Chlorofluorocarbon Sources of Environmental Contamination

Abstract. *The quantities of chlorofluorocarbons (FCC's) used commercially in the United States and globally are reviewed, and estimates of environmental release from the applications are made. The results indicate that sizable quantities of the FCC's that have been produced have not yet reached the environment and that regulation of U.S. applications would partly reduce, but not end, the possible destruction of stratospheric ozone.*

For several years, chlorofluorocarbons (FCC's) have been known to be environmental contaminants (*1–5*). Both CCl_2F_2 and CCl_3F have been detected at concentrations varying from background levels of 50 to 100 parts per trillion (ppt) over oceans and remote areas to high averages of several hundred ppt in urban areas. The initial interest in monitoring these compounds was prompted by their unique usefulness as unequivocal anthropogenic tracers (*6*). However, the FCC's have been cited recently as atmospheric pollutants because of their suspected contribution to the destruction of O_3 in the upper atmosphere (*7*). It is theorized that the high stability of these compounds allows them to persist long enough to diffuse to the stratosphere where they decompose upon exposure to high-energy ultraviolet light (chiefly 175 to 220 nm) to yield atomic chlorine, which can catalyze the destruction of O_3. It is possible that chlorine-catalyzed O_3 destruction may exceed the other natural sinks of O_3, thus resulting in a reduction of the total stratospheric O_3. Depletion of stratospheric O_3 may lead to increased incidences of skin cancer, sunburn, and premature aging of the skin, and perhaps produce growth retardation in crops and climatological effects (*8*).

The rate and magnitude of such an effect and the possibility of corrective action, as well as a clear assessment of the relative impact of FCC's by comparison with other sources of chlorine atoms in the stratosphere (*9*), are all dependent upon the various applications of FCC's and the resulting quantities of these materials released from these applications. As part of a review of the potential environmental hazards from the commercial use of the FCC's (*10*), we have considered the production and application quantities and the resulting environmental releases of these materials in great detail.

Table 1 presents a breakdown of FCC's by compound, production quantity, and application in the United States. The quantities of each compound were determined from published sources (*11, 12*) and from discussions with major manufacturers. By far, the largest application is as aerosol propellants, although the quantities used in the other applications are not insignificant. Small quantities of FCC's are used as feedstock in the production of plastics monomers (for example, $CF_2{=}CF_2$ from $CHClF_2$) but are not considered here since the material is not released in appreciable quantities to the atmosphere. On the basis of the information in Table 1, as well as historical data on FCC applications (*13*) and several assumptions discussed below, the quantities of FCC's released from U.S. applications have been calculated (Fig. 1).

The loss during production, transport, and storage is considered to be negligible as compared to other sources. With aerosol cans, all the propellant is lost during propulsion of the active ingredients of the aerosol. However, because of an inventory lag of approximately 1 year, the cumulative quantity released is less than the quantity produced by an amount equal to the current year's production. Refrigerant applications can be divided into prefabricated units, for which charging with the FCC's takes place at the factory, and large commercial units, for which the charging is conducted after the units are in place. In order to arrive at the result depicted in Fig. 1, we assumed that approximately equal amounts of FCC's are used in the small and large units. The average life of a prefabricated unit is 10 years (*14*); therefore, the annual loss for the year N is approximately equal to the annual quantity produced for prefabricated units in the year $N - 10$. The losses from large commercial units were based on the assumption that the units will be recharged every 5 years and that 80 percent of the original refrigerant will be recovered. For solvent applications, a recovery system efficiency of 80 percent was assumed. For FCC's used as foaming or blowing agents there is an approximately equal division between open-cell and closed-cell applications. Loss from the closed-cell foams should be negligible, whereas all the FCC's used with open-cell foams should be released to the atmosphere immediately. Thus half of the quantity of FCC's used as foaming agents will be lost immediately, while the other half would remain tied up in the foam matrix for an extended period.

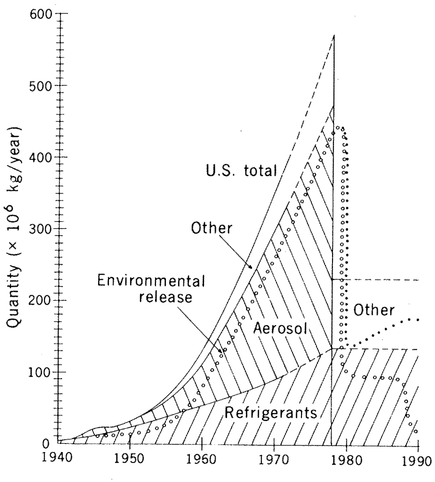

Fig. 1. Data on U.S. production and environmental release of FCC's. Data to 1972 were based on known production information. Trends were extrapolated to 1978, and then release calculations were made on the basis of the following assumptions: (i) zero production after 1978 (ooooo) and (ii) no aerosol propellant use, with production for refrigerant and other uses remaining equal to the 1978 levels (·····).

These assumptions were based upon discussions with major manufacturers of FCC's, major manufacturers of by-products (for example, companies manufacturing refrigerators and air-conditioners), and large users of FCC by-products (for example, apartment house landlords). The accuracy of these assumptions varies substantially, but we consider them to be very close to the actual situation, at least for aerosol propellants and refrigerants (84 percent of the market in 1972). The assumption for solvent losses is the least accurate and is probably dependent upon the quantity of solvent being used at each particular geographic location (determines the incentive for recycling). However, inaccuracies in the solvent loss assumption would have little effect on the total losses depicted in Fig. 1. For FCC's used in closed-cell foams, it could be argued that substantial losses might occur during disposal (especially incineration) of the plastic products, which usually have fairly short useful lives. However, since only a small percentage [~10 percent (*15*)] of the solid waste that is dumped each year is incinerated, it is unlikely that large quantities of FCC's would be released by incineration. The proportion of the FCC's in the closed-cell foams [usually polyurethanes (*13*)] released during disposal is unknown. The amount of FCC's released by degradation of the plastic is probably quite small since the more commercially important (*16*) polyether polyurethanes are resistant to fungal attack (*17*).

Comparison of the estimates in Fig. 1 with atmospheric monitoring data is most difficult since we have reported total FCC's released whereas monitoring data is reported for individual compounds (usually CCl_3F and CCl_2F_2). The relative production proportions noted in Table 1 pro-

Table 1. Applications of FCC's in the United States in 1972 (*11, 12*).

Compound	Aerosol propellants ($\times 10^6$ kg)	Refrigerants ($\times 10^6$ kg)		Solvents ($\times 10^6$ kg)	Foaming agent ($\times 10^6$ kg)	Total ($\times 10^6$ kg)
		Prefabricated units	Large commercial units			
CCl_3F	111		4		21	136
CCl_2F_2	119	31	29		20	199
$CHClF_2$		21	15			36
$CClF_2CFCl_2$				23		23
$CClF_2CClF_2$	9					9
Total	239	52	48	23	41	403
Percentage of total	59	13	12	6	10	100

vide some insight but the quantities of each individual compound released are dependent upon the quantity used and the particular application. Lovelock *et al.* (*5*) assumed that the integrated world production of CCl_3F in mid-1971 was 900×10^6 kg in order to calculate a global mean concentration of 53 ppt. This calculated value agreed fairly well with the observed global mean concentration of 48 ppt, but it is lower than the mean aerial concentration of 61 ppt observed by Wilkness *et al.* (*4*). Wilkness *et al.* (*4*) concluded that an inconsistency existed between predicted and observed concentrations. Our integrated quantity of total FCC's from the United States through 1971 is approximately 2500×10^6 kg. If it is assumed that CCl_3F makes up one-third of the total FCC's released (Table 1), the quantity of CCl_3F released from U.S. sources would be approximately 830×10^6 kg. Considering the uncertainty that can be introduced from the assumed volume of the atmosphere, the nonuniform global distribution of FCC's, and the FCC release from outside the United States, our U.S. release calculations seem to agree relatively well with the background monitoring data.

Hester and his co-workers (*2*) noted an average ratio of 1.1 (weight to weight) in the CCl_2F_2/CCl_3F concentrations at various sampling sites in the Los Angeles Basin. That ratio agrees with the relative quantities of CCl_2F_2 and CCl_3F being used as aerosol propellants (Table 1). Simmonds *et al.* (*3*) determined that the highest concentration of both CCl_3F and CCl_2F_2 in the Los Angeles Basin is observed at 8 a.m.; they attribute the time relationship to the early morning release of aerosol propellants. The relative ratio and time relationship noted above is in agreement with the obvious conclusion that a major source of FCC release is aerosol propellant use.

The FCC's are used in the various applications noted in Table 1 because they are noncorrosive, nonflammable, have convenient boiling points, and exhibit a low order of toxicity, the last characteristic being perhaps the most important. Although a comprehensive review of alternatives to FCC's has not been conducted, the possibility of replacing these chemicals with other compounds which exhibit the desired properties listed above but would not affect the stratospheric O_3 seems relatively remote. Thus, it appears quite likely that, if the suspected destruction of O_3 due to FCC's is demonstrated, restrictions may be placed on some or perhaps all of the present applications of FCC's. Propellant applications are an obvious candidate, in view of the large quantity of FCC's used in that application and the fact that the use is primarily one of convenience rather than necessity. In addition, aerosol packaging has been under attack for reasons unrelated to O_3 destruction, such as health hazards and the explosive nature of the packaging (*18*). However, the desirability of such restrictions needs to be considered in terms of the potential to significantly reduce environmental pollution by FCC's.

Table 2. Quantities of CCl_3F and CCl_2F_2 produced in the United States and in the world (*20*). The U.S. production figures are based on the U.S. Tariff Commission reports (*11*) and probably have an error of less than 5 percent. The figures for world production have an estimated overall error of 20 percent (*20*).

Year	CCl_3F ($\times 10^6$ kg)		CCl_2F_2 ($\times 10^6$ kg)	
	U.S.	World	U.S.	World
1958	23	23	59	59
1959	27	27	71	71
1960	33	40	75	87
1961	41	52	78	94
1962	56	72	94	117
1963	63	83	98	129
1964	67	93	103	143
1965	77	112	123	175
1966	77	122	130	196
1967	83	139	141	225
1968	93	165	148	256
1969	108	197	167	300
1970	111	217	170	327
1971	117	241	177	363
1972	136	285	199	422
1973	147	313	221	469

Two alternatives and their resulting effects on FCC release are illustrated in Fig. 1. We have assumed that the production and use of FCC's will continue to grow at their present rate until the possible effects of FCC's on the stratospheric O_3 can be evaluated (probably not before 1978). In the event that FCC use is found to be substantially hazardous, two possibilities seem likely: (i) all FCC use in the United States will be stopped, or (ii) all aerosol propellant use in the United States will be stopped, and refrigerant and other uses will be maintained at their 1978 levels. The resulting release curves demonstrate the relationship between FCC applications and immediate or delayed release to the environment. All the FCC's produced will eventually be released to the environment. Release can take place almost immediately as with propellant applications, or an inventory may slowly build up, reducing the quantity immediately released but increasing the quantity that will eventually be released even if production of FCC's is halted. For example, even if all production of FCC's is halted in 1978, approximately 100×10^6 kg would continue to be emitted each year for the next 10 years, most of this derived from an inventory of refrigerant FCC's. Our results also indicate that, although aerosol propellant use is a major source of FCC's in the atmosphere, sizable quantities (30 percent in 1972 to 1978) of the chemicals can be released from nonpropellant uses. Furthermore, the calculations suggest that the quantity released to the atmosphere is 65 to 70 percent of the total quantity that has been produced (in 1972, 2800×10^6 kg out of 4300×10^6 kg produced; in 1978, 5100×10^6 kg out of 7300×10^6 kg produced). This result should be taken into account in projections of possible O_3 destruction.

Projections of possible O_3 destruction also require that global sources of FCC's be considered. Unfortunately, data on the worldwide production of FCC's and on the quantities used in various applications can only be approximated. In 1960, when the United States had an estimated FCC capacity of 186×10^6 kg/year and an estimated FCC production of 136×10^6 kg/year, the rest of the free world had an estimated FCC capacity of 67×10^6 kg/year and an estimated FCC production of 38×10^6 kg/year. It is estimated that the total world production is at present approximately twice the U.S. production (Table 2). Moreover, it is projected that in 1974 sources outside the United States will have produced 47 percent of the free-world aerosol products (in terms of aerosol units)

(*19*). Furthermore, during the 10-year period from 1963 to 1972 when aerosol production in the United States nearly tripled, the output of spray packaging in the free world outside the United States almost quadrupled (*19*), an indication of the higher growth rate of aerosol production outside the United States. Data on FCC production outside the free world are not available, but the quantity produced is estimated to be relatively low. From this information and the review given above of the relationship between applications and environmental release, it is apparent that annual FCC losses from sources outside the United States are presently approximately equal to and in the future will probably exceed U.S. losses. More detailed conclusions from the available data do not seem warranted. However, even from these qualitative estimates, it would appear that restrictions on FCC production and use in the United States would only partly reduce, rather than end, destruction of stratospheric O_3, if, in fact, the chlorine-catalyzed O_3 destruction due to FCC compounds can exceed all natural sinks of stratospheric O_3.

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References and Notes

J. E. Lovelock, *Nature (Lond.)* **230**, 379 (1971); *Atmos. Environ.* **6**, 915 (19 C. W. Su and E. D. Goldberg, *Nature (Lond.)* **245**, 27 (1973).

2. N. E. Hester, E. R. Stephens, O. C. Taylor, *J. Air Pollut. Contr. Assoc.* **24**, 591 (1974).

P. G. Simmonds, S. L. Kerrin, J. E. Lovelock, F. H. Shair, *Atmos. Environ.* **8**, 209 (1974).

P. E. Wilkness, R. A. Lamontagne, R. E. Larson, J. W. Swinnerton, C. R. Dickson, T. Thompson, *Nature (Lond.)* **245**, 45 (1973).

J. E. Lovelock, R. J. Maggs, R. J. Wade, *ibid.* **241**, 194 (1973).

J. E. Lovelock, *ibid.* **252**, 292 (1974).

M. J. Molina and F. S. Rowland, *ibid.* **249**, 810 (1974); R. J. Cicerone, R. S. Stolarski, S. Walters, *Science* **185**, 1165 (1974).

8. A. L. Hammond and T. H. Maugh II, *Science* **186**, 335 (1974).
9. Lovelock (*6*) presents evidence suggesting that chlorocarbons may be a major source of chlorine atoms in the stratosphere.
10. P. H. Howard, P. R. Durkin, A. Hanchett, *Environmental Hazard Assessment of One- and Two-Carbon Fluorocarbons* (Syracuse Univ. Research Corporation, Syracuse, N.Y., 1974).
11. U.S. Tariff Commission, *Synthetic Organic Chemicals: U.S. Production and Sales, 1972* (U.S. Tariff Commission Publication 681, Government Printing Office, Washington, D.C., 1974).
12. *Chem. Market. Rep.*, "Chemical profile: fluorocarbons" (1 January 1973).
13. J. M. Hamilton, Jr., *Advan. Fluorine Chem.* **3**, 117 (1962).
14. "Engineered refrigeration systems (industrial and commercial)," in *ASHRAE Handbook* (American Society of Heating, Refrigerating, and Air-Conditioning Engineers, New York, 1973), p. 241.

I. C. T. Nisbit and A. F. Sarofim, *Environ. Health Perspect.* **1**, 21 (1972).

16. J. K. Backus and P. G. Gemeinhardt, in *Plastic Foams,* K. C. Frisch and J. H. Saunders, Eds. (Dekker, New York, 1973), part 2, p. 459.
17. R. T. Darby and A. M. Kaplan, *Appl. Microbiol.* **16**, 900 (1968).
18. J. Crossland, *Environment (St. Louis)* **16** (No. 6), 16 (1974); A Fritsch, B. Hogan, S. Guhl, *How Aerosol Spray Can Affect Your Health* (Center for Science in the Public Interest, Washington, D.C., 1973).
19. *Chem. Market. Rep.*, "Aerosol production growth throughout the world despite problems" (13 May 1974).
20. R. L. McCarthy, "Fluorocarbons in the environment," paper presented at the American Geophysical Union meeting, San Francisco, Calif., 13 December 1974.
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Angiotensin II Stimulation of Prostaglandin Production in Cultured Human Vascular Endothelium

Abstract. *Immunoreactive material resembling prostaglandin E accumulates in the medium of cultured human umbilical vein endothelial cells. Production is inhibited by indomethacin and stimulated by angiotensin II. Prostaglandin secretion by endothelium may be important in platelet-dependent thrombotic phenomena, and in local control of vascular permeability and tone in vivo.*

Exogenous prostaglandins (PG's) are potent mediators of several cardiovascular phenomena (*1*). In particular, prostaglandin E (PGE) can induce changes in vascular tone and permeability (*2*), and modify the behavior of blood platelets (*3*). Little is known, however, about the specific origins of endogenous PG's or the physiologic factors controlling their biosynthesis within the circulatory system. Recent work in our laboratory (*4*) and by others has led to the culture of homogeneous populations of vascular endothelial cells for biochemical and morphological studies. We now report the secretion of immunoreactive PGE-like material (iPGE) by cultured human endothelium and stimulation of basal levels of production by the vasoactive octapeptide angiotensin II.

Human endothelial cells were obtained, free of contamination by vascular smooth muscle, fibroblasts, and circulating blood elements, by brief collagenase treatment of the luminal surface of term umbilical cord veins (*4*). Cells from each vein were plated in replicate in 12 to 24 Linbro multidish culture wells and were allowed to grow to confluent densities (1 to 2 × 10^5 cells per square centimeter) in medium 199 supplemented with fetal bovine serum (20 percent) at 37°C under a humidified atmosphere consisting of 5 percent CO_2 in air. Primary cultures obtained in this manner form uniform epithelioid monolayers that exhibit differentiated ultrastructural characteristics of vascular endothelium. All experiments were performed on 5- to 10-day-old confluent cultures.

The concentration of PGE-like material was determined on frozen samples of culture medium or on samples of sonicated cells by a specific radioimmunoassay (*5*). After acidification to *p*H 3.5 and extraction with ethyl acetate, prostaglandin E was separated by silicic acid chromatography and converted to prostaglandin B by treatment with 0.1*N* methanolic potassium hydroxide. Radioimmunoassay was performed with sheep antiserum to PGA_1. At a final dilution of 1 : 75,000 it bound $[^3H]$PGB, and gave a standard curve ranging from 0.08 to 2.0 ng of PGB_2. Fifty percent inhibition of binding for PGB_2, PGB_1, PGE_2, PGE_1, and $PGF_{2\alpha}$ occurred with 0.5, 0.09, 12.0, 5.5, and >100 ng, respectively. Recoveries of known amounts of PGE_2, ranging from 0.8 to 5.6 ng, added to plasma and handled in this manner were 104 ± 19.8 percent (mean ± 1 S.D.), with a mean absolute error of 0.22 ng over the entire range. This assay procedure measures both PGE_1 and PGE_2, which we refer to as iPGE.

Culture medium incubated with endothelial cells for 24 hours contained 13.6 ± 1.5 ng of iPGE per milliliter (mean ± S.E.M.; six cultures), while washed, rapidly frozen cells from these cultures that were sonicated and suspended in phosphate-buffered saline (in a volume equal to that of the culture medium) yielded 1.35 ± 0.11 ng of iPGE per milliliter. Fresh culture medium and medium incubated in the absence of cells contained less than 0.2 ng of iPGE per milliliter.

To establish that the extracellular accumulation of iPGE reflected new synthesis, rather than release of stored material, indomethacin, a potent, selective inhibitor of prostaglandin biosynthesis (*6*), was added to the culture medium at the start of the 24-hour incubation. A dose-related reduction in iPGE production resulted (Fig. 1). Fifty percent inhibition occurred at 6 × 10^{-9} g per milliliter of indomethacin. Cytotoxic changes were not observed by phase-contrast microscopy in cultures exposed to indomethacin at any of the concentrations tested. These data indicate that the appearance of iPGE in the medium was the result of de novo synthesis by the cultured endothelial cells.

Robertson and Khairallah have demonstrated endothelial cell contraction and transient permeability changes in the walls