

Table 37.1 Formulae and physicochemical properties of chlorofluorocarbons (CFCs) and hydrofluoroalkanes (HFAs) used in pMDI formulations

Number	Formula	Boiling point (°C)	Vapour pressure (kPa at 20°C)	Density (g/mL at 20°C)
11	CCl <sub>3</sub> F	23.7	89 (0.89 bar)	1.49
12	CCl <sub>2</sub> F <sub>2</sub>	-29.8	568 (5.68 bar)	1.33
114	C <sub>2</sub> Cl <sub>2</sub> F <sub>4</sub>	3.6	183 (1.83 bar)	1.47
134a	C <sub>2</sub> F <sub>4</sub> H <sub>2</sub>	-26.5	660 (6.6 bar)	1.23
227	C <sub>3</sub> F <sub>7</sub> H	-17.3	398 (3.98 bar)	1.41

CFCs and HFAs are numbered using a universal system. The first digit is the number of carbon atoms minus 1 (omitted if zero), the second is the number of hydrogen atoms plus 1, and the third is the number of fluorine atoms. Chlorine fills any remaining valencies, given the total number of atoms required to saturate the compound. If asymmetry is possible, this is designated by a letter. The symmetrical isomer is assigned the number described above; of the asymmetrical isomers, that designated the letter *a* is the most symmetrical, *b* the next most symmetrical, and so on. The CFCs are perfectly miscible with each other and suitable blends give a useful intermediate vapour pressure, usually about 450 kPa. The vapour pressure of the mixture of propellants is given by Raoult's Law, i.e. the vapour pressure of a mixed system is equal to the sum of the mole fraction of each component multiplied by its vapour pressure:

$$P = p_a + p_b \quad (37.5)$$

where  $P$  is the total vapour pressure of the system and  $p_a$  and  $p_b$  are the partial vapour pressures of the components, *a* and *b*:

$$p_a = x_a p_a^0 \quad (37.6)$$

$$p_b = x_b p_b^0 \quad (37.7)$$

where  $x_a$  and  $x_b$  are the mole fractions and  $p_a^0$  and  $p_b^0$  are the partial vapour pressures of components *a* and *b*, respectively.

The reaction of CFCs with the ozone in the earth's stratosphere, which absorbs ultraviolet radiation at 300 nm, and their contribution to global warming are major environmental concerns. CFCs pass to the stratosphere, where in the presence of UV they liberate chlorine, which reacts with ozone. The depletion of stratospheric ozone results in increased exposure to the UV-B part of the UV spectrum, resulting in a number of adverse effects, in particular an increased incidence of skin cancer. The Montreal Protocol of 1987 was a global ban on the production of the five worst ozone-depleting CFCs by the year 2000. This was amended in 1992, so that production of CFCs in developed countries was phased out by January 1996. In the European Union and USA, all ozone-depleting CFCs were banned by the end of 1995, except for certain limited uses. The inclusion of CFCs in pMDIs currently has an 'essential use exemption', which will remain until medically acceptable non-ozone depleting alternatives to the remaining CFC-based pMDIs are available. This exemption is reviewed regularly and very few CFC-based pMDIs are now marketed. In household and cosmetic aerosols, CFCs have been replaced by hydrocarbons, such as propane and butane. Alternatively, non-toxic compressed gases such as nitrogen dioxide, nitrogen and carbon dioxide may be used, for instance in food products. However, compressed gases do not maintain a constant pressure within the canister throughout its use, as the internal pressure is inversely proportionate to the head volume, and so product performance changes with usage. For reasons of toxicity and inflammability, hydrocarbons are not considered appropriate alternatives to CFCs for inhalation products and so non-ozone depleting alternatives to CFCs have been developed.