968).

In a perfusion experiment with rat liver, Stier *et al.* (1972) showed that NaTFA enhanced lactate and pyruvate turnover and uptake without apparent stimulation of the tricarboxylic acid cycle or glucose synthesis.

Single intraperitoneal doses of $2.1 \text{ mmol}\cdot\text{kg}^{-1}$ of TFE and TFAlD produced significant bone marrow and intestinal toxicity, which is characterized by leucopenia and loss of intestinal dry weight. This eventually leads to a lethal septicemia in male Wistar rats. HTFA, when administered at $240 \text{ mg}\cdot\text{kg}^{-1}$ (a dose equimolar to TFE and TFAlD) did not produce any similar toxic effects (Fraser and Kaminsky, 1988).

Repeated Dose Toxicity

When HTFA or NaTFA were added to drinking water to a concentration of $114 \text{ g}\cdot\text{l}^{-1}$ ($1 \text{ N}\cdot\text{l}^{-1}$), male Sprague-Dawley rats rejected the solutions which resulted in dehydration and body weight loss (Blake *et al.*, 1970). As a consequence, an increase ($<30\%$) in the liver-to-body weight ratio was observed within 10 days. In contrast, daily intragastric administration of $1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ of 1 N NaTFA ($114 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) to rats, for 8 days, did not cause dehydration or body weight loss and did not significantly affect the liver-to-body weight ratio. Furthermore, 1 N NaTFA did not affect the duration of hexobarbital-induced hypnosis suggesting no change in the metabolic activity of the liver.

In one other report (Stier *et al.*, 1972), NaTFA was administered via drinking water to male Wistar rats such that the animals were provided with approximately $130 \text{ }\mu\text{mol}$ NaTFA per 100 g body weight per 24 hours (equivalent to $150 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$, based on an assumed normal consumption of water) for 5 to 6 days. After 5 days of treatment, the relative liver weight was increased by about 43%. Furthermore, the glycogen content of the liver was decreased.

Male Wistar rats were fed trifluoroacetate, perfluorobutyrate, and perfluorooctanoate in their diets for 5 to 14 days at concentrations of 5000 ppm ($500 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) for the TFA, and 2500 ppm for the latter two compounds (Just *et al.*, 1989). All three compounds induced hepatomegaly, anorexia, and peroxisome proliferation. The relative liver weight increased by 20 to 30%. With TFA, the body weight gain was similar to controls. Perfluorobutyrate and

perfluorooctanoate were found to be more active than TFA. The rise in activity of peroxisomal fatty acid β -oxidation was only slight for TFA, amounting to about a 2-fold increase, whereas the increase in activity was 9- to 10-fold after perfluorobutyrate and perfluorooctanoate treatment.

Male rats and male guinea pigs were fed diets containing 7500 ppm (rat: $750 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$) for 25 days. A decrease of body weight without concomitant changes in food consumption was observed for rats. Decreases in serum cholesterol, triglycerides, glucose, and insuline levels were reported in rats and to a lesser extent in guinea pigs. Increased liver weights and diffuse liver hypertrophy were observed in treated rats, but in guinea pig the liver weights were reduced. The rate of hepatic peroxisomal β -oxidation was increased in rats but not in guinea pigs supporting the conclusion that peroxisome induction is a rodent-specific phenomena (Warheit, 1993).

Studies on repeated inhalation exposures of animals to HTFA are limited to one report (Kheilo and Kremneva, 1966). Rats were exposed for 4-hours daily 6 times a week at concentrations of 0.4 to $0.7 \text{ mg} \cdot \text{l}^{-1}$ (86 to 150 ppm) HTFA for 5 months. Effects observed included: irritation of mucous membranes, increased proteinuria, and "altered neuromuscular excitability." These investigators noted that chronic exposure to 0.025 to $0.05 \text{ mg} \cdot \text{l}^{-1}$ (~5 to 11 ppm) caused only very slight symptoms and suggested that they can be considered to be close to the threshold concentrations for chronic exposures.

In conclusion, the major target organ in TFA-exposed rats is the liver, showing mild effects (increased weight, hypertrophy and induction of peroxisomes) at $150 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ by gavage for 5 days.

Irritation

Application of solutions of HTFA to the skin of rats or guinea pigs, at concentrations of 20% or greater, caused marked coagulation, necrosis; 10% concentration was moderately severely irritating and concentrations of from 2 to 5% were moderately irritating (Patty, 1963). Kheilo and Kremneva (1966) reported HTFA to be corrosive to rabbit skin.

Corrosivity

As with any strong acid, severe eye irritation would be expected from contact with HTFA (Patty, 1963). Ocular irritation was observed during the Russian acute inhalation studies in rats and mice (Kheilo and Kremneva, 1966).

Sensitization

TFA, when conjugated to human and guinea pig albumin, was shown to induce a specific delayed-type hypersensitivity in guinea pigs (Mathieu *et al.*, 1974). Erythema and induration were observed 24 to 48 hours after intradermal challenge with antigen, as evidence for cutaneous hypersensitivity. Perivascular mononuclear infiltration was observed, histologically. This prompted the investigators to conclude that TFA may serve as a hapten able to elicit specific cellular immune responses.

Several reports relating to cellular-mediated immune response have appeared in the literature. These have included demonstrations of trifluoroacetylated neoantigens such as: TFA-albumin (Reves and McCracken, 1976a,b), TFA-ovalalbumin (Ford *et al.*, 1984), TFA-neoantigen (present in microsomal carboxylesterase) (Satoh *et al.*, 1984), and trifluoroacetylated hepatocytes (Satoh *et al.*, 1985) that have resulted from exposure to halothane or TFA.

However, the role of TFA in cell-mediated immunity is questionable because TFA, as well as halothane, did not stimulate DNA formation in cultured lymphocytes obtained from the blood of human subjects previously exposed to halothane (Waldron and Ratra, 1972), and the delayed hypersensitivity response to TFA had no effect on halothane-induced liver damage in mice and rats (Ford *et al.*, 1984). Furthermore, skin test hypersensitivity reactions with TFA, prepared as a complex with autologous serum protein, did not correlate with hepatic necrosis induced by halothane exposure in guinea pigs (Reves and McCracken, 1976b).

Mutagenicity

NaTFA was tested for mutagenicity in the standard Ames assay (Blake *et al.*, 1981). NaTFA was found to be nonmutagenic to *Salmonella typhimurium* strains TA98, TA100, and TA1535, both in the presence and absence of Aroclor 1254-induced rat liver or rat testes S-9 activation systems. HTFA was tested in another laboratory (Waskell, 1978) using *Salmonella typhimurium* strains TA98 and TA100, both with and without rat liver S-9 activation, and was also found to be nonmutagenic. Additionally, HTFA was tested using the repair-deficient strains TS24, TA2322, and TA1950 of *Salmonella typhimurium*. HTFA did not inhibit the growth of any of the above DNA repair-deficient strains relative to a normal repair-proficient *hisG*, thus indicating a lack of genetic activity. In yet another laboratory (Baden *et al.*, 1976), HTFA or urine from patients anesthetized with halothane were all found to be nonmutagenic to *Salmonella typhimurium* strains TA98 and TA100, either in the presence or absence of Aroclor 1254-induced rat liver S-9 activating medium.

Carcinogenicity

No information was found with regard to the carcinogenic potential of TFA.

Toxicity for Reproduction

TFA has not been tested for teratogenicity or fetotoxicity.

RISK CHARACTERIZATION

Present and Future Environmental Concentrations

As described in detail in previous sections, the present contributions to environmental levels of trifluoroacetic acid can be summarized as follows.

Production and Use of Trifluoroacetic Acid

Trifluoroacetic acid is manufactured at about 1000 metric tons per year and is widely used in the fine chemicals industry and as a laboratory reagent. It is either consumed or becomes part of a chemical waste stream. The quantities released into the atmosphere from this source are very small indeed and do not appear to be a significant contribution to global environmental levels.

Use of Fluorocarbon Anaesthetics

Halothane and isoflurane anaesthetics, which have been in use since the 1970s, both yield trifluoroacetate when degraded. Halothane is the most used of the fluorocarbon anaesthetics at a maximum of 1500 metric tons per year globally. All the material used is assumed to be emitted to the atmosphere. The global deposition rate of trifluoroacetic acid from this source is estimated to be 800 metric tons per year.

Use of Certain CFC Substitutes

CFCs substitutes — HCFCs and HFCs — break down in the environment to give predominantly carbon dioxide, water, and inorganic salts of chlorine and fluorine. However, some substances, most notably HFC-134a, HCFC-124, and HCFC-123, also break down to yield trifluoroacetic acid (HTFA), which is resistant to further atmospheric degradation. Because the HCFCs and HFCs have until now been produced only in limited commercial quantities, their contribution to present environmental levels of TFA has been estimated to be small — around 2000 metric tons per year.

In total, the present known emission sources of all fluorocarbon precursors (anaesthetics + CFC substitutes) will yield trifluoroacetic acid at a rate of 2800 metric tons per year.

To derive future environmental concentrations, predicted production and releases of the relevant HCFCs and HFCs, along with their rates of transformation into TFA, have been modeled.

Substances that decompose in the atmosphere by oxidation or photolysis will give rise to diffuse fluxes of decomposition products in the atmosphere as the first compartment. HCFCs and HFCs that break down to trifluoroacetic acid have atmospheric lifetimes ranging from about 1.4 to 14.6 years, so that most decomposition occurs at or near the background concentration of the substance after it has become well mixed in the atmosphere. The decomposition mechanisms depend on physical and chemical properties and processes that are relatively well understood so that it is possible to calculate accurately the future atmospheric concentrations of precursors to trifluoroacetate, given a particular set of scenarios for emissions.

It has been calculated (see earlier section for details) that in the year 2020 the global deposition of trifluoroacetic acid as a breakdown product of the HCFCs and HFCs will be about 160,000 metric tons per year.

Based on the physico-chemical properties of TFA, the preferred environmental compartment will be water, rather than air, ground, or biota. Thus, trifluoroacetic acid that is emitted from processes as a vapor, or trifluoroacetate

that is formed from other materials by reaction in the atmosphere will partition rapidly into cloud, rain, or surface water.

In rain water a range of concentrations has been calculated, taking into account geographical variations (OH radical concentrations, amount of rain, regional releases of parent compound). Because most of the rainfall and the highest regional concentrations of hydroxyl occur in the tropics, the mass deposition rate of trifluoroacetic acid is highest in this region. It was calculated that in 2020 the tropical concentration would be $2 \mu\text{mol}\cdot\text{m}^{-2}\cdot\text{yr}^{-1}$ or $100 \text{ ng}\cdot\text{l}^{-1}$ in rainwater. Over Europe, the deposition rate would be about $0.5 \mu\text{mol}\cdot\text{m}^{-2}\cdot\text{yr}^{-1}$ and over the United States levels would be up to double this.

For this risk assessment, a maximum level of TFA in rain water in the region of $0.1 \mu\text{g}\cdot\text{l}^{-1}$ ($0.0001 \text{ mg}\cdot\text{l}^{-1}$) in the year 2020 was adopted as the standard for the predicted environmental concentration.

In surface water, it appears to be possible to accumulate a riverborne flux of TFA in lakes or seas from which there is no outflow, only evaporation. However, consideration of the volumes and flows indicates significant local accumulation over global levels takes many hundreds of years.

A possible buildup in special ecosystems, such as seasonal wetlands (special aquatic ecosystems that dry out periodically and are replenished only by rainfall), has been postulated but significant buildup over background levels can only be anticipated if a number of low probability events occur at the same time and endure for a long period of time. Therefore, although some accumulation of TFA may take place in special ecosystems like vernal pools, accumulation over several orders of magnitude appears to be highly improbable.

Generally, soil retention of TFA is poor although soils with high levels of organic matter have been shown to have a greater affinity for TFA when contrasted with soils with low levels of organic matter. This appears to be an adsorption phenomenon, not irreversible binding. Based on the maximum observed partition coefficient (K_d) of 20, the maximum concentration bound to soil — in equilibrium with the projected rainfall concentration (from CFC alternatives) in 2020 of $0.0001 \text{ mg}\cdot\text{l}^{-1}$ — would be $0.002 \text{ mg}\cdot\text{kg}^{-1}$.

Degradation mechanisms of TFA that could mitigate future concentrations of this compound have been studied quite extensively. Given the high thermodynamical stability of the CF_3 group, no significant abiotic mineralization process has been observed or is forecast in environmentally relevant conditions.

TFA is highly resistant to both microbial oxidative and reductive degradation. Although biodegradation has been observed under specific conditions, the relevance of these results to the real world are considered to be doubtful. For the purpose of this risk assessment, we will assume, as a reasonable worst case, that no degradation of TFA is likely to occur in the environment.

TFA's low octanol/water partition coefficient ($\log P_{ow} = -2.1$) indicates no potential to bioaccumulate. TFA does not accumulate significantly in lower aquatic life forms such as bacteria, small invertebrates, oligochaete worms and some aquatic plants including *Lemna gibba* (duckweed). In terrestrial higher plants such as sunflower and wheat, some bioaccumulation was seen (bioconcentration factors up to 43 based on fresh weight). This appeared to be related to uptake with water and then concentration due to transpiration water loss.

In the event that TFA is degraded, it may be transformed into monofluoroacetic acid (MFA). However, as the rate of breakdown of MFA (hydrolytically by fluoroacetate dehalogenases) is so much higher than for TFA, any MFA formed would rapidly degrade. Therefore, there would be no buildup of MFA regardless of the levels of TFA present in the environment.

Effect Assessment

Given the fact that deposited TFA would remain in water, a number of studies have been conducted aiming to derive a no-effect concentration in the aquatic compartment. Standard acute tests on fish and *Daphnia* carried out with NaTFA show that they are insensitive to large concentrations (up to $1 \text{ g} \cdot \text{l}^{-1}$ TFA). This low toxicity of TFA is reinforced by toxicological data on mammals developed previously, namely, in the context of TFA being a metabolite of several anaesthetics (see earlier section). On the other hand, the no-effect concentration for the standard algae species *Selenastrum capricornutum* is around $0.10 \text{ mg} \cdot \text{l}^{-1}$ (as TFA). To see if this sensitivity was general among algae, 10 other species belonging to 4 different classes have been tested; these other species were not sensitive to NaTFA (no-effect concentration $>100 \text{ mg} \cdot \text{l}^{-1}$). Even among the chlorophyceae, *Selenastrum capricornutum* seems to be unique; therefore, even if this species was affected above $0.1 \text{ mg} \cdot \text{l}^{-1}$, the ecology of the system (*i.e.*, the functionality) where it lives would not be affected. Consequently, it is considered that for the protection of the aquatic environment the no-effect concentration of $0.1 \text{ mg} \cdot \text{l}^{-1}$ of this alga can be used.

Extensive research has been devoted to effects on higher plants, as they could be exposed to TFA in rainwater through leaves and stems and TFA in pore water through roots. A number of species were tested, with particular emphasis on those having an important role in feeding people and cattle. Exposure of the leaves was shown to be less important than exposure of the roots. By application to the soil, the most sensitive species was sunflower, with an effects threshold of $1 \text{ mg NaTFA} \cdot \text{kg}^{-1}$ (dry soil). The same soil concentration had no effect on the germination, growth and nitrogen-fixing capacity of soya seedlings. However, because of the limited binding of TFA to soil, effects are better defined as concentrations in the soil water. By exposure of the roots to aqueous solutions, the no-effect concentration was $1 \text{ mg NaTFA} \cdot \text{l}^{-1}$ for the long-term growth of wheat and soya. Therefore, as a conservative figure, the no-effect concentration in soil-water is considered to be $0.1 \text{ mg} \cdot \text{l}^{-1}$.

Risk Assessment

In comparing the present and future environmental concentrations of TFA (maximum of $0.0001 \text{ mg} \cdot \text{l}^{-1}$ in rainwater in 2020) with the no-effect concentrations in both surface water and soil ($0.1 \text{ mg} \cdot \text{l}^{-1}$), it is concluded that no noticeable risk for the environment can be anticipated as there is a 1000-fold difference. The local enrichments in certain aquatic systems and organic rich soils do not influence this conclusion.

For the time being, an important question remains concerning the origin of the large present levels of TFA that have been measured in the environment (fresh and marine surface waters, rain, and air) and cannot be explained by the known industrial sources. These levels, in the range of $0.1 \mu\text{g}\cdot\text{l}^{-1}$ for water and $50 \text{ ng}\cdot\text{l}^{-1}$ for air, are roughly 60 times what is estimated to arise from known sources today and more or less equal to what is anticipated in 25 years from now.

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