Number 5

VOLATILE SUBSTANCE ABUSE

Practical Guidelines for Analytical Investigation of Suspected Cases and Interpretation of Results

R.J. Flanagan, P.J. Streete, J.D. Ramsey

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PREFACE

Most societies utilise products which contain substantial amounts of volatile organic solvents. Common household products which often contain organic solvents include cleaning and polishing fluids, contact adhesives, and paint and nail-polish removers. Organic solvents and other volatile compounds are also used extensively in industry and in the laboratory. Long-term exposure to solvent vapour as a result of industrial or domestic use of these substances is thus a common occurrence.

One aspect of human exposure to the vapour of volatile substances of particular concern is deliberate self-administration by inhalation in order to achieve intoxication. Many volatile substances, if inhaled in sufficient quantity, produce effects similar to those of central nervous system depressants such as ethanol and barbiturates. Their abuse potential is directly related to their ability to produce intoxication and repeated abuse may result in psychological dependence or other harmful health effects.

In many developed and developing countries volatile substance abuse is a significant public health problem. Originally confined to the abuse of gases such as nitrous oxide, "glue sniffing" has now been reported from practically every region of the world. The prevalence and public health effects of volatile substance abuse are often underestimated and local knowledge of the phenomenon is often inadequate. The situation is further complicated by the range of organic solvents available in many common products. Volatile substances which can be abused by inhalation are not subject to the international control measures which apply to many narcotics, for example, although bulk supplies of acetone, diethyl ether and toluene have been controlled since 1988 with the aim of preventing their use in the synthesis or purification of illicit drugs.

Volatile substance abuse is closely linked to the domain of illicit drug abuse in many ways. Since they are cheap and widely available, volatile substances are the "drugs" of choice for adolescents in many countries, with lifetime prevalence rates of 1-10 per cent in this age group. The large number and varied physical and chemical characteristics of abusable volatile substances make this an extremely difficult area for health and law enforcement agencies. Precise identification of the substances abused may be important in a variety of situations. It is, however, a task which requires sound knowledge and the appropriate laboratory instrumentation and support.

Recognizing the need for a more rigorous knowledge base in this area, various expert consultations have suggested that assistance in the form of technical guidelines and procedures as well as basic technology should be made available to drug control services in countries with limited resources. One area where national laboratories need urgent advice, even though the materials/substances involved are not all under international control, is the compilation of a practical analytical guide for the analysis of organic solvents contained in glues and paints. The present paper is intended to provide such assistance. The United Nations International Drug Control Programme (UNDCP), in fulfilment of its normative and technical functions, commissioned the authors, as experts in the field, to prepare the paper.

The authors thank the Royal Society of Chemistry for permission to reproduce data and illustrations (Section 4 and Appendix 1) first published in *The Analyst* (1992; 117: 1111-1127).

1. INTRODUCTION

If anaesthesia is excluded, acute poisoning with volatile substances usually follows the deliberate inhalation of vapour in order to become intoxicated. This phenomenon is known as "glue sniffing", inhalant abuse, solvent abuse or volatile substance abuse (VSA). Those who accidentally or deliberately ingest, or more rarely inject, solvents or solvent-containing products and the victims of industrial and domestic accidents may also be poisoned by such compounds. Vapour-phase poisoning with relatively toxic solvents, for example, acetonitrile and methanol may also be encountered, often in an occupational setting, although such compounds are not normally abused. Amyl and butyl nitrites, however, are often inhaled deliberately in order to experience their vasodilator properties; the hazards associated with the abuse of the latter compounds have been reviewed (Haverkos and Dougherty 1988).

Volatile substance abuse has clearly much in common with other forms of substance abuse on the one hand and with ethanol (alcohol) use on the other. Solvents or other abusable volatile compounds can produce dose-related central nervous system (CNS) effects similar to those of other sedatives. Small doses can lead to euphoria and other behavioural disturbances, and may also induce more profound effects such as delusions and hallucinations. Psychological dependence is common in chronic users, although withdrawal symptoms are rarely severe (Jacobs and Fehr 1987). Higher doses may produce life-threatening effects such as convulsions and coma. Death may ensue indirectly, for example, after inhalation of vomit or from direct cardio- or CNS-toxicity (Shepherd 1989). Chronic high-dose usage of toluene and of chlorinated solvents such as 1,1,1-trichloroethane can produce severe organ damage, especially to the liver, kidneys, and brain (Flanagan et al. 1990).

There are, however, significant differences between volatile substance abuse and some other forms of substance abuse. In most subjects volatile substance abuse is a transient phenomenon, i.e. long-term addiction or habituation is rare. However, progression to alcohol or illicit drug use has been documented (D'Amanda et al. 1977; Altenkirch and Kindermann 1986). A further factor is that young children are involved with volatile substance abuse to an extent that is unusual with other forms of substance abuse.

In contrast to the situation with respect to illicit drugs, in most countries there is little or no criminal involvement in supply. Although bulk supplies of acetone, diethyl ether and toluene have been under international control since 1988 with the aim of preventing their use in the synthesis or purification of illicit drugs, this is of no relevance as regards volatile substance abuse. Indeed, the widespread availability of products that can be abused by inhalation, all of which are safe when used correctly and for their intended purpose, means that it is virtually impossible to control volatile substance abuse by controlling the availability of the products abused.

There is a clear need for regulatory authorities to be aware of the problems posed by volatile substance abuse and of prevention strategies. The aim of the present paper is to provide information to facilitate the analysis of biological and other relevant samples to help diagnose acute poisoning with organic solvents and some other volatile compounds. In contrast to the situation with illicit drugs and pharmaceuticals, the chemical analysis of abuseable volatile substances is normally only relevant in the context of a particular poisoning or suspected poisoning incident.

Instances where an analytical toxicology laboratory may be asked to perform analyses for solvents and other volatiles in biological samples include the following: (a) clinical diagnosis of acute poisoning; (b) confirmation of a suspicion of chronic volatile substance abuse that is denied by the patient and/or a caretaker; (c) investigation of deaths where poisoning by volatile compounds is a possibility; (d) investigation of rape, other assault or other offences such as driving a motor vehicle or operating machinery while under the influence of drugs or other agents; (e) investigation of incidents such as rape or other

assault in which volatile substances may have been administered to the victim, (f) investigation of fire or explosion where volatile substance abuse might have been a contributory factor; and (g) assessment of occupational or environmental exposure to solvent vapour. Other techniques such as ambient air monitoring or the measurement of urinary metabolite excretion may, however, be more appropriate in this latter context.

The laboratory analysis of volatile substances presents particular problems. First, many of the compounds abused occur commonly in laboratories. Thus, special precautions against contamination of the sample and interference in the analysis are required. Secondly, sample collection, storage and transport must be controlled as far as practicable in order to minimize loss of analyte. Thirdly, blood (or other tissues in fatalities) is the sample of choice because many compounds of interest are excreted unchanged via the lungs; polar metabolites from only a few compounds are excreted in urine. Fourthly, quantitative work can be futile with very volatile compounds such as butane unless the sample is taken quickly and loss of analyte from the sample prior to the analysis is prevented. Finally, the interpretation of results can be difficult, especially if legitimate exposure to solvent vapour is a possibility. Thus, it is necessary to take a broad approach to the problems posed by volatile substance abuse and other situations where poisoning by volatiles may be encountered.

2. VOLATILE SUBSTANCE ABUSE

Compounds such as diethyl ether, chloroform and nitrous oxide have been deliberately inhaled for recreational purposes since the early 1800s. Abuse of substances such as trichloroethylene in Germany and of products such as petrol (gasoline) in the United States of America was recorded as they became widely available during this century. Volatile substance abuse has now been reported from most parts of the world. Solvents from adhesives, notably toluene, typewriter correcting fluids and thinners (until recently often 1,1,1-trichloroethane), hydrocarbons such as those found in cigarette lighter refills [forms of liquified petroleum gas (LPG), largely butane], aerosol propellants, halocarbon fire extinguishers and gases such as nitrous oxide are among the compounds or products which may be abused in this way (see Tables 1 and 2). Petrol (gasoline) is often abused, especially in developing communities. Acetone (propanone) too is often said to be abuseable in this way, although this compound is relatively water soluble and might not be expected to be a good intoxicant. Neither petroleum distillates such as white spirit and paraffin (kerosene), nor alcohols such as ethanol, 2-propanol, 2-methoxyethanol (methyl cellosolve) and ethylene glycol, are sufficiently volatile to be abused by inhalation.

Many reviews, monographs, proceedings of meetings and consultation documents on volatile substance abuse have been published in recent years (Crider and Rouse 1988; Flanagan and Ives 1994; Flanagan et al. 1989; Flanagan et al. 1990; Kozel et al. 1995; Sharp et al. 1992; World Health Organization 1993). Many of the substances which have been abused by inhalation remain in widespread use. Since the mid-1970s, however, concern as to the consequences of the release of massive quantities of volatile organochlorine and organobromine compounds such as chlorofluorocarbon (CFC) refrigerants and aerosol propellants into the atmosphere has led to the planned, phased withdrawal of many chlorinated solvents and of CFCs as a result of the Montreal Protocol (see Figure I). Deodorized liquefied petroleum gas and dimethyl ether, which is often used as a non-flammable azeotrope with chlorodifluoromethane, have already largely replaced fully halogenated CFCs as aerosol propellants in many countries. Polyfluorinated compounds such as 1,1,1,2-tetrafluoroethane have been developed for use as refrigerants. Such changes alone are unlikely to have a major impact on volatile substance abuse since the replacement compounds have just the same abuse potential as CFCs.

The abuse of volatile substances involves deep breathing via the nose and/or the mouth. Re-breathing exhaled air may add to the effect if a plastic or paper bag is used to contain the abused substance. It is virtually impossible to assess dosage. It seems likely that the intensity of abuse (and the consequent exclusion of oxygen) is a risk factor in sudden deaths. The occurrence of chronic toxicity is, however, related to the compounds abused, also to the intensity and duration of the abuse.

Table 1. Some volatile substances which may be abused by inhalation

1. Hydrocarbons: Aliphatic	Acetylene
	Butane[1]
	Hexane[2]
	Isobutane (2-methylpropane)[1]
	Propane[1]
Aromatic	Toluene (toluol, methylbenzene, phenylmethane)
	Xylene (xylol, dimethylbenzene)[3]
Mixed	Petrol (gasoline)[4]
	Petroleum ethers[5]
Halogenated	Bromochlorodifluoromethane (BCF, FC 12B1)
	Carbon tetrachloride (tetrachloromethane)
	Chlorodifluoromethane (FC 22, Freon 22)
	Chloroform (trichloromethane)
	Dichlorodifluoromethane (FC 12, Freon 12)
	Dichloromethane (methylene chloride)
	1,2-Dichloropropane (propylene dichloride)
	Ethyl chloride (monochloroethane)
	Fluorotrichloromethane (FC 11, Freon 11)
	Halothane (2-bromo-2-chloro-1,1,1-trifluoroethane)
	Tetrachloroethylene (perchloroethylene)
	1,1,1-Trichloroethane (methylchloroform, Genklene)
	1,1,2-Trichlorotrifluoroethane (FC 113)
	Trichloroethylene (“trike”, Trilene)
2. Oxygenated compounds	Butanone (2-butanone, methyl ethyl ketone, MEK)
	Butyl nitrite[6]
	Enflurane (2-chloro-1,1,2-trifluoroethyl difluoromethyl ether)
	Ethyl acetate
	Diethyl ether (ethoxyethane)
	Dimethyl ether (DME, methoxymethane)
	Isobutyl nitrite (“butyl nitrite”)[6]
	Isoflurane (1-chloro-2,2,2-trifluoroethyl difluoromethyl ether)
	Isopentyl nitrite (3-methylbutyl nitrite, isoamyl nitrite, “amyl nitrite”)[6,7]
	Methyl acetate
	Methyl isobutyl ketone (MIBK, isopropyl acetone)
	Methyl *tert.*-butyl ether (MTBE)
	Nitrous oxide (dinitrogen monoxide, “laughing gas”)
	Sevoflurane (fluoromethyl 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether)

1 Components of liquified petroleum gas (LPG) - gas intended for use as a fuel may contain 30-40 per cent unsaturates (propene, butenes)
2 Commercial "hexane" mixture of hexane and heptane with small amounts of higher aliphatic hydrocarbons
3 Mainly *meta*-xylene (1,3-dimethylbenzene)
4 Mixture of aliphatic and aromatic hydrocarbons with boiling range 40-200 °C
5 Mixtures of pentanes, hexanes, etc. with specified boiling ranges (for example 40-60 °C)
6 Abused primarily for its vasodilator properties
7 Commercial “amyl nitrite” mainly isopentyl nitrite but other nitrites also present

Table 2. **Some products which may be abused by inhalation** (See Table 1 for full chemical names of some compounds. Halocarbon shorthand nomenclature is summarized in Section 3.3)

Product		Major volatile components
Adhesives:	Balsa wood cement	Ethyl acetate
	Contact adhesives	Butanone, hexane, toluene and esters
	Cycle tyre repair cement	Toluene and xylenes
	Polyvinylchloride (PVC) cement	Acetone, butanone, cyclohexanone, trichloroethylene
	Woodworking adhesives	Xylenes
Aerosols:	Air freshener	Butane, dimethyl ether and/or fluorocarbons
	Deodorants, antiperspirants	Butane, dimethyl ether and/or fluorocarbons
	Fly spray	Butane, dimethyl ether and/or fluorocarbons
	Hair lacquer	Butane, dimethyl ether and/or fluorocarbons
	Paint	Butane, dimethyl ether and/or fluorocarbons and esters
Inhalational anaesthetics		Nitrous oxide, diethyl ether, enflurane, halothane, isoflurane
Topical analgesics		FC 11, FC 12, ethyl chloride
Cigarette lighter refills		Butane, isobutane, propane
Commercial dry cleaning and degreasing agents		Dichloromethane, FC 113, methanol, 1,1,1-trichloroethane, tetrachloroethylene, toluene, trichloroethylene (now rarely carbon tetrachloride, 1,2-dichloropropane)
Dust removers (“air brushes”)		Dimethyl ether, FC 22
Domestic spot removers and dry cleaners		Dichloromethane, 1,1,1-trichloroethane, tetrachloroethylene, trichloroethylene
Fire extinguishers		Bromochlorodifluoromethane, FC 11, FC 12
Fuel gases	“Butane”	Butane, butenes, isobutane, propane, propenes
	“Propane”	Butane, butenes, isobutane, propane, propenes
Nail varnish/nail varnish remover		Acetone and esters
Paints/paint thinners		Acetone, butanone, esters, hexane, toluene, trichloroethylene, xylenes

Table 2. Some products which may be abused by inhalation (continued)

Product	Major volatile components
Paint stripper	Dichloromethane, methanol, toluene
"Room odorizer"	Isobutyl nitrite
Surgical plaster/chewing gum remover	1,1,1-Trichloroethane, trichloroethylene
Typewriter correction fluids/thinners	1,1,1-Trichloroethane
Whipped cream dispensers	Nitrous oxide

Montreal Protocol of 1987, as revised in November 1992

The Montreal Protocol is an international agreement on the manufacture, import and export of the volatile chlorinated and brominated compounds listed below. Originally it was planned to gradually reduce the amount of these controlled substances used to zero by the year 2000 (2005 in the case of 1,1,1-trichloroethane) with a 10-year extension granted for less developed countries. Manufacture of some controlled substances was still to be permitted for safety-critical and other "essential" (but undefined) applications (bromofluorocarbon fire extinguishers, for example, may be exempted) or for captive use as chemical intermediates. Not all states have signed the Protocol. A revised timetable for cutbacks from 1986 production (see below) was adopted at Copenhagen in November 1992. The European Community has advocated tighter controls, including the phase out of chlorofluorocarbons containing at least 1 hydrogen atom (HCFCs) by 2014.

Controlled substances (N.B. Details of fluorocarbon nomenclature are given in Section 3.3).

a. Chlorofluorocarbons (denoted as CFCs in the Protocol) - FCs 11, 12, 113, 114, 115 and all other fully halogenated chlorofluorocarbons with 1, 2 or 3 carbon atoms, including all isomers: 75 per cent cut in production by 1.1.1994; complete phaseout by 1.1.1996.

b. Bromofluorocarbons (denoted halons in the protocol) - FCs 12B1, 13B1 and 114B2, including all isomers: complete phaseout by 1.1.1994.

c. Carbon tetrachloride: 85 per cent cut in production by 1.1.1995; complete phase-out by 1.1.1996.

d. 1,1,1-Trichloroethane: 50 per cent cut in production by 1.1.1994; complete phase-out on 1.1.1996.

e. Chlorofluorocarbons with 1, 2 or 3 carbon atoms containing at least one hydrogen atom (HCFCs, e.g. FC 21, FC 22, etc.): no increase in production from 1996; complete phase out by 2030.

f. Bromomethane: cut in production (to 1991 levels) by 1995; further cuts likely in future.

Figure I

2.1. Modes of abuse of volatile substances

The physical form of a product often determines the way it is abused. Contact adhesives are usually poured into plastic bags such as empty potato crisp packets or paper bags. The top is then gathered together and placed over the mouth and the vapour is inhaled. It is said that cans of glue may be heated to increase the yield of vapour. Instances where an abuser has used litres of adhesive per day have been reported. The vapour of petrol and other relatively volatile solvents may be inhaled directly from the container, or after pouring onto fabric (a coat sleeve or handkerchief) or into plastic bottles such as empty detergent or bleach containers. Gasoline "sniffing" is associated with a risk of fire and explosion, and perhaps lead poisoning. Aerosol propellants or halon-containing fire extinguishers may be inhaled directly, or after spraying into plastic bags or release under bedclothes.

Aerosols are usually liquid or solid suspensions supplied in cans containing a liquified propellant gas; at room temperature one volume of liquid propellant may generate 200 to 300 volumes of vapour. The normal use of aerosols is largely irrelevant, although products containing a high proportion of propellant, such as topical analgesic sprays (100 per cent propellant), deodorants and fly sprays rather than those with little (shaving foam, for example), are preferred. If some constituents are not respirable, for example aluminium chlorhydrate (an active ingredient in antiperspirants), then the product may be first bubbled through water, filtered through a cloth held firmly over the mouth, or sprayed into a plastic bag and the aerosol allowed to settle. Alternatively, the container may be inverted to allow direct access to the propellant via the dip tube. Abuse of nitrous oxide from cylinders designed for use, for example, with whipped cream dispensers has also been described.

Domestic piped fuel ("natural") gas is rarely abused, primarily because the principal component, methane, does not induce desirable pharmacological effects. However, the liquified petroleum gas used in cigarette lighter refills, small blow torches and camping gas stoves usually consists of butane, isobutane and propane in various proportions - products other than cigarette lighter refills may, however, contain up to 40 per cent of unsaturated hydrocarbons (propene and the butenes). Such products are available in small, inexpensive packs and are very attractive to misusers. Use of 5-10 (250 ml) cans per day has been reported. Gas from large cylinders (often primarily propane) is also sometimes abused. Such cylinders usually need a valve with which to obtain the gas. Cigarette lighter refills may be misused by simply clenching the nozzle between the teeth and pressing to release the gas. If the can is tilted, however, a jet of fluid cooled to at least -60 ^{o}C by expansion may be inhaled directly. There is an obvious risk of fire and explosion associated with the abuse of cigarette lighter refills.

2.2. Prevalence of volatile substance abuse

The prevalence of previous or current volatile substance abuse was 5.9 per cent in adolescent school children in 16 schools in the United Kingdom, 1984-1986 (Chadwick et al. 1989). The proportion of abusers ranged from 0.5 to 9.6 per cent surveyed with no marked sex difference. However, if subjects who had never been "intoxicated" were excluded, the mean prevalence fell to 3.6 per cent. Similarly, in a 1985 survey of 4,766 pupils in the United Kingdom aged 11 to 19 years, 6.1 per cent had tried volatile substance abuse and a further 0.7 per cent were current abusers; three pupils (0.1 per cent) "sniffed" every day (Cooke et al. 1988). Of those who had experimented with volatile substance abuse, 58 per cent had already "sniffed" by age 13 years. More recent studies have reported higher prevalence rates (3 per cent of 14-16 year olds in a recent study, with a further 5 per cent misusing solvents in conjunction with illegal drugs). Thus, it seems that 3.5 to 10 per cent of young people in the United Kingdom have at least experimented with volatile substance abuse and current users comprise some 0.5 to 1 per cent of the secondary school population.

Similar, if not slightly higher, figures for the prevalence of volatile substance abuse have been reported from other countries within the last 10 years. Some 10 per cent of young people aged 15 to 20 years in Oslo, Norway, had "sniffed" at some stage (Lavik 1987). An epidemiological study carried out in three secondary schools in Yugoslavia showed that among 2254 pupils, aged 14-18 years, 15.2 per cent of the boys and 11 per cent of the girls were sniffers (Grubisic-Greblo et al. 1989). In the United States of America, it has been estimated that 7 to 12 per cent of high school pupils have "sniffed" at least once and that about 4 per cent "sniff" regularly (Sharp and Korman 1981). Similar findings were reported in a study of Navajo adolescents in the United States of America (Coulehan et al. 1983). Of 1836 students aged 9 to 18 years from a low socio-economic background in Sao Paulo, Brazil, in 1988 some 24 per cent had abused volatile substances at some stage; 4.9 per cent had "sniffed" within the previous month (Carlini-Cotrim and Carlini 1988). The substances most commonly abused were "lança-perfume" (a mixture of chloroform and diethyl ether) (36 per cent), acetone (34 per cent), petrol (32 per cent), finger-nail polish (31 per cent) and glue (25 per cent). In Singapore, while not a criminal offence, volatile substance abuse warrants police intervention - arrests of inhalant abusers (mostly aged 15-19 years) increased from 24 in 1980 to 763 in 1984 (Teck-Hong 1986).

Volatile substance abuse is clearly a significant problem in many countries (World Health Organization 1993), though it is not usually considered to be illegal. Several factors contribute to its continuing popularity. The products abused are cheap and readily available. Furthermore, the containers, for example those of typewriter correction fluid and thinner, are often conveniently sized and are either easily concealed or their possession can appear legitimate. Volatile substance abuse is often a group activity and peer-group influence may be a factor in encouraging the persistence of the practice. It has been suggested that toluene users are more likely to "sniff" in a group setting, possibly because of the relatively long duration of toluene intoxication. In general, however, the onset of effects and recovery are relatively rapid, a distinct advantage over alcohol because a child who "sniffs" after school can still return home sober. This is especially true of the abuse of butane and other very volatile compounds.

2.3. Clinical features of volatile substance abuse

In general, the acute central nervous system depressant and cardiotoxic effects of volatile substances are similar, being related more to their physical properties than to their chemical structure. The occurrence of toxicity such as peripheral neuropathy and hepatorenal damage, however, often results from metabolism and can differ markedly between compounds with ostensibly similar structures. Volatile substance abuse is characterised by a rapid onset of intoxication and a relatively rapid recovery; a "high" can be maintained for several hours by repeated "sniffing". As with the ingestion of ethanol, euphoria, disinhibition and a feeling of invulnerability may occur. Higher doses often lead to less pleasant and more dangerous effects. Changes in perception may precede bizarre and frightening hallucinations while tinnitus, ataxia, agitation and confusion are often reported; dangerous delusions such as those of being able to fly or swim may also occur. Nausea and vomiting with the risk of aspiration can occur at any stage. Flushing, coughing, sneezing and increased salivation are further characteristic features. Coma, depressed respiration and even convulsions may ensue in severe cases (Meredith et al. 1989). Methanol poisoning arising from the deliberate inhalation of a dichloromethane/methanol/toluene mixture by a 17-year-old male has also been described (McCormick et al. 1990).

With volatile substance abusers, opportunities to intervene in the acute phase of intoxication are rare. However, if the opportunity does arise care must be taken not to stress or excite the individual concerned further because of the risk of inducing a cardiac arrhythmia. If possible, exposure should be stopped either by taking away the source of intoxication or removing the individual from the contaminated atmosphere. Gastrointestinal symptoms may predominate after solvent ingestion, but the later features of toxicity are similar to those following inhalation of vapour.

Chronic sequelae of volatile substance abuse include recurrent epistaxis, halitosis, oral and nasal ulceration, conjunctivitis, chronic rhinitis and increased bronchial expectoration. Anorexia, thirst, weight loss and fatigue may also occur. Loss of concentration, depression, irritability, hostility and paranoia are further reported complications. In addition, neuropsychological impairment is often present in volatile substance abusers with well-defined neurological abnormalities. Studies have also found that abusers without reported neurological abnormalities obtain lower psychometric test scores than non-abusers, but this may not be caused by volatile substance abuse (Chadwick and Anderson 1989; Chadwick et al. 1989).

Peripheral neuropathy, cerebellar dysfunction, chronic encephalopathy and dementia have been described after chronic volatile substance abuse (Flanagan et al. 1990). Schizophrenia has been associated with petrol abuse (Daniels and Latchman 1984). Chronic abuse of toluene and of 1,1,1-trichloroethane and trichloroethylene have both been associated with permanent organ damage, especially to the kidney, liver and heart. There are many other reports of chronic toxicity following toluene abuse. Lead poisoning from alkyl leads used as "antiknock" agents has been reported as a complication of petrol (gasoline) "sniffing".

2.4. Sudden death from "sniffing"

The major risk associated with volatile substance abuse is that of sudden death. Bass (1970) reported 110 such deaths in the United States of America from the abuse of aerosol propellants and chlorinated solvents during the 1960s. Further series of fatalities have been noted, again from the United States of America (Garriott and Petty 1980) and from Scandinavia (Kringsholm 1980). In the United Kingdom, sudden deaths from volatile substance abuse have been monitored systematically since 1983 (Anderson et al. 1985; Taylor et al. 1995) and have increased from 2 in 1970 to 151 in 1990; there were 73 such deaths in 1993 (see Figure II).

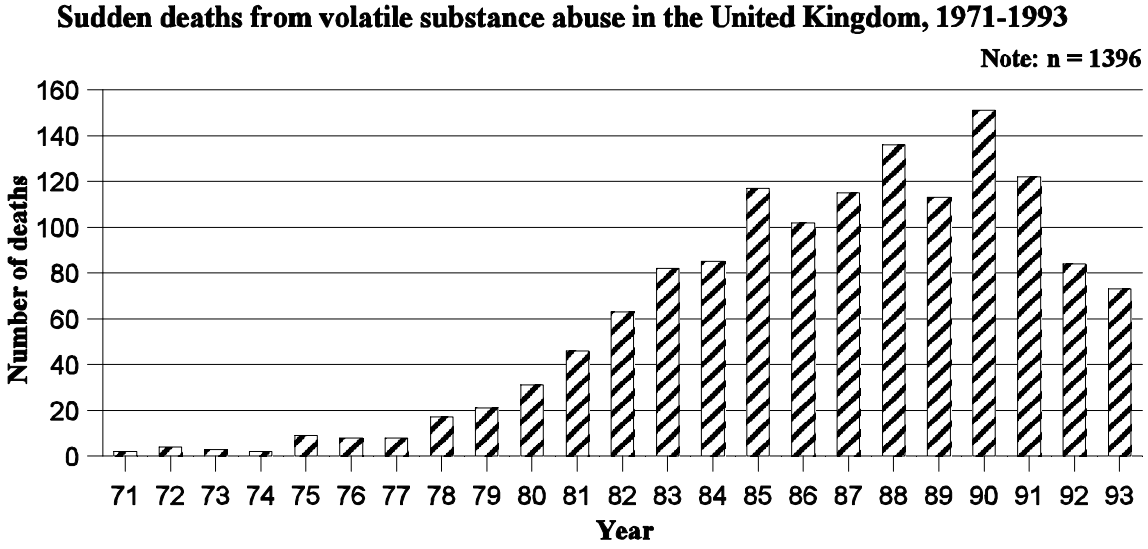


Figure II

It is possible that volatile substance abuse-related deaths were under-reported in the United Kingdom in the 1970s, but it is unlikely that the increase in such deaths recorded since the early 1980s is simply the result of better reporting. The average annual increase from 1983 to 1991 was 5.4 per cent per year. Nevertheless, volatile substance abuse deaths are relatively rare in the United Kingdom given the numbers of abusers indicated by prevalence studies (Section 2.2). Such deaths occur in all social classes

and in all parts of the country. The age at death has ranged from 9 to 76 years, but most deaths (73 per cent) occur in adolescents aged less than 20 years (see Figure III).

Sudden deaths from volatile substance abuse in the United Kingdom, by age in years, 1971-1993

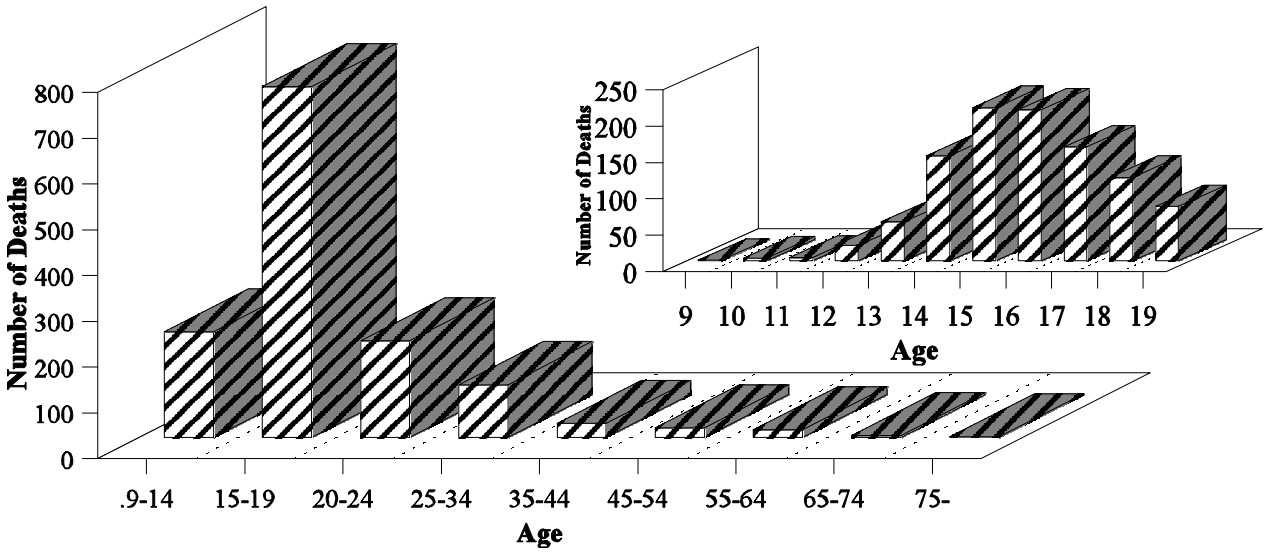


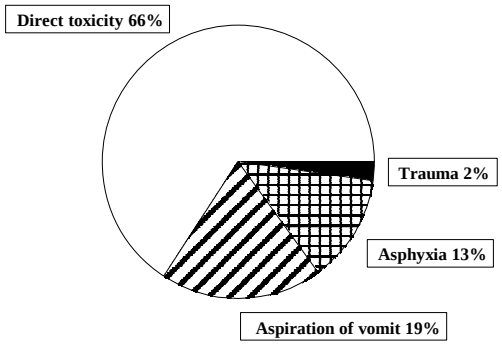
Figure III

In contrast to the sex distribution noted in prevalence studies, most volatile substance abuse-related deaths in the United Kingdom (88 per cent) have occurred in males. In 1993, in 28 (38.3 per cent) of United Kingdom volatile substance abuse-related deaths either death occurred on the first occasion (or on one of the first occasions) of abuse, or there was no evidence of the abuser ever having indulged in volatile substance abuse before (Taylor et al. 1995). The compounds encountered in United Kingdom volatile substance abuse-related deaths are: fuel gases, mainly butane from cigarette lighter refills (37 per cent of cases); aerosol propellants - fluorocarbons and/or butane (20 per cent); solvents from adhesives (18 percent); other solvents, notably 1,1,1-trichloroethane (20 per cent); and fire extinguishers (mainly bromochlorodifluoromethane) (4 per cent).

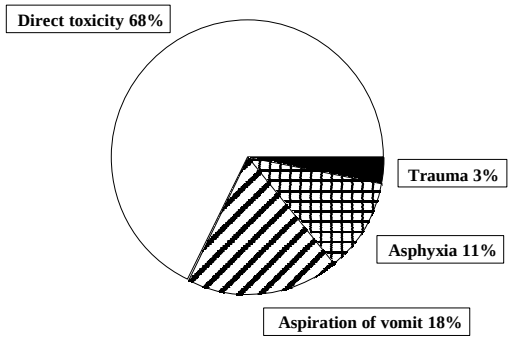
The precise mechanism of sudden death related to volatile substance abuse is seldom clear, but indirect effects such as trauma, aspiration of vomit and asphyxia associated with the use of a plastic bag predominate in deaths associated with solvents from adhesives (see Figure IV). Four possible modes of death which may be related directly to volatile substance abuse have been suggested: anoxia, vagal stimulation leading to bradycardia and cardiac arrest, respiratory depression and cardiac arrhythmia (Shepherd 1989). Of these, cardiac arrhythmia leading to cardiac or cardiorespiratory arrest is presumed to cause most deaths. Sudden alarm, exercise or sexual activity may precipitate an arrhythmia since volatile substance abuse may sensitize the heart to circulating catecholamines; in many deaths related to volatile substance abuse the immediate ante-mortem event is fright and running (Bass 1970).

Mortality from volatile substance abuse in the United Kingdom, by mechanism of death and product abused, 1971-1993

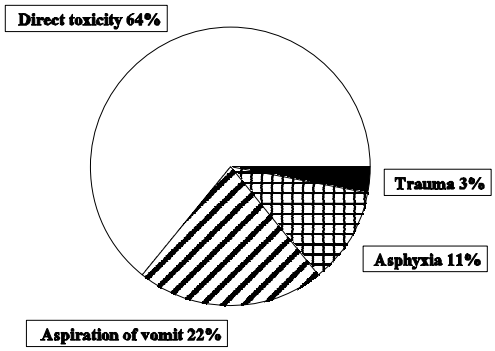
(a) Aerosol propellants



(b) Gas fuels



(c) Chlorinated and other solvents



(d) Solvents from adhesives

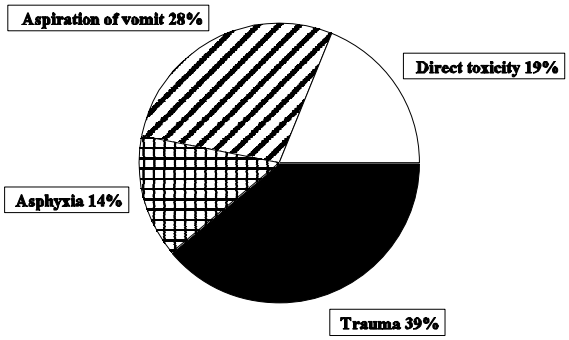


Figure IV

There are no published data on sudden deaths related to volatile substance abuse from other countries comparable to those available in the United Kingdom, although individual cases and small series of deaths are reported spasmodically. Mortality statistics do, however, provide a crude measure of the problem of volatile substance abuse in a particular country and can thus help to assess the efficacy of preventative programmes. Experience in the United Kingdom has shown that deaths related to volatile substance abuse can be easily overlooked if sudden deaths in children and adolescents are not investigated thoroughly. This is because well-meaning friends or parents may remove the paraphernalia of volatile substance abuse (e.g. the product abused or a plastic bag) from the scene prior to an investigation.

2.5. Treatment of abusers and strategies for prevention

Volatile substance abuse is habit-forming and in some cases addictive. It is thought that adolescents tend to abandon volatile substance abuse after a few months or years, although some individuals continue to abuse volatile substances for a long period. In the United Kingdom few abusers of volatile substances appear to progress to heavy alcohol or illicit drug use. Progression to opioid addiction has been reported in New York (D'Amanda et al. 1977) and in Berlin (Altenkirch and Kindermann 1986). The psychosocial aspects of volatile substance abuse, for example the disruption caused to the families and friends of abusers and criminal activities performed while intoxicated (Gjerde et al. 1990), must not be neglected.

Early recognition of individual problems by health professionals and by the abusers themselves is important if treatment is to be successful. Indeed, the best approach seems to be to prevent individuals from becoming abusers in the first place. In this regard, the main effort in the United Kingdom has been in education, not only of school children and their parents and teachers, but also of retailers and health care professionals. Education packs for use in schools and in the community have been produced; some of these aids have been produced together with organizations in other countries. Monographs aimed at health care professionals have also been produced.

In the United Kingdom, legislation has also been enacted. In Scotland, the Solvent Abuse (Scotland) Act of 1983 defines the offence of "recklessly" selling solvents to children. In certain cases children who are thought to be in need of care and protection may be referred to Children's Panels rather than to court. In the period 1983 to 1991, 3487 such referrals were made. In England and Wales, the Intoxicating Substances (Supply) Act of 1985 made it an offence to sell, or to offer for sale, substances to children under the age of 18 years if the vendor knows or has grounds for believing that those substances are likely to be inhaled to achieve intoxication.

Whatever preventive strategies are adopted it is important to at least attempt to monitor their effects. The increase in sudden deaths in the United Kingdom in the late 1980s was mainly due to an increase in deaths from abuse of butane and other very volatile substances (see Figure V). It is possible that this could have been caused by undue emphasis on prevention of "glue sniffing" *per se* while neglecting the dangers of abuse of products such as cigarette lighter refills.

Sudden deaths from volatile substance abuse in the United Kingdom, by type of product abused, 1981-1993

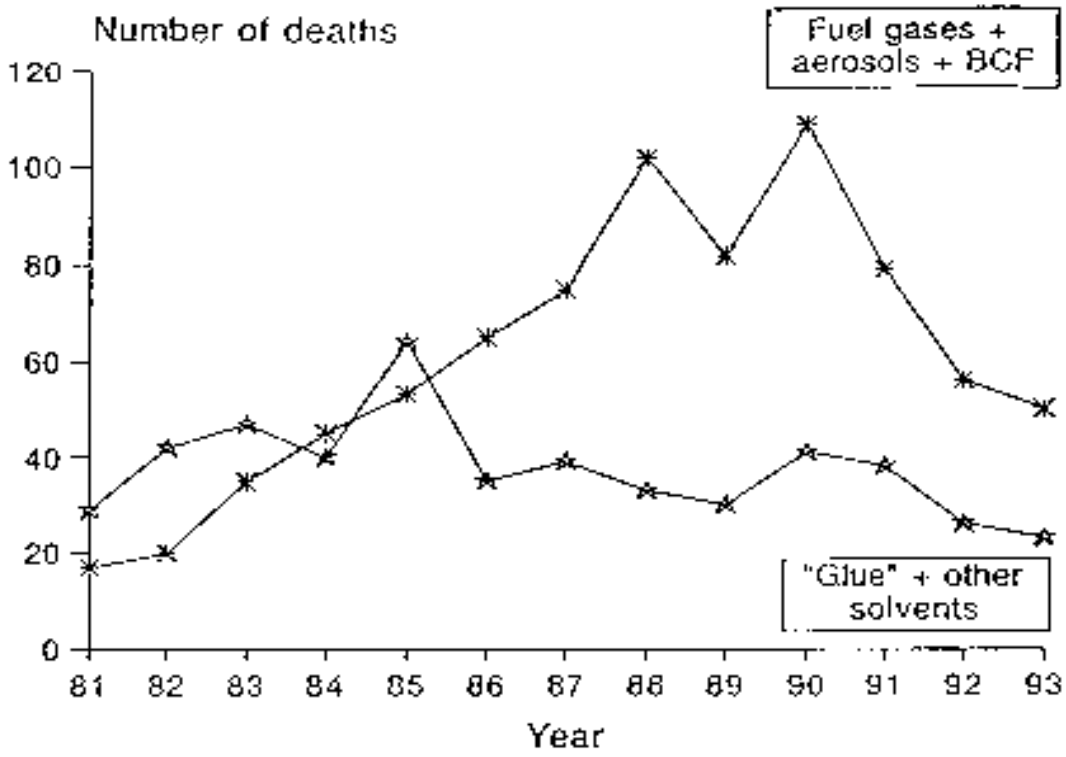


Figure V

3. DIAGNOSIS OF POISONING DUE TO VOLATILE SUBSTANCES

3.1. Clinical and circumstantial evidence

Many of the problems associated with volatile substance abuse may appear similar to the normal problems of adolescence. However, such abuse should be suspected in children and adolescents that display "drunken" behaviour, unexplained listlessness, anorexia and moodiness. Their hair, breath and clothing may smell of solvent, and empty adhesive tubes or other containers, potato crisp bags, cigarette lighter refills, or aerosol spray cans are often found. The smell of solvent on the breath is related to the dose and duration of exposure, and may persist for many hours. The so-called "glue-sniffer's rash" (perioral eczema) is caused by repeated contact with glue poured into a plastic bag. However, in one study only 2 of 300 children who regularly "sniffed" glue were found to exhibit this feature (Sourindhrin and Baird 1984). It is important to consider all circumstantial evidence in cases that are possibly related to volatile substance abuse since suicide or even homicide cannot be excluded simply on the basis of the toxicological examination.

3.2. Role of toxicological analyses

In terms of the analytical procedure, the analysis of biological samples for solvents and other volatiles that may be abused by inhalation has clear parallels with the analysis of such samples for methanol, ethanol and 2-propanol. Headspace gas chromatography provides a viable method for the analysis of volatiles such as solvents in blood and other biological specimens that may be obtained without

using special apparatus such as breath-collection tubes (Ramsey and Flanagan 1982). Direct mass spectrometry of expired air can also detect many compounds several days after exposure. The use of this technique is limited, however, by the need to take breath directly from the patient. Vapour-phase infra-red spectrophotometry may be useful in the analysis of abused products.

Toxicological investigations should be considered mandatory in all deaths thought to be due to volatile substance abuse, and indeed in all deaths which could have been due to poisoning in young people (Shepherd 1989). Such analyses can also be helpful, for example, in cases of unexplained abnormal behaviour, especially in adolescents. Nevertheless, a diagnosis of volatile substance abuse should be based on a combination of circumstantial, clinical and analytical evidence rather than on any one factor alone. The likelihood of detecting exposure to volatile substances by headspace gas chromatography of blood is influenced by the dose and duration of exposure, the time of sampling in relation to the time elapsed after exposure and the precautions taken in the collection and storage of the specimen. The possible loss of analyte from the sample prior to the analysis must always be considered, especially in the case of very volatile analytes such as propane, butane and the halon aerosol propellants.

3.2.1. Sample collection and storage

Most volatile compounds are relatively stable in blood if simple precautions are taken. The container should be glass, preferably with a cap lined with metal foil; greater losses may occur if plastic containers are used. The tube should be as full as possible and should only be opened when required for analysis and then only when cold (4 °C) (Gill et al. 1988). If the sample volume is limited, it is advisable to select the container to match the volume of blood so that there is minimal headspace. An anticoagulant (lithium heparin) should be used. Specimen storage between -5 and 4 °C is recommended and, in the case of esters such as ethyl and methyl acetates, 1 per cent (w/v) sodium fluoride should be added to minimize esterase activity. However, many samples submitted in conditions far from ideal still give useful qualitative results.

Products thought to have been abused should be packed, transported and stored entirely separately from biological specimens to avoid cross-contamination. In a fatality that could be due to volatile substance abuse, analysis of tissues (especially fatty tissues such as brain) may prove useful since high concentrations of volatile compounds may be present even if very little is detectable in blood. Tissues should be stored before analysis in the same way as blood. Analysis of urine is only useful if a significant proportion of the abused compound is metabolised (see Section 3.4.2).

3.3. Nomenclature of abusable compounds

One problem encountered when discussing volatile substances is the multiplicity of chemical and trivial names in common use (see Table 1 and Appendix 1). Straight-chain (normal) alkanes are referred to by name with no suffix (hexane, for example) in the text and tables. In some cases widely used trivial names (chloroform, carbon tetrachloride) have been preferred to systematic names. In the case of mixed ethers and ketones, the convention has been adopted whereby the substituent with the lowest carbon number is cited first, for example methyl tert.-butyl ether, and not in alphabetical order. Compounds used as drugs (halothane, isoflurane) are best referred to by their approved names. The Chemical Abstracts Registry Number (see Appendix 1) provides a unique reference.

With the halons (halocarbons, aliphatic hydrocarbons in which one or more hydrogens are replaced by halogen atoms) much additional confusion is generated by the existence of two separate "shorthand" numbering systems. The simplest system was promulgated by the United States of America Army Corps of Engineers in the late 1950s and uses the word "halon" together with a number denoting (reading from left to right) the numbers of carbon, fluorine, chlorine and bromine atoms in the molecule; terminal zeros

are omitted. The number of hydrogen atoms is calculated by difference. Clearly for anything but very simple molecules this notation gives a "group" classification.

A second fluorocarbon numbering system was devised by the American Society of Refrigeration Engineers (ASRE) for substituted alkane and cycloalkane refrigerants. In this system all fluorocarbons (FCs) have an identifying number, the first digit (reading from right to left) being the number of fluorine atoms in the molecule, the second from the right being the number of hydrogens plus 1, and the third from the right being the number of carbons minus 1 (omitted if zero). The number of chlorine atoms in the molecule is ascertained by difference. In unsaturated compounds the number of double bonds is shown by the fourth number from the right; bromine is indicated by a capital "B" followed (on the right) by a number indicating the number of bromine atoms present; various isomers are indicated by lower case suffixes ("a", "b", etc.) allocated in order of decreasing symmetry; and so on.

Clearly the ASRE fluorocarbon numbering system becomes unwieldy with complex molecules. A further complication is that the numerical values derived in this manner are sometimes used together with the words "propellant" or "refrigerant", or with a variety of trade (brand) names including Arcton (ICI), Freon (Du Pont), Frigen (Hoechst), Genetron (Allied-Signal), Isceon (Rhône-Poulenc), Isotron (Pennsalt), KLEA (ICI) and Ucon (Union Carbide). These trade names are sometimes used with additional numbers not derived using the ASRE system to denote azeotropic mixtures of FCs. To add to the confusion, numbers based on the FC numbering system are sometimes used with the suffixes "C" and/or "H" to denote the presence of chlorine or hydrogen, respectively, in the molecule. It is possible to denote nonfluorinated halons using the ASRE fluorocarbon system but this becomes a bit nonsensical - all (H)(C)FCs are halons, but not all halons are (H)(C)FCs. The best policy is to fully define any abbreviation when it is first used in any publication.

3.4. Pharmacokinetics of volatile substances

The United Kingdom Maximum Exposure Level (MEL) or Occupational Exposure Standard (OES) provide information on the relative toxicities of volatile compounds (see Table 3). Some knowledge of the pharmacokinetics of volatile compounds is important in understanding the rate of the onset, intensity, and duration of intoxication with these substances, as well as the rate of recovery. Such an understanding is also helpful when attempting to interpret the results of toxicological analyses performed on biological samples from poisoned patients.

3.4.1. Absorption, distribution and elimination

Inhaled compounds may rapidly attain high concentrations in vital, well-perfused organs such as the brain and heart, while concentrations in muscle and adipose tissue may be very low. Should death occur, this situation is "frozen", but if exposure continues, the compound will slowly accumulate in less accessible (poorly perfused) tissues, only to be slowly released once exposure ceases. Thus, the plasma concentrations of some compounds may appear to fall monoexponentially, while others may exhibit two (or more) separate phases of decline (half-lives).

Published data on the elimination half-lives of volatile substances are not easily comparable, either because too few samples were taken or the analytical methods used did not have sufficient sensitivity to measure accurately the final half-life. The partition coefficients of a number of compounds between air, blood and various tissues have been measured *in vitro* using animal tissues, and some *in vivo* distribution data have been obtained from post-mortem tissue measurements in human fatalities (see Table 3). These latter data must be used with caution, however, since there are many difficulties inherent in such measurements (sampling variations, analyte stability, external calibration etc.).

3.4.2. Metabolism

Many volatile substances are eliminated unchanged in exhaled air. Others are partly eliminated in exhaled air and metabolized in the liver and elsewhere, the metabolites being largely eliminated in exhaled air or in urine (see Table 4). After ingestion, extensive hepatic metabolism can reduce systemic availability ("first-pass" metabolism). Exogenous compounds may be metabolized in a number of ways, a frequent result being the production of metabolites of greater polarity (water solubility) and thus lower volatility than the parent compound.

As with other exogenous compounds, Phase I reactions (usually oxidation, reduction or hydrolysis) and Phase II reactions (conjugation with glucuronic acid, sulphate, acetate or an amino acid) occur with certain solvents. The rate and extent of metabolism may be affected by many factors such as age, disease, dose and exposure to other drugs or solvents. Co-ingestion of paracetamol, for example, has been reported to increase blood toluene concentrations (Lof et al. 1990). The pharmacological activity and pharmacokinetics of the metabolites often differ from those of the parent compounds.

Although metabolism normally results in detoxification, enhanced toxicity may also result. This is especially true of solvents and other volatile compounds; aspects of the toxicity of, for example, acetonitrile, carbon tetrachloride, chloroform, dichloromethane, hexane, methanol, trichloroethylene and possibly halothane can be attributed to the formation of toxic metabolites (see Table 4). Many other compounds including butane, many fluorocarbons, tetrachloroethylene and 1,1,1-trichloroethane, are largely excreted unchanged in expired air.

Table 3. Physical properties and pharmacokinetic data of some volatile compounds (sources: Baselt and Cravey 1990; Fiserova-Bergerova 1983; Moffat 1986)

Compound	MEL/ OES[1]	Inhaled dose absorbed (per cent)	*Proportion Absorbed Dose* Eliminated unchanged (per cent)	Metabolized (per cent)	Half-life[2] (h)	Partition distribution ratio (deaths)	Brain:blood coefficient (blood:gas) (37 °C)
Acetone	1000	-	-	-	3-5[3]	-	243-300
Benzene	5	46	12	80	9-24	3-6	6-9
Butane	1000[4]	30-45	-	-	-	-	-
Isobutane	1000[4]	-	-	-	-	-	-
Butanone	200	70	99+	0.1	0.5	-	116
Carbon disulphide	10	40	<30	50-90	<1	-	2.4
Carbon tetrachloride	5	-	50?	50?	48	-	1.6
Chlorodifluoromethane	1000	-	-	-	-	1.9	-
Chloroform	10	-	20-70 (8 h)	>30	-	2-4	8
Cyclopropane	-	-	99	0.5	-	1.5-3.6	0.55
Dichlorodi-fluoromethane	1000	35	99	<0.2	-	1.4	0.15
Dichloromethane	200	-	50?	<40	0.7	0.5-1	5-10
Diethyl ether	400	-	>90	-	-	1.1	12
Enflurane	-	90+	>80 (5 d)	2.5	36	-	1.9
Ethyl acetate	400	-	-	-	-	-	-
Fluorotrichloromethane	1000	92	89	<0.2	1.5	2.5	0.87
Halothane	-	90+	60-80 (24 h)	<20	0.5	2-3	2.4
Hexane	20	-	-	-	-	-	-
Methoxyflurane	-	-	19 (10 d)	>44	-	2-3	11
Methyl isobutyl ketone	50	-	-	-	-	-	-
Nitrous oxide	-	-	>99?	-	-	1.1	0.47
Propane	1000[4]	-	-	-	-	-	-
Styrene	100	-	1-2	>95	13	-	32
Tetrachloroethylene	50	60+	>90	1-2	72	9-15	9-19
Toluene	50	53	<20	80	7.5	1-2	8-16
1,1,1-Trichloroethane	350	-	60-80 (1 w)	2	10-12	2	1-3
Trichloroethylene	100	50-65	16	>80	30-38	2	9.0
"Xylene"	100	64	5	>90	20-30	-	42.1

Key
1 United Kingdom Maximum Exposure Limit/Occupational Exposure Standard (8 hours time-weighted average), 1992 (parts per million)
2 Terminal phase elimination half-life
3 Longer after high doses
4 As components of liquified petroleum gas (LPG)

Table 4. Summary of the metabolism of some solvents and other volatile substances

Compound	Principal metabolites (per cent absorbed dose)	Notes
Acetone	2-Propanol (minor) and intermediary metabolites (largely excreted unchanged at higher concentrations)	Endogenous compound produced in large amounts in diabetic or fasting ketoacidosis; also the major metabolite of 2-propanol in man (Kawai et al. 1990).
Acetonitrile	Inorganic cyanide (at least 12 per cent) thence to thiocyanate	Cyanide/thiocyanate may accumulate during chronic exposure.
Benzene	Phenol (51-87 per cent), catechol (6 per cent), hydroquinone (2 per cent), *trans,trans*-muconic acid	Excreted in urine as sulphate and glucuronide conjugates. Urinary phenol excretion has been used to indicate exposure but is variable and subject to interference.
Bromomethane	Inorganic bromide (and others?)	Serum bromide has been used to monitor exposure, although the concentrations associated with toxicity are much lower than when inorganic bromide is given orally.
Butane	2-Butanol, butanone (both <1 per cent?)	-
Butanone	3-Hydroxybutanone (0.1 per cent)	3-Hydroxybutanone excreted in urine. Most of an absorbed dose of butanone excreted unchanged in exhaled air.
Carbon tetrachloride	Chloroform, carbon dioxide, hexachloroethane and others	Trichloromethyl free radical (reactive intermediate) probably responsible for hepatorenal toxicity.
Chloroform	Carbon dioxide (ca. 50 per cent), diglutathionyl dithiocarbonate	Phosgene (reactive intermediate) depletes glutathione and is probably responsible for hepatorenal toxicity.
Cyclohexanone	Cyclohexanol (ca. 50 per cent)	Cyclohexanol excreted in urine largely as glucuronide (Sakata et al. 1989).
Dichloromethane	Carbon monoxide (ca. 50 per cent)	Carbon monoxide half-life 13 hours (breathing air, atmospheric pressure). Blood carboxyhaemoglobin measurement useful indicator of chronic exposure.
Dimethylsulphoxide	Dimethylsulphide (3 per cent), dimethylsulphone (18-22 per cent)	After oral/dermal administration, dimethylsulphide excreted in exhaled air and dimethylsulphone in urine.
Dioxane	Beta-hydroxyethoxyacetic acid (HEAA)	HEAA excreted in urine.
Enflurane	Difluoromethoxydifluoroacetic acid (>2.5 per cent), inorganic fluoride	-
Ethyl acetate	Ethanol, acetic acid	Rapid reaction catalysed by plasma esterases.

Table 4. Summary of the metabolism of some solvents and other volatile substances (continued)

Compound	Principal metabolites (per cent absorbed dose)	Notes
Ethylbenzene	Methylphenylcarbinol (5 per cent), mandelic acid (64 per cent), phenylglyoxylic acid (25 per cent)	Methylphenylcarbinol excreted in urine as conjugate, others as free acids. Mandelic acid excretion has been used to monitor ethylbenzene exposure.
Halothane	Chlorotrifluoroethane, chlorodifluoroethylene, trifluoroacetic acid, inorganic bromide and others	The formation of reactive metabolites may be important in the aetiology of the hepatotoxicity ("halothane hepatitis") which may occur in patients exposed to halothane.
Hexane	2-Hexanol, 2-hexanone, 2,5-hexanedione	2-Hexanol excreted in urine as glucuronide. 2,5-Hexanedione thought to cause neurotoxicity. Methyl butyl ketone also neurotoxic and also metabolised to 2,5-hexanedione.
Isobutane	2-Methyl-2-propanol (<1 per cent?)	-
Isobutyl nitrite	2-Methyl-1-propanol (99 per cent), inorganic nitrite	Parent compound not detectable in blood. Blood methaemoglobin can be used to monitor exposure.
Isopentyl nitrite	3-Methyl-1-butanol (99 per cent), inorganic nitrite	Parent compound not detectable in blood. Blood methaemoglobin can be used to monitor exposure.
Methanol	Formaldehyde (up to 60 per cent), formic acid	Urinary formic acid excretion has been advocated for monitoring methanol exposure.
Propane	2-Propanol, acetone (<1 per cent?)	-
2-Propanol	Acetone (80-90 per cent)	2-Propanol half-life ± 2 hours, acetone half-life ± 22 hours.
Styrene	Mandelic acid (85 per cent) and phenylglyoxylic acid (10 per cent)	Urinary mandelic acid excretion indicates exposure. Ethanol inhibits mandelic acid excretion (Wilson et al. 1983).
Tetrachloroethylene	Trichloroacetic acid (<3 per cent)	Urinary trichloroacetic acid excretion serves only as qualitative index of exposure.
Toluene	Benzoic acid (80 per cent) and *o*-, *m*- and *p*-cresol (1 per cent)	Benzoic acid largely conjugated with glycine giving hippuric acid which is excreted in urine (half-life 2-3 hours). Not ideal index of exposure since there are other (dietary) sources of benzoic acid.
1,1,1-Trichloroethane	2,2,2-Trichloroethanol (2 per cent), trichloroacetic acid (0.5 per cent)	Urinary metabolites serve as qualitative index of exposure only (compare tetrachloroethylene).

Table 4. Summary of the metabolism of some solvents and other volatile substances (continued)

Compound	Principal metabolites (per cent absorbed dose)	Notes
Trichloro-ethylene	2,2,2-Trichloroethanol (45 per cent), trichloroacetic acid (32 per cent)	Trichloroethanol (glucuronide) and trichloroacetic acid excreted in urine (half-lives ca. 12 and 100 hours). Trichloroacetic acid excretion can indicate exposure.
Xylenes	Methylbenzoic acids (95 per cent) and xylenols (2 per cent)	Methylbenzoic acids conjugated with glycine and urinary methylhippuric acid excretion used as index of exposure - no dietary sources of methylbenzoates.

4. GAS CHROMATOGRAPHY OF SOLVENTS AND OTHER VOLATILES IN BIOLOGICAL SAMPLES

Headspace sample preparation together with temperature programmed gas chromatography and split flame ionization/electron capture detection (FID/ECD) provides a simple method of screening for a wide range of volatiles in biological specimens. Ramsey and Flanagan (1982) used a packed column (2 m x 2 mm i.d. 0.3% (w/w) Carbowax 20M on Carbopack C) programmed from 35 to 175 °C. On-column septum injections of as much as 400 µl of headspace could be performed and thus good sensitivity (of the order of 0.1 mg/l or better using 200 µl of sample) could be obtained. Moreover, most compounds of interest were retained without resort to sub-ambient operation and the system could be used isothermally at an appropriate temperature for quantitative analyses. Disadvantages included the poor resolution of some very volatile substances, the long total analysis time (40 min), and variation in the peak shape given by alcohols between batches of column packing.

Bonded-phase wide-bore capillary columns permit relatively large volume septum injections and can offer advantages of improved efficiency, reproducibility and reliability. A 60 m x 0.53 mm i.d. fused silica capillary coated with the dimethylpolysiloxane phase SPB-1 (5 µm film thickness) offers many advantages over the packed column described above (Streete et al. 1992), including the following: (a) improved resolution of very volatile compounds is obtained even at an initial temperature of 40 °C, (b) the total analysis time can be reduced to 26 min, and (c) good peak shapes are obtained even for alcohols. Septum injections of up to 300 µl headspace can be performed with no noticeable effect either on the reproducibility of the retention data or on column efficiency, hence sensitivity is as least as good as that attainable with a packed column.

Some authors have emphasized the need to use retention data from two different packed columns when analyzing solvents in biological samples (Goebel 1982; de Zeeuw et al. 1992). As in any toxicological investigation, however, the results must never be considered in isolation from any clinical or circumstantial evidence. The use of the capillary column together with two different detectors confers a high degree of selectivity, particularly for low formula weight compounds where there are very few alternative structures. If more rigorous identification is required, gas chromatography combined with mass spectrometry or Fourier transform infrared spectrometry may be used. However, gas chromatography-mass spectrometry can be difficult when the fragments produced are less than m/z 40, particularly if the instrument is used for other applications in addition to solvent analyses. In particular, the available sensitivity and spectra of the low molecular weight alkanes renders them very difficult to confirm by gas chromatography-mass spectrometry. Gas chromatography-Fourier transform infrared spectrometry is more appropriate to the analysis of volatiles, but sensitivity is relatively poor particularly when compared with electron-capture detection. In addition, interference, particularly from water and carbon dioxide in the case of biological specimens, can be troublesome.

4.1. Headspace capillary gas chromatography

The headspace capillary gas chromatographic method presented here is that of Streete et al. (1992). The sample preparation procedure is that described by Ramsey and Flanagan (1982), although some parameters have been adjusted to accommodate the use of the capillary column. An outline of the method is given in Figure VI. A high-performance gas chromatograph and supplies of pure helium and pure nitrogen together with appropriate moisture, oxygen and oil filters are required. Use of data capture systems on the ECD and FID channels is mandatory if full advantage is to be taken of the reproducibility of the retention data which can be achieved. The dimensions of the column are important. The reduction in cost and time taken to recycle the oven temperature which arises from the use of the relatively high starting temperature (40 °C) are considerable, especially if liquid carbon dioxide or liquid nitrogen cooling would otherwise have been necessary.

Although the retention data have proved highly reproducible in routine use, it is prudent to analyze an authentic specimen of the suspected poison before reporting results. The sensitivity of the method has been aimed at detecting solvents and other volatiles in biological specimens at the concentrations associated with acute poisoning with those substances. Of course, it is possible to increase the sensitivity of the method by, for example, purge-and-trap apparatus, but interpretation of results then becomes an even greater problem (see Section 4.5).

A substantial workload is necessary to justify use of expensive apparatus. In forensic or occupational toxicology laboratories, it may prove possible to combine the use of the analytical procedure described here with other tasks such as ethanol analysis. There is, however, no viable alternative to gas chromatography for the analysis of solvents and other volatiles in biological fluids.

Outline of headspace capillary gas chromatography of solvents and other volatiles

Gas chromatography operation ("cold start")

1. The temperature program (Section 4.1.1) should be run to clear any compounds which may have accumulated on the column since it was last used.

2. A portion (1-5 µl) of the qualitative standard mixture prepared in a 125 ml gas sampling bulb (Section 4.2.2) should be analyzed.

3. If necessary, the carrier gas flow-rate should be adjusted so that retention times of the components of the mixture match those in Table 8.

Sample analysis - liquid analytes

1. A portion (100-300 µl) of headspace obtained on incubation (65 °C, 15 min) of 200 µl of the internal standard solution (Section 4.2.3) in a sealed vial (Section 4.2.4) should be analyzed.

2. The sample (200 µl) should be added to the vial containing the internal standard solution and re-incubated (65 °C, 15 min). A portion (100-300 µl) of the headspace should be analyzed (Section 4.2.4).

3. If there is a possibility that either ethylbenzene or 1,1,2-trichloroethane are present in the sample, the sample analysis should be performed without addition of the internal standard solution.

4. Any compounds present in the sample should be identified by reference to the chromatogram obtained on analysis of the standard mixture and the table of retention data (Appendix 1).

Sample analysis - tissues

1. Dissect 20-50 mg wet weight of tissue from the centre of the specimen (preferably whilst frozen) and add to headspace vial (Section 4.2.4). Add internal standard solution (200 µl) and Subtilisin A (approximately 1 mg) and incubate (65 °C, 15 min).

2. A portion (100-300 µl) of headspace should be analyzed. The internal standard analysis should be performed in a separate vial.

Figure VI

4.2. Apparatus

The equipment and apparatus listed below is that used in the authors' laboratory - equivalent items should be obtainable from alternative suppliers in most if not all cases.

4.2.1. Gas chromatography

- Gas chromatograph: Hewlett-Packard Model 5890 fitted with Hewlett-Packard splitless capillary septum injector;
- Column: 60 m x 0.53 mm i.d. fused silica capillary coated with SPB-1 (5 µm film) (Supelco);
- Carrier gas: helium (flow-rate 8.6 ml/min);
- Injector and detector oven temperatures: 150 and 275 °C, respectively;
- Temperature program: 6 min isothermal period, then programmed from 40 to 80 °C at 5 °C/min, and then to 200 °C at 10 °C/min (total analysis time 26 min);
- Detection: dual FID/^{63}Ni constant current ECD (SGE outlet splitter system OSS-2, split ratio approximately 5:1);
- Hydrogen and air (FID) inlet pressures: 15 and 22 p.s.i., respectively;
- ECD purge (nitrogen) flow: approximately 35 ml/min;
- Data capture: Hewlett-Packard 3396A recording integrators and associated connections to the gas chromatograph;
- Column conditioning: program from 30 to 260 °C with carrier flow at 2 °C/min and hold for 16 h.

4.2.2. Volumetric and other apparatus

- 125 ml Glass gas sampling bulb fitted with a septum port (Supelco 2-2146);
- 10 ml Glass septum vial (Schubert);
- Teflon-lined silicone disc and disposable aluminium vial cap (Kontron);
- Electrically-powered vial heating block;
- 1.0 ml Plastic disposable syringe fitted with a 1 inch, 25 gauge Luer needle;
- 50 and 100 ml Glass volumetric flasks;
- 200 µl Air displacement pipette (Eppendorf);
- 500 µl Gas-tight glass syringe (Scientific Glass Engineering);
- 10 µl Gas-tight glass syringe (Scientific Glass Engineering);
- 125 ml Septum bottles.

4.3. Experimental

4.3.1. Establishment of retention data

Retention and detector response data for 248 compounds are given in Appendix 1. Pure compounds were obtained from standard laboratory chemical suppliers or donated by manufacturers. The compounds were first sampled in the vapour phase (60 °C); direct liquid injection was used for compounds which were not sufficiently volatile to be analyzed in this way. Such compounds are identified by an asterisk in Appendix 1; they are included in the database to facilitate analysis of products and other non-biological specimens.

The compounds studied included those listed in Table 1 and other common halons, solvents and metabolites as well as products of putrefaction such as methyl sulphide. Generally, the amount of compound injected was sufficient to give full-scale deflection (FSD) or thereabouts at the detector sensitivities normally used in sample analyses (FID 80 pA FSD, ECD 2 kHz FSD). ECD responses were coded as nil (0), poor (1) or good (2) as a guide to aid peak assignment. Retention times were measured from the injection point and were also calculated relative to 1,1,2-trichloroethane which responds on both detectors. Kovats retention indices were calculated from the data generated on the temperature program by applying the following formula during the isothermal period or during the individual ramps of the program:

$$RI(x) = 100z + 100 \frac{RT(x) - RT(z)}{RT(z+1) - RT(z)}$$

Where: $RI(x)$ = Retention index of compound x
z = Number of carbon atoms in alkane eluting before compound x
$RT(x)$ = Retention time of compound x
$RT(z)$ = Retention time of alkane with carbon atoms z
$RT(z+1)$ = Retention time of alkane with z+1 carbon atoms eluting after compound

4.3.2. Qualitative standard mixture

A qualitative standard mixture may be prepared by adding the appropriate volume of the gaseous components (see Table 5 (A)) to a clean, sealed 125 ml gas-sampling bulb and adding a portion (10 µl) of the liquid components stock mixture (see Table 5 (B) - this mixture is stable for at least 6 months when stored in a glass-stoppered vessel at -5 to -20 °C). The qualitative standard mixture should be analyzed prior to sample analyses by obtaining a portion (1-5 µl) of the mixture via the septum port of the gas sampling bulb using a 10 µl gas-tight syringe and injecting the vapour into the gas chromatography column. The composition of the mixture can be adjusted to serve local needs as appropriate.

Table 5. Preparation of the GC qualitative standard mixture

A. Vapour mixture

Compound	Amount added (ml)[1]
Bromochlorodifluoromethane	0.005
Butane[2]	-
Dichlorodifluoromethane	0.3
Dimethyl ether	1.0
Fluorotrichloromethane	0.02
Isobutane[2]	-
Propane[2]	-
1,1,1-Trichlorotrifluoroethane	0.5

Key 1 Volume of vapour phase in headspace vial
2 2.0 ml commercial liquified petroleum gas added (see Table 1)

B. Liquid components mixture (prepared in 50 ml stoppered glass bottle)

Compound	Amount added (ml)
Acetone	7.5
Butanone	5.0
Carbon tetrachloride	0.05
Chloroform	0.5
Ethanol	5.0
Ethylbenzene	2.5
Halothane	0.1
Hexane	5.0
Methyl isobutyl ketone	2.5
2-Propanol	5.0
Tetrachloroethylene	0.025
Toluene	2.5
1,1,1-Trichloroethane	0.25
1,1,2-Trichloroethane	1.0
2,2,2-Trichloroethanol	0.015
Trichloroethylene	0.25

4.3.3. Preparation of internal standard solution

Ethylbenzene and 1,1,2-trichloroethane should be tested by gas chromatography for the presence of contaminants, especially toluene and 1,1,1-trichloroethane, before use. Approximately 50 mg of each compound are measured into 50 ml glass volumetric flasks containing outdated blood-bank whole blood. After thorough mixing, 1.0 ml of the 1,1,2-trichloroethane solution and 2.5 ml of the ethylbenzene solution are diluted to 100 ml using outdated blood-bank whole blood:deionised water (1+24) to give the working internal standard solution. The final ethylbenzene and 1,1,2-trichloroethane concentrations are approximately 25 and 10 mg/l, respectively. This solution remains useable for not less than two years if stored in 5 ml portions at -5 to -20 ºC in screw-topped glass bottles.

4.3.4. Sample preparation and analysis

The internal standard solution is first analyzed by gas chromatography to monitor any interference from the laboratory atmosphere etc. ("blank" analysis). In the case of liquid specimens, a portion for analysis is added to the same vial via the rubber septum and, after re-incubation, the headspace from the vial is again analyzed by gas chromatography. Any volatiles present in the samples are revealed by comparing the "blank" and sample chromatograms.

Blood and urine

Internal standard solution (200 µl) is added to a 10 ml glass septum vial using an air displacement pipette. The vial is then sealed with a crimped-on Teflon-lined silicone disc. The vial is incubated at 65 ºC in a heating block and, after 15 min, a portion (100-300 µl) of the headspace is injected into the gas chromatography column using a 0.5 ml gas-tight glass syringe, which is warmed beforehand by being placed on the heating block (10 min).

Subsequently, the sample (whole blood, plasma, serum, or urine) (200 µl) is added to the same vial using a 1.0 ml hard plastic disposable syringe fitted with a 1 inch, 25 gauge Luer needle and, after at least 15 min, a further portion of the headspace is taken using the 0.5 ml gas-tight syringe and injected into the gas chromatography column. After each injection, the plunger should be removed from the gas-tight syringe and the assembly placed on the heating block until the next injection to ensure evaporation of any remaining analyte. The syringe should also be rinsed occasionally with methanol to remove deposits and dried by purging with compressed air.

Tissues

Samples of solid tissues should be analyzed as above after adding a proteolytic enzyme to the incubation mixture. Thus, 20-50 mg wet weight of tissue is dissected from the centre of the specimen, preferably while the specimen is frozen. Duplicate portions of the specimen are incubated (65 ºC, 15 min) with internal standard solution (200 µl) and approximately 1 mg of Subtilisin A (Novo) or equivalent, prior to the analysis of 100-300 µl headspace as described above. The "blank" analysis of the internal standard solution should be performed in a separate vial.

Products

It is very important that all products sent for analysis are packaged, stored, and analyzed entirely separately from biological samples to prevent cross-contamination. Aerosols and fuel gases can be analyzed after releasing a portion of the product into a headspace vial, and then transferring a few µl of the vapour to another vial for analysis. Liquids can be analyzed in the same way except that it is often possible to

withdraw a portion (5-50 µl) of the headspace directly from the container. Adhesives and other liquid or semi-liquid products can be introduced into a glass vial. The vial is sealed and after incubation (65 ºC, 15 min), a portion (50-100 µl) of the headspace is transferred to a sealed pre-incubated vial (65 ºC, 15 min) containing internal standard solution. After re-equilibration (65 ºC, 5 min) 100-200 µl of headspace are taken for analysis.

4.3.5. Quantitative analyses

Quantitative assays should be performed in duplicate either isothermally or on a temperature program using the appropriate detector. If concentrations of ECD-responding compounds are very high it is sometimes more convenient to use the FID. Assay calibration should be by analysis of standard solutions prepared as described below; the same solutions are used in the analysis of blood and of tissue digests. Analyte concentrations in the range 0.1-10 or 0.5-50 mg/l are usually adequate in cases of acute poisoning. The method is amenable to automation using, for example, the Tekmar 7000 headspace system fitted with a heated transfer line. The use of such apparatus not only permits unattended operation, but also gives much better reproducibility in quantitative work.

Liquid and solid analytes

Calibration solutions are prepared by adding a known volume of the liquid analyte to a volumetric flask containing "blank" blood by using a positive displacement pipette and ascertaining the exact amount added by weighing. Solid analytes are weighed in directly. After allowing time for equilibration, appropriate volume to volume dilutions are performed, taking care to minimize loss of analyte by handling reagents and glassware at 4 ºC and storing samples and standards at 4ºC with minimal headspace. Small (2 ml) glass vials with caps lined with aluminium foil are convenient for performing standard dilutions. Portions of the standards are transferred to headspace vials for analysis as described above and a calibration graph of peak height ratio of analyte to internal standard against analyte concentration is prepared. Often, either 1,1,2-trichloroethane or ethylbenzene can be used as the internal standard. Carbon tetrachloride, fluorotrichloromethane and 1,1,1-trichloroethane are best analyzed isothermally at a column temperature of 120 ºC, while 1-butanol, chloroform, paraldehyde, tetrachloroethylene, toluene, 2,2,2-trichloroethanol and trichloroethylene are best analyzed at 150 ºC.

Gaseous analytes

Calibration solutions are prepared directly into headspace vials (Gill et al. 1993). Septum bottles of approximately 125 ml capacity are calibrated by weighing the amount of deionised water each could contain. Each bottle is then dried and filled with nitrogen. A piece of aluminium foil (approximately 1 cm^2) is added to aid mixing and the vial is sealed. After recording atmospheric pressure, the pure analyte, usually supplied in a small cylinder, is transferred to a 125 ml gas sampling bulb at atmospheric pressure. The selected volume of vapour is then taken from the gas sampling bulb using a gas-tight syringe and added to a calibrated septum bottle. Care should be taken to ensure that the contents of all vessels remain at atmospheric pressure. Thus, if the volume of gas transferred is greater than 0.1 ml a short vent needle should be inserted through the septum well away from the point of the gas-tight syringe needle. After thorough mixing, further dilutions may be prepared as required. Finally, measured volumes of diluted analyte vapour are transferred using a gas-tight syringe into headspace vials containing the same volume of "blank" blood as used in sample analyses. A constant volume of appropriately diluted internal standard (2,2-dimethylpropane in the case of butane) vapour is also added to the sample vial and to the vials containing the calibration mixtures.

4.4. Retention and relative detector response data

The gas chromatograph temperature program should be run each day before any sample analyses to remove contaminants which might have accumulated on the column since the system was last used. The analysis of the qualitative standard mixture (see Table 5) is illustrated in Figure VII. Note especially the good peak shapes given by ethanol and 2-propanol. No deterioration in peak shape has been observed in 6 years of routine use. The column is operated well below its maximum recommended temperature (320 °C) and thus column life should be long.

Compounds which do not elute during the program generally have boiling points (atmospheric pressure) of 170 °C or above and Kovats retention indices on SE-30/OV-1/OV-101 packed columns of 1000 or more (see Appendix 1). Among the compounds which do not elute are: camphor, 1-chlorooctane, cycloheptanone, decane, 1,2-dichlorobenzene, 1,4-dichlorobenzene, 2,6-dimethyl-4-heptanone, ethchlorvynol, 2-ethyl-1-hexanol, 2-ethylhexyl acetate, hexachloroethane, 4-methylbenzaldehyde, N-methylformamide, 2-nonanone, 5-nonanone, 1-octanol and octylamine.

The injection of hydrogen (retention time 2.49 min, relative retention to 1,1,2-trichloroethane 0.134) provides a measure of the void volume of the system (retention time of methane 2.52 min, see Appendix 1). There is a slight difference in the absolute retention time of compounds which respond at each detector because of the effect of the effluent splitter. Retention times are calculated relative to 1,1,2-trichloroethane since this compound responds on both detectors at the sensitivities normally employed. However, the retention data quoted in Appendix 1 were derived from the ECD for compounds responding on that detector. Compounds responding strongly on ECD are primarily halogenated substances such as halons, but many compounds containing nitro- or keto-moieties also respond. Other substances such as allyl isothiocyanate and nitrous oxide show a good response. In contrast, the response to some halogenated compounds such as 1,1,1,2-tetrafluoroethane is relatively poor and some ketones, for example the heptanones, show no response.

The relative retention data have proved to be highly reproducible in routine use over a six-month period in the authors' laboratory (see Table 6) and should be applicable to other SPB-1 columns (and indeed to other dimethylpolysiloxane-coated capillaries (OV-1, SE 30, etc.)) of similar dimensions and film thickness. The carrier gas flow might have to be adjusted, however, to give retention data identical to those given in Appendix 1. Experience has shown that the relative retention time is more convenient than the retention index when evaluating peaks given by unknowns. Nevertheless, the Kovats retention indices (alkane) calculated for each compound on the temperature program on the SPB-1 column are given in Appendix 1. Literature values for Kovats retention indices on SE-30/OV-1/OV-101 packed columns, if available, are also given; if two different packed column indices were reported, the mean is given.

As noted above, only compounds with a retention index of <1000 eluted from the SPB-1 column on the temperature program used. Thus, in order to calculate the retention indices for compounds eluting between 23.56 min (retention time of nonane) and 26.00 min, it was necessary to ascertain the retention time of decane. This was measured by continuing the final ramp for a further 2 min (retention time of decane 26.06 min).

Table 6. Inter-assay reproducibility of the GC retention data (n = 30 in each case) (GC conditions as Figure VII; see Table 1 for full chemical names of certain compounds)

Compound	Retention time (min)	RSD (per cent)	Relative retention time	RSD (per cent)
Propane	3.050	0.27	0.163	0.32
Dichlorodifluoromethane	3.179	0.67	0.170	0.64
Dimethyl ether	3.338	0.25	0.179	0.28
Isobutane	3.613	0.24	0.193	0.29
Bromochlorodifluoromethane	4.065	0.90	0.217	0.89
Butane	4.091	0.23	0.219	0.19
Ethanol	4.795	0.23	0.257	0.25
Acetone	5.664	0.20	0.303	0.20
2-Propanol	6.036	0.23	0.323	0.20
Trichlorofluoromethane	6.128	0.71	0.327	0.67
1,1,1-Trichlorotrifluoroethane	8.013	0.51	0.428	0.49
Halothane	8.763	0.19	0.468	0.13
Butanone	10.173	0.14	0.545	0.12
Hexane	11.512	0.11	0.616	0.08
Chloroform	11.651	0.19	0.622	0.15
1,1,1-Trichloroethane	13.559	0.14	0.724	0.09
Carbon tetrachloride	14.703	0.12	0.785	0.09
Trichloroethylene	16.245	0.09	0.868	0.05
Methyl isobutyl ketone	17.602	0.06	0.942	0.04
1,1,2-Trichloroethane	18.720	0.06	1.000	-
Toluene	19.143	0.05	1.025	<0.01
Tetrachloroethylene	20.892	0.05	1.116	0.04
2,2,2-Trichloroethanol	22.292	0.07	1.191	0.08
Ethylbenzene	22.377	0.04	1.198	<0.01

Analysis of the GC qualitative standard mixture (see Table 5). Column: 60 m x 0.53 mm i.d. SPB-1 (5 µm film). Oven temperature: 40 ^{0}C (6 min), then to 80 ^{0}C at 5 ^{0}C/min, then to 200 ^{0}C at 10 ^{0}C/min. Injection: approximately 10 µl vapour. Detector sensitivities (FSD): FID 3.2 nA, ECD 64 kHz. Peaks: 1 = propane, 2 = dichlorodifluoromethane, 3 = dimethyl ether, 4 = isobutane, 5 = butane, 6 = bromochlorodifluoromethane, 7 = ethanol, 8 = acetone, 9 = 2-propanol, 10 = trichlorofluoromethane, 11 = 1,1,1-trichlorotrifluoroethane, 12 = halothane, 13 = butanone, 14 = hexane, 15 = chloroform, 16 = 1,1,1-trichloroethane, 17 = carbon tetrachloride, 18 = trichloroethylene, 19 = methyl isobutyl ketone, 20 = 1,1,2-trichloroethane (internal standard), 21 = toluene, 22 = tetrachloroethylene, 23 = 2,2,2-trichloroethanol, 24 = ethylbenzene (internal standard).

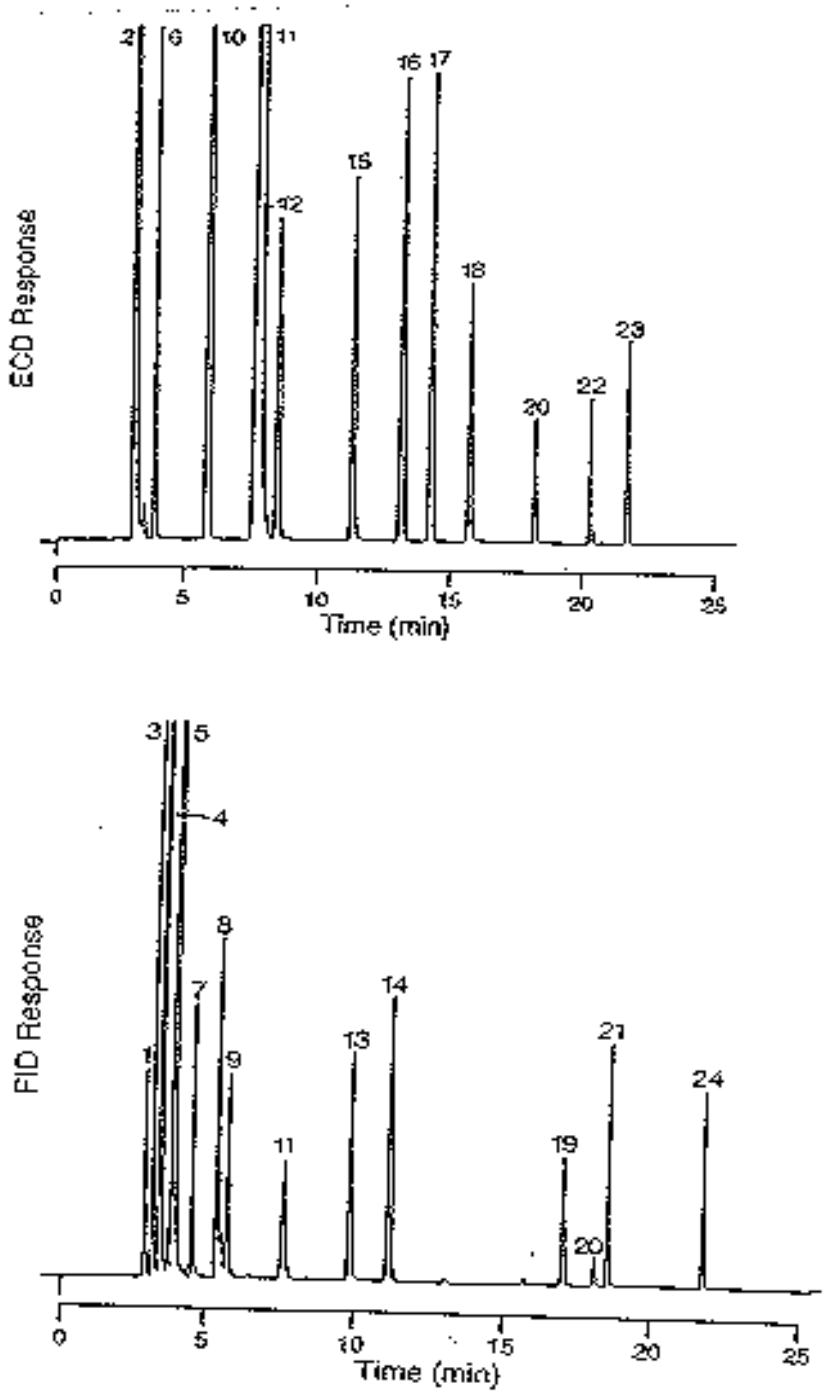


Figure VII

4.5. Application to sample analyses

The chromatograms discussed below illustrate some practical aspects of analyses for volatile substances in biological samples. A typical "reagent blank" analysis from the authors' laboratory is shown in Figure VIII. In addition to the internal standards, the only identifiable compounds were small amounts of methanol, which may have originated from the laboratory atmosphere, and chloroform, which may have arisen either from the laboratory atmosphere or from chlorination of the public water supply used to feed the laboratory deioniser. The latter compound can be removed by passing through a bed of activated charcoal, for example that in the Elga UHQ water purifier.

The analysis of a blood specimen from an adolescent who died after abusing a cigarette lighter refill and vapour from a typewriter correcting fluid is shown in Figure IX. The analysis of a blood specimen from a patient who died after inhaling vapour from an electrical component cleaner is illustrated in Figure X. It is clear that the concentrations of the components of interest were well above the limit of detection of the system. Indeed, although no formal studies have been performed, the sensitivity attainable appears to be similar to that obtained using an FID to ECD split ratio of 10 to 1 with the modified Carbopack packed column system (Ramsey and Flanagan 1982), i.e. of the order of 0.01 mg/l for ECD-responding compounds and 0.1 mg/l for the remainder.

Of the commonly encountered compounds only isobutane and methanol are not resolved. Isobutane is unlikely to be found in the complete absence of butane and propane (see Table 7). Methanol is rapidly oxidized in aqueous solution on mixing with potassium dichromate (5 per cent w/v) in aqueous sulphuric acid (6 mol/l). Methanol cannot be directly removed from blood in this way, but can be oxidized after headspace transfer to a second, warmed vial before adding the dichromate reagent. Such transfer may, however, be associated with considerable loss of sensitivity.

It may prove difficult to differentiate toluene and paraldehyde if either compound is present in great excess. Simply reducing the amount injected in order to measure the relative retention time accurately is normally all that is required. Alternatively, addition of 6 mol/l aqueous sulphuric acid (200 µl) to the vial and re-incubation (65 ºC, 10 min) should remove the paraldehyde peak and lead to an increase in the acetaldehyde peak. Measurement of released acetaldehyde has been advocated for metaldehyde assay in biological specimens (Griffiths 1984), although this approach has not proved successful when attempted by the authors.

Analysis of the internal GC standard solution. Gas chromatography conditions: as Figure VII. Sample volume: 200 µl. Injection: 300 µl headspace. Detector sensitivities (FSD): FID 80 pA, ECD 2 kHz.

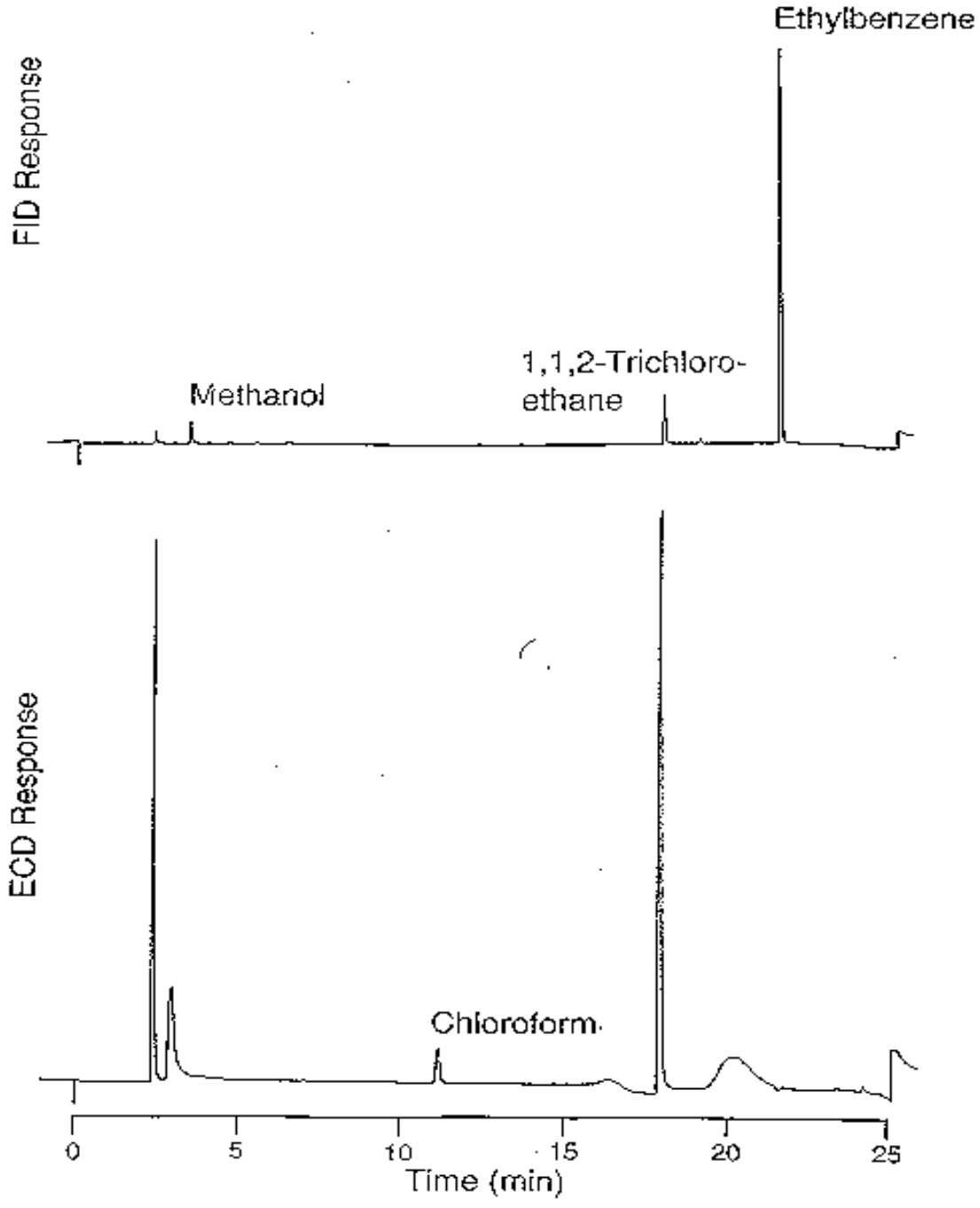


Figure VIII

GC Analysis of a whole blood specimen (200 µl) from a patient who died after abusing a cigarette lighter refill and a typewriter correcting fluid containing 1,1,1-trichloroethane. Gas chromatography conditions: as Figure VII. Injection: 300 µl headspace. Detector sensitivities (FSD): FID 80 pA, ECD 2 kHz. Whole blood 1,1,1-trichloroethane concentration 1.2 mg/l.

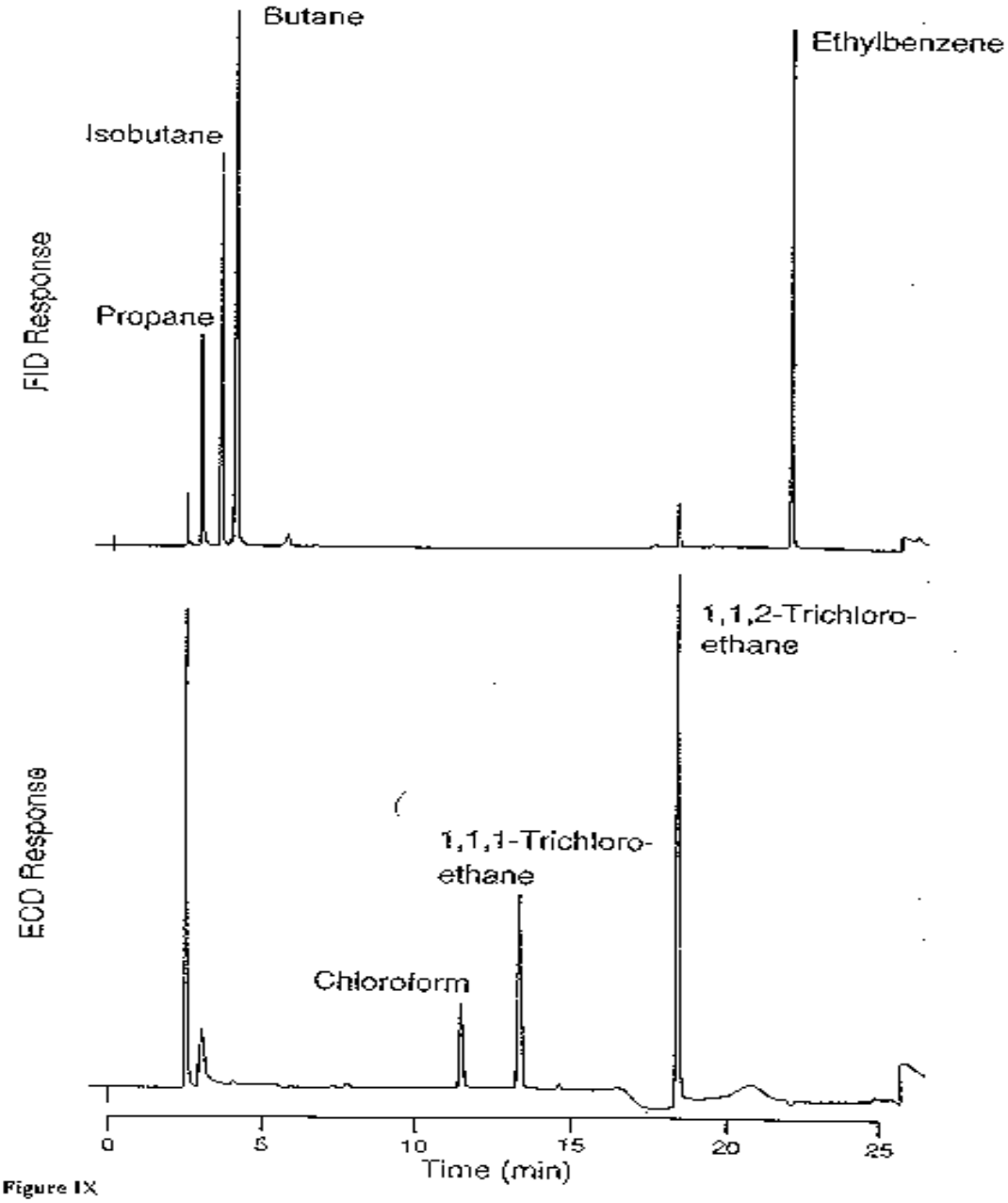


Figure IX

GC Analysis of a whole blood specimen (200 µl) from a patient who died after abusing an aerosol designed for cleaning electrical components which contained FCs 11, 12 and 113. Gas chromatographic conditions: as Figure VII. Injection: 150 µl headspace. Detector sensitivities (FSD): FID 160 pA, ECD 4 kHz. Whole blood fluorotrichloromethane (FC 11) and 1,1,2-trichlorotrifluoroethane (FC 113) concentrations 3.2 and 1.0 mg/l, respectively.

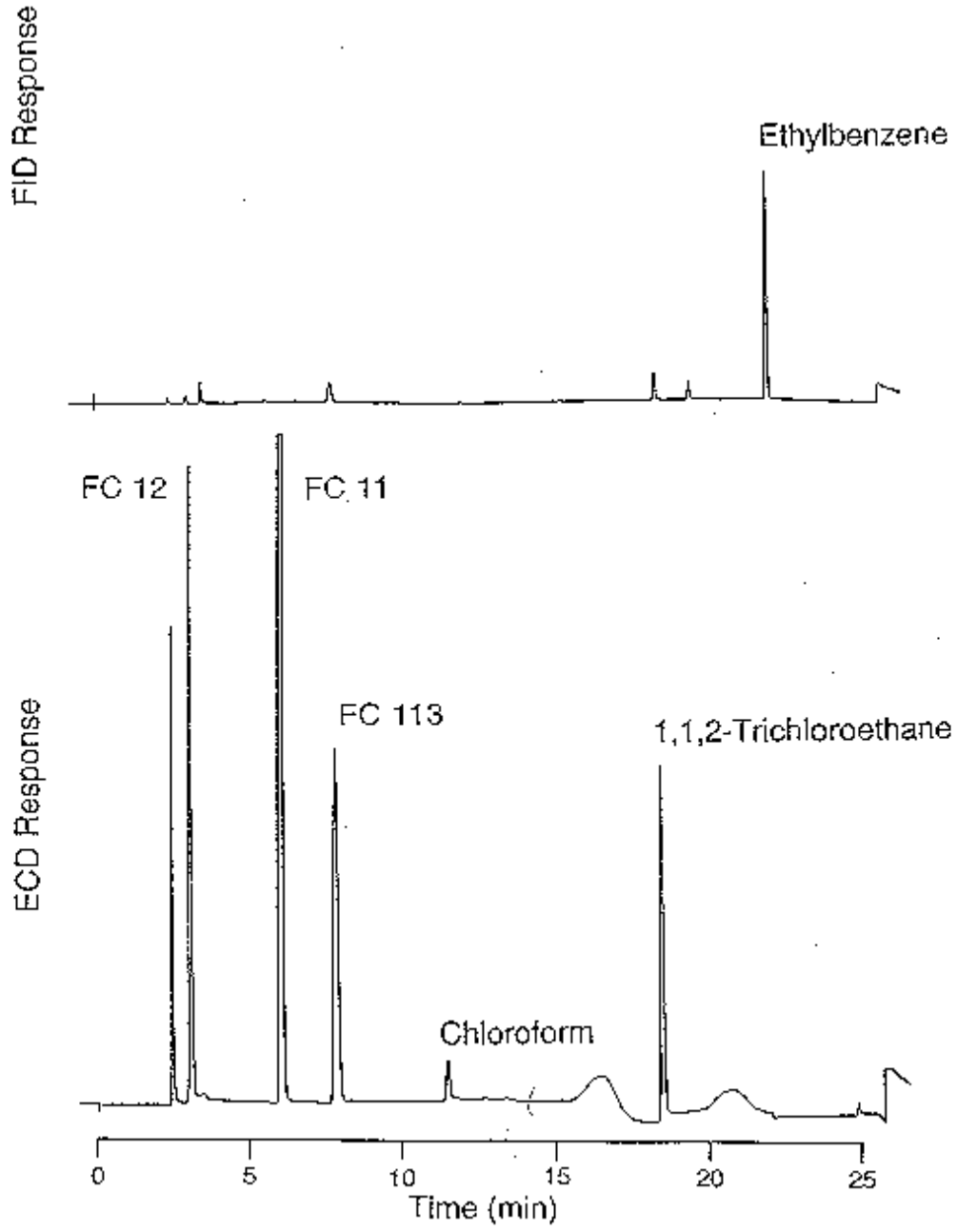


Figure X

Table 7. Volatile compounds which often occur together in blood

Compound	Associated compound
Acetone	Butanone and higher ketones in ketoacidosis, 2-propanol (metabolite, rare)
Bromochlorodifluoromethane	Fluorotrichloromethane
Butane	Butanone, 2-butanol (metabolites, rare), isobutane, propane
Cyclohexanone	Cyclohexanol (metabolite)
Dimethyl ether	Chlorodifluoromethane
Ethanol	Propanols and higher alcohols if fermentation has occurred
Ethyl acetate[1]	Ethanol (metabolite)
Ethylbenzene	Toluene, xylenes
Fluorotrichloromethane	Bromochlorodifluoromethane, dichlorodifluoromethane
Dichlorodifluoromethane	Fluorotrichloromethane
Chlorodifluoromethane	Dimethyl ether
Halothane	2-Chloro-1,1-difluoroethylene, 2-chloro-1,1,1-trifluoroethane (metabolites, rare)
Isobutane	Butane, 2-methyl-2-propanol (metabolite, rare), propane
Isobutyl nitrite[1]	2-Methyl-1-propanol (degradation product)
Isopentyl nitrite[1]	3-Methyl-1-butanol (degradation product)
Methyl acetate[1]	Methanol (metabolite)
Propane	Acetone (metabolite, rare), butane, isobutane, 2-propanol (metabolite, rare)
2-Propanol	Acetone (metabolite)
1,1,1-Trichloroethane	Isopropyl nitrate (stabiliser, rare)
2,2,2-Trichloroethanol	Trichloroethylene (also metabolite of the drugs chloral hydrate, dichloralphenazone and triclofos)
Trichloroethylene	2,2,2-Trichloroethanol (metabolite), chloroform [in headspace gas chromatography possibly from thermal degradation of trichloroacetic acid (metabolite) *in vitro*]
Xylenes	*o*-, *m*- and *p*-Xylene occur together in technical xylene, *m*-xylene predominating. Ethylbenzene may also be present

Key 1 Parent compound not normally detected in blood

4.6. Interpretation of qualitative analytical data

The likelihood of detecting exposure to volatile substances by headspace gas chromatography of blood is influenced by the nature of the compounds involved, the extent and duration of exposure, the time of sampling in relation to the time elapsed since exposure and the precautions taken when collecting and storing the sample. In one series of suspected abusers, volatile compounds or metabolites were detected in 79 of 125 cases. In 69 of the positive cases (87 per cent) the samples were obtained within 10 hours of the suspected exposure (Meredith et al. 1989). Nevertheless, exposure can be detected using later samples - in separate cases toluene was detected at 40 hours and 2,2,2-trichloroethanol (from trichloroethylene) at 48 hours.

Analysis of urinary metabolites may extend the time in which exposure may be detected but, of the compounds commonly abused, only toluene, the xylenes and some chlorinated solvents, notably trichloroethylene, have suitable metabolites (see Table 4). Chronic petrol "sniffing" has been diagnosed by the measurement of blood lead concentrations or detection of aromatic components such as toluene and ethylbenzene (Matsumoto et al. 1992). However, with some petrols and other complex mixtures such as petroleum ethers (see Table 1) the blood concentrations of the individual components are often below the limit of detection of headspace gas chromatographic methods even after significant inhalational exposure.

Detection of a volatile compound in blood does not always indicate volatile substance abuse or occupational/environmental exposure to solvent vapour. Acetone and some homologues may occur in high concentrations in ketotic patients. Large amounts of acetone and butanone may also occur in blood and urine from children with acetoacetylcoenzyme A thiolase deficiency and may indicate the diagnosis. In addition, acetone is the major metabolite of 2-propanol in man (see Table 4). Conversely, 2-propanol has recently been found in blood from ketotic patients (Bailey 1990). Other ketones may also give rise to alcohols *in vivo*. Cyclohexanol, for example, is the principal metabolite of cyclohexanone in man (see Table 4). Other volatile compounds such as halothane and paraldehyde may be used in therapy. Some compounds usually occur in association one with another (see Table 7).

It is important to remember when collecting samples that use of aerosol disinfectant preparations, for example, may contaminate the sample if an aerosol propellant is used. Contamination of blood samples with ethanol or 2-propanol may also occur if an alcohol-soaked swab is used to cleanse skin prior to venepuncture. Gross contamination with technical xylene (a mixture of *o*-, *m*- and *p*-xylene together with ethylbenzene) has been found in blood collected into Sarstedt Monovette Serum Gel blood collection tubes (Streete and Flanagan 1993); contamination with toluene (up to 22 mg/l), 1-butanol, ethylbenzene and xylene has been found in more recent batches of these same tubes (Dyne et al. 1996). Contamination with 1-butanol or 2-methyl-2-propanol occurs commonly in blood collected into tubes coated with ethylenediamine tetra-acetic acid (EDTA).

The interpretation of case data involving chloroform is particularly difficult, especially since this compound is still sometimes used in the course of crimes such as rape and murder (McGee et al. 1987). Post-mortem blood chloroform concentrations in fatalities involving this agent have been reported as 10-50 mg/l (Baselt and Cravey 1990). In addition to sometimes being present in drinking water at low concentrations, chloroform is found in a variety of medicinal preparations, in cigarette smoke, soft drinks, margarines, and in swimming pools if a chlorination plant is in operation.

A further possible source of chloroform on headspace gas chromatography is from thermal decomposition of trichloroacetic acid (Aggazzotti et al. 1987). Trichloroacetic acid is a metabolite of several compounds including the solvent trichloroethylene (see Table 4) and the drugs chloral hydrate, dichloralphenazone and triclofos. Trichloroacetic acid has a half-life in blood of 3-5 days and thus may be detected for a relatively long time after exposure to, or ingestion of, a precursor. Trichloroacetic acid

plasma concentrations of up to 40 mg/l have been reported after occupational exposure to trichloroethylene vapour (Baselt & Cravey 1990).

Pfaffenberger and Peoples (1982) measured plasma chloroform concentrations in 25 Caucasian adult women in Florida, United States of America, over a period of six months. All subjects were carefully screened to exclude occupational and recreational exposure to chloroform and other compounds which could give rise to chloroform on headspace gas chromatography. Average plasma chloroform concentrations were generally less than 25 µg/l, but in 2 subjects plasma chloroform concentrations of 2.9 and 4.0 mg/l, respectively, were found during routine sampling. Neither subject was aware that they had been exposed recently to chloroform or a compound giving rise to chloroform on headspace gas chromatography.

A further chlorinated compound, chlorobutanol (1,1,1-trichloro-2-methyl-2-propanol), has been used in doping racing greyhounds (Smith and Thorpe 1978). However, this compound is still sometimes employed as a sedative and a preservative (Tung et al. 1982), and thus caution is needed in the interpretation of results.

It is well-known that ethanol may be both produced and metabolized by microbial action in biological specimens (Corry 1978). Small amounts of hexanal may arise from degradation of fatty acids in blood on long-term storage even at -5 to -20 °C (Gill et al. 1988). Hexanal is resolved from toluene on the capillary gas chromatographic system described in Section 4, but resolution may be lost if an isothermal quantitative analysis is performed. Interference from hexanal is only likely to be important, however, if very low concentrations of toluene (0.1 mg/L or less) are to be measured.

The alkyl nitrites which can be abused by inhalation (isobutyl nitrite, isopentyl nitrite) are a special case in that (a) they are extremely unstable and break down rapidly *in vivo* to the corresponding alcohols (Figure XI), and (b) usually also contain other isomers (butyl nitrite, pentyl nitrite). Any products submitted for analysis will usually contain the corresponding alcohols as well as the nitrites. Aspects of the analysis of alkyl nitrites have been reviewed (Baselt and Cravey 1990; Osterloh 1984).

Breakdown of alkyl nitrites in humans (Note: Pentyl=amyl)

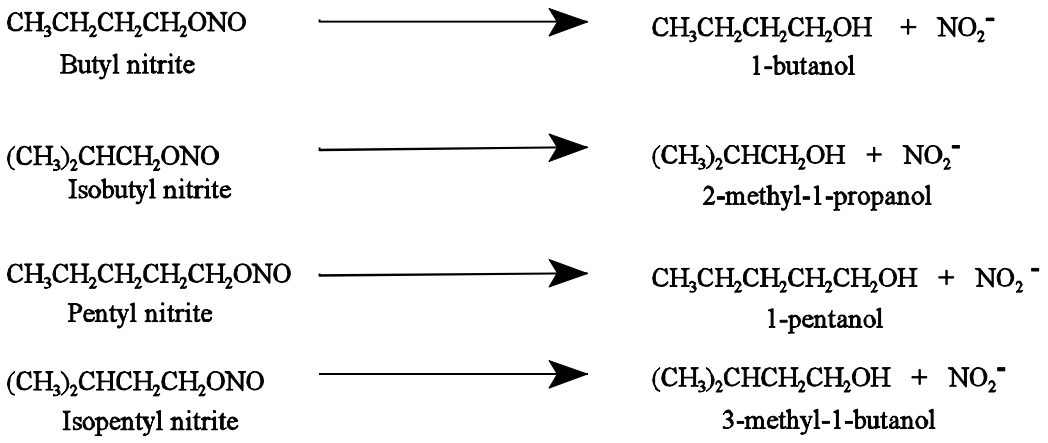


Figure XI

4.7. Interpretation of quantitative analytical data

Data to aid the interpretation of results in individual cases are given in Baselt and Cravey (1990) and Moffat (1986). Conversion factors for ambient air concentrations [parts per million (ppm) to milligrams per cubic metre (mg/m^3)] and for concentrations in blood and other fluids (Système Internationale (SI) mass to molar units) for a number of volatile compounds are given in Table 8.

Table 8. Volatile compounds: conversion factors (25 °C, 760 mm Hg)

Compound	Formula mass	Ambient air concentrations[1]		Blood concentrations	
		parts per million to mg/m^3	mg/m^3 to parts per million	mg/l to µmol/l	µmol/l to mg/l
Acetone	58.1	2.37	0.422	17.21	0.058
Benzene	78.1	3.20	0.313	12.80	0.078
Butane	58.1	2.38	0.422	17.21	0.058
Butanone	72.1	2.95	0.339	13.87	0.072
Carbon disulphide	76.1	3.11	0.322	13.14	0.076
Carbon tetrachloride	153.8	6.29	0.159	6.50	0.154
Chlorodifluoromethane	86.5	3.54	0.283	11.56	0.087
Chloroform	119.4	4.89	0.205	8.38	0.119
Cyclopropane	42.1	1.72	0.582	23.75	0.042
Dichlorodifluoromethane	120.9	4.95	0.202	8.27	0.121
Dichloromethane	84.9	3.48	0.288	11.78	0.085
Diethyl ether	74.1	3.03	0.330	13.50	0.074
Enflurane	184.5	7.57	0.133	5.42	0.185
Ethanol	46.1	1.88	0.532	21.7	0.046
Ethyl acetate	88.1	3.60	0.278	11.35	0.088
Ethylbenzene	106.2	4.34	0.231	9.42	0.106
Fluorotrichloromethane	137.4	5.62	0.178	7.28	0.137
Halothane	197.4	8.08	0.124	5.07	0.197
Hexane	86.2	3.53	0.283	11.60	0.086
Isobutane	58.1	2.37	0.422	17.21	0.058
Methanol	32.0	1.31	0.764	31.25	0.032
Methoxyflurane	165.0	6.75	0.148	6.06	0.165
Methyl isobutyl ketone	100.2	4.10	0.244	9.98	0.100
Nitrous oxide	44.0	1.80	0.556	22.73	0.044
Propane	44.1	1.80	0.556	22.68	0.044
2-Propanol	60.1	2.55	0.408	16.67	0.060
Styrene	104.1	4.25	0.235	9.61	0.104
Tetrachloroethylene	165.9	6.79	0.147	6.02	0.166
Toluene	92.1	3.76	0.266	10.86	0.133
1,1,1-Trichloroethane	133.4	5.46	0.183	7.69	0.130
Trichloroethylene	131.4	5.38	0.186	7.61	0.131
Xylene	106.2	4.35	0.231	9.42	0.106

Key 1 Data from Clayton and Clayton (1981)

4.7.1. Blood toluene concentrations and clinical features of toxicity

Oliver (1984) reported that 50 per cent of patients with blood toluene concentrations between 5 and 10 mg/l showed marked intoxication, and that virtually all patients with concentrations greater than 10 mg/l were comatose or dead at the time of sampling. Shortly after exposure, however, only signs of moderate intoxication (e.g. slurred speech, unsteady movements) have been associated with blood toluene concentrations as high as 30 mg/l (Garriott et al. 1981).

Blood toluene concentrations in samples from 132 patients who were thought to have engaged in volatile substance abuse ranged from 0.2 to 70 mg/l and were in excess of 5 mg/l in 22 of the 25 deaths reported (Meredith et al. 1989). Although there was a broad correlation between blood concentration and severity of poisoning, there were large variations within each patient group. Thirteen patients with blood toluene concentrations greater than 10 mg/l were either asymptomatic or only mildly intoxicated (headache, nausea, vomiting and/or drowsiness), although these manifestations of toxicity can lead to "indirect" acute volatile substance abuse-related death (Shepherd 1989). Similar findings have been reported in Japan (Miyazaki et al. 1990). Aside from individual differences in tolerance and possible loss of toluene from the sample prior to analysis (Gill et al. 1988), the lack of a strong correlation between blood concentrations and clinical features of poisoning is probably due to rapid initial tissue distribution and elimination. In the occupational setting, blood toluene concentrations after exposure to up to 127 parts per million toluene (United Kingdom Occupational Exposure Limit = 100 parts per million) for 8 hours ranged between 0.4 to 6.7 mg/l (Campbell et al. 1987).

Some 80 per cent of a dose of toluene is converted to hippuric acid (see Table 4). Similarly, more than 90 per cent of a dose of xylene is metabolized to methylhippuric (toluric) acids. The principal isomer found in urine is 3-methylhippurate since *m*-xylene is the principal component of technical grade xylene (see Table 1). Methylhippurates are not normal urinary constituents, but hippuric acid may arise from the metabolism of benzoates in foods and medicines, and thus caution is needed in the interpretation of analytical results. Hippurate and methylhippurate excretion are often expressed as a ratio to creatinine since this obviates the need for timed urines. Occupational exposure to toluene can give rise to ratios of 1 gram of hippurate per gram of creatinine or more; in patients suspected of volatile substance abuse a ratio of more than 1 g/g suggests, but does not prove, toluene exposure (Meredith et al. 1989). Measurement of urinary *o*-cresol has been proposed as an alternative means of monitoring toluene exposure selectively, particularly in occupational circumstances, but the assay procedure is relatively complex and is thus not widely used.

4.7.2. Blood 1,1,1-trichloroethane concentrations and clinical features of toxicity

After exposure of 12 subjects to 350 parts per million (United Kingdom maximum exposure limit) for one hour, the mean blood 1,1,1-trichloroethane concentration was 2.6 mg/l (Mackay et al. 1987). Blood 1,1,1-trichloroethane concentrations ranged from 0.1 to 60 mg/l in samples from 66 patients suspected of volatile substance abuse, 29 of whom died (Meredith et al. 1989). There was again a broad relationship between blood concentration and the severity of poisoning but there were large variations within each patient group. As with toluene, the absence of a strong correlation between blood concentration and clinical features is probably due to rapid initial distribution into tissues. In addition, other compounds were present in many non-fatal cases, further complicating recognition of any dose-response relationship.

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APPENDIX Retention and relative detector response data on the SPB-1 column system
(see Figure VII for chromatographic conditions and Notes on Page 56).

(a) Alphabetical order

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Acetaldehyde	3.59	0.192	0	352	372	44.1	21	75-07-0
Acetone	5.66	0.303	1	460	469	58.1	57	67-64-1
Acetonitrile	5.22	0.279	0	443	455	41.1	82	75-05-8
Acetonylacetone: see 2,5-Hexanedione								
Acetylacetone: see 2,4-Pentanedione								
Acetylene	2.63	0.141	0	165	-	26.0	-81	74-86-2
Acrylonitrile	6.50	0.348	0	492	590	53.1	77	107-13-1
Allyl glycidyl ether	22.62	1.211	0	869	880	114.2	154	106-92-3
Allyl isothiocyanate	22.31	1.192	2	585	-	99.2	151	57-06-7
Amyl ... : see Pentyl ...								
Aniline	25.13	1.345	0	963	970	93.1	183	62-53-3
BCF: see Bromochlorodifluoromethane								
Benzene	14.39	0.770	0	655	660	78.1	80	71-43-2
Benzaldehyde	24.75	1.325	0	948	956	106.1	179	100-52-7
Benzonitrile	25.16	1.347	0	965	-	103.1	191	100-47-0
Bicyclo(4.3.0)nonane	25.48	1.364	0	977	-	124.2	167	496-10-6
Bromoacetonitrile	17.65	0.943	2	725	-	120.0	62[1]	590-17-0
Bromobenzene	24.45	1.306	2	936	945	157.0	156	108-86-1
Bromochlorodifluoromethane	4.07	0.217	2	398	405	165.4	-3	353-59-3
Bromochloromethane	11.40	0.609	2	598	660	129.4	68	74-97-5
2-Bromo-2-chloro-1,1,1-trifluoroethane: see Halothane								
Bromodichloromethane	16.16	0.863	2	690	715	163.8	90	75-27-4
1-Bromo-2,3-epoxypropane	19.54	1.044	2	773	805	137.0	136	3132-64-7
Bromoform	22.82	1.219	2	875	911	252.8	149	75-25-2
Bromomethane	4.47	0.239	2	414	-	94.9	-94	74-83-9
1-Bromopropane	12.24	0.654	2	614	-	123.0	71	106-94-5
Bromotrichloromethane	18.98	1.014	2	859	810	198.3	103	75-62-7
Bromotrifluoromethane	2.77	0.148	2	222	-	148.9	-58	75-63-8
1,3-Butadiene	4.04	0.215	0	393	-	54.1	-5	106-99-0
Butanal	9.98	0.534	0	568	-	72.1	75	123-72-8
2,3-Butanedione	9.72	0.519	2	563	-	86.1	89	431-03-8
Butane	4.09	0.219	0	*400*	*400*	58.1	-1	106-97-8
1-Butanol	14.08	0.754	0	650	651	74.1	117	71-36-3
2-Butanol	10.80	0.578	0	585	624	74.1	100	78-92-2
tert.-Butanol: see 2-Methyl-2-propanol								
Butanone	10.18	0.545	1	572	579	72.1	80	78-93-3
1-Butene	3.94	0.211	0	386	390	56.1	-6	106-98-9
2-Butoxyethanol	23.39	1.244	0	889	-	118.2	171	111-76-2
Butyl acetate	20.36	1.090	0	795	794	116.2	125	123-86-4
Butyl cellosolve: see 2-Butoxyethanol								
Butyl chloride: see 1-Chlorobutane								
Butyl formate	17.02	0.911	0	708	701	102.1	107	592-84-7
Butyl iodide: see 1-Iodobutane								
Butyl nitrite	12.41	0.663	2	617	608	103.1	78	544-16-1

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Butyraldehyde: see Butanal								
Caprylene: see 1-Octene								
Carbon disulphide	8.03	0.429	1	527	524	76.1	47	75-15-0
Carbon tetrachloride	14.70	0.785	2	661	659	153.8	77	56-23-5
Chloral hydrate	16.60	0.887	2	698	705	165.4	98	302-17-0
1-Chlorobutane	13.64	0.730	2	641	642	92.6	79	106-69-3
Chlorbutol: see Chlorobutanol								
Chlorobenzene	21.90	1.170	1	844	860	112.6	131	108-90-7
Chlorobutanol	25.44	1.359	2	976	949	177.5	167	57-15-8
2-Chloro-1,1-difluoroethane	3.41	0.182	1	335	-	100.5	-10	75-68-3
2-Chloro-1,1-difluoroethylene	3.46	0.185	1	339	-	98.5	-18	359-10-4
Chlorodifluoromethane	2.90	0.155	1	258	-	86.5	-41	75-45-6
1-Chloro-2,3-epoxypropane	16.42	0.877	2	695	720	92.5	118	106-89-8
Chloroethane: see Monochloroethane								
2-Chloroethanol	13.57	0.725	2	640	643	80.5	129	107-07-3
Chloroform	11.65	0.622	2	603	605	119.4	61	67-66-3
1-Chloro-2-methylbenzene	24.96	1.336	1	956	-	126.6	159	95-49-8
1-Chloro-3-methylbenzene	25.03	1.337	1	959	-	126.6	162	108-41-8
1-Chloro-4-methylbenzene	25.05	1.343	1	960	-	126.6	162	106-43-4
2-Chlorophenol	25.83	1.380	2	992	-	128.6	175	95-57-8
1-Chloropropane	8.31	0.444	1	533	570	78.5	47	540-54-5
2-Chloro-1,1,1-trifluoroethane	3.73	0.199	1	365	375	118.5	7	75-88-7
1-Chloro-2,2,2-trifluoroethyl difluoromethyl ether: see Isoflurane								
2-Chloro-1,1,2-trifluoroethyl difluoromethyl ether: see Enflurane								
Cryofluorane: see 1,2-Dichlorotetra-fluoroethane								
Cumene		24.19	1.295	0	925	905	120.2	1 5 2 98-82-8
Cyanogen bromide	6.25	0.334	2	482	-	105.9	62	506-68-3
Cyclohexane	14.91	0.798	0	666	664	84.2	81	110-82-7
Cyclohexanol	22.77	1.219	0	874	899	100.2	161	108-93-0
Cyclohexanone	22.90	1.226	1	878	875	98.1	156	108-94-1
Cyclohexene	15.69	0.840	0	681	703	82.1	83	110-83-8
Cyclopropane	8.29	0.444	0	533	-	42.1	-33	75-19-4
Diacetone alcohol: see 4-Hydroxy-4-methyl-2-pentanone								
Diacetyl: see 2,3-Butanedione								
Dibromodifluoromethane	6.12	0.327	2	477	-	209.8	25	75-61-6
1,2-Dibromoethane	20.20	1.079	2	790	823	187.9	133	106-93-4
Dibromomethane	15.80	0.844	2	683	733	173.8	98	74-95-3
2,2-Dichloro-1,1-difluoroethyl methyl ether: see Methoxyflurane								
Dichlorodifluoromethane	3.18	0.170	2	313	305	120.9	-30	75-71-8
1,1-Dichloroethane	9.57	0.511	2	559	563	99.0	58	75-34-3
1,2-Dichloroethane	13.09	0.699	2	630	631	99.0	83	107-06-2
1,1-Dichloroethylene	7.28	0.389	2	512	-	96.9	61	156-59-2

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
1,2-Dichloroethylene (both isomers)	9.19	0.491	2	552	556	96.9	60	540-59-0
Dichloromethane	7.45	0.398	2	515	515	84.9	40	75-09-2
1,2-Dichloropropane	15.87	0.848	1	684	-	113.0	96	78-87-5
1,3-Dichloropropane	19.20	1.026	2	765	-	113.0	122	142-28-9
1,3-Dichloro-2-propanol	22.74	1.215	2	873	885	129.0	174	96-23-1
1,2-Dichlorotetrafluoroethane	3.59	0.192	2	352	361	170.9	4	76-14-2
Diethylamine	9.53	0.510	0	559	-	73.1	56	109-89-7
Diethyl ether	6.69	0.358	0	499	515	74.1	35	60-29-7
Diethyl ketone: see 3-Pentanone								
1,1-Difluoroethane	2.84	0.152	1	242	-	66.1	-25	75-37-6
1,1-Difluorotetrachloroethane	16.77	0.896	2	702	785	203.8	92	76-11-9
1,2-Difluorotetrachloroethane	16.90	0.903	2	704	730	203.8	93	76-12-0
Diisopropyl ether	11.43	0.612	0	598	594	102.2	69	108-20-3
Dimethoxymethane: see Methylal								
N,N-Dimethylacetamide	21.61	1.157	0	835	-	87.1	167	127-19-5
Dimethyl disulphide: see Methyl disulphide								
Dimethyl ether	3.34	0.179	0	328	-	46.1	-24	115-10-6
N,N-Dimethylformamide	18.47	0.989	0	746	-	73.1	153	68-12-2
2,5-Dimethylfuran	16.53	0.885	1	697	697	96.1	94	625-86-5
Dimethyl ketone: see Acetone								
2,2-Dimethylpropane	4.32	0.231	0	409	-	72.2	10	463-82-1
2,6-Dimethylpyridine	22.62	1.211	0	869	-	107.1	144	108-48-5
Dimethyl sulphide: see Methyl sulphide								
Dimethyl sulphoxide	19.97	1.069	0	784	-	78.1	191	67-68-5
Dinitrogen monoxide: see Nitrous oxide								
Dipropyl ketone: See 4-Heptanone								
Dioxane	16.16	0.865	0	690	696	88.1	101	123-91-1
1,3-Dioxolane	11.13	0.596	0	592	635	74.1	76	646-06-0
DME: see Dimethyl ether								
DMF: see Dimethylformamide								
DMSO: see Dimethyl sulphoxide								
Enflurane	6.14	0.328	2	478	462	184.5	57	13838-16-9
Epibromohydrin: see 1-Bromo-2,3-epoxypropane								
Epichlorohydrin: see 1-Chloro-2,3-epoxypropane								
1,2-Epoxybutane	10.63	0.569	0	582	600	72.1	65	106-88-7
Ethane	2.69	0.144	0	*200*	*200*	30.1	-88	74-84-0
Ethanol	4.80	0.257	0	427	421	46.1	79	64-17-5
Ethanolamine[2]	13.75	0.736	0	643	780	61.1	70	141-43-5
2-Ethoxyethanol	16.38	0.877	0	694	701	90.1	135	110-80-5
2-Ethoxyethyl acetate	22.83	1.222	0	876	874	132.2	156	111-15-9
Ethyl acetate	11.42	0.611	0	598	596	88.1	77	141-78-6
Ethylamine	4.30	0.230	0	408	-	45.1	17	75-04-7
Ethylbenzene	22.38	1.198	0	861	860	106.2	136	100-41-4
Ethyl cellosolve: see 2-Ethoxyethanol								

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Ethyl chloride: see Monochloroethane								
Ethylene	2.63	0.141	0	165	-	28.1	-104	74-85-1
Ethylene chlorohydrin: see 2-Chloroethanol								
Ethylene glycol[2]	15.15	0.811	0	670	772	62.1	198	107-21-1
Ethylene glycol monobutyl ether: see 2-Butoxyethanol								
Ethylene oxide	4.22	0.226	0	405	400	44.1	11	75-21-8
Ethyl formate	6.82	0.365	0	521	545	74.1	53	109-94-4
Ethyl iodide: see Iodoethane								
4-Ethylmorpholine	22.68	1.214	0	871	-	115.2	139	100-74-3
Ethyl propionate	16.42	0.879	0	695	679	102.1	99	105-37-3
Ethyl propyl ketone: see 3-Hexanone								
FC 11: see Fluorotrichloromethane								
FC 12: see Dichlorodifluoromethane								
FC 12B1: see Bromochlorodifluoromethane								
FC 22: see Chlorodifluoromethane								
FC 112: see 1,2-Difluorotetrachloroethane								
FC 113: see 1,1,1-Trichlorotrifluoroethane								
FC 114: see 1,2-Dichlorotetrafluoroethane								
FC 134a: see 1,1,1,2-Tetrafluoroethane								
FC 142: see 1-Chloro-2,2-difluoroethane								
FC 152a: see 1,1-Difluoroethane								
Fluoromethyl 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether: see Sevoflurane								
Fluorotrichloromethane	6.13	0.327	2	478	484	137.4	24	75-69-4
Formaldehyde	2.86	0.153	0	247	-	30.0	-20	50-00-0
Formaldehyde dimethyl acetal: see Methylal								
Furfural	20.74	1.108	1	806	825	96.1	162	98-01-1
Halothane	8.76	0.468	2	543	533	197.4	50	151-67-7
2,2,3,3,4,4,4-Heptafluoro-1-butanol	9.25	0.494	2	553	-	200.1	103	375-01-
Heptanal	23.05	1.234	0	883	883	114.2	153	111-71-7
Heptane	16.70	0.894	0	*700*	*700*	100.2	98	142-82-5
1-Heptanol	24.88	1.332	0	953	955	116.2	176	111-70-6
2-Heptanone	22.79	1.220	0	874	880	114.2	152	110-43-0
3-Heptanone	22.62	1.211	0	869	-	114.2	148	106-35-4
4-Heptanone	22.27	1.192	0	857	857	114.2	144	123-19-3
1-Heptene	16.18	0.866	0	690	-	98.2	94	592-76-7
Hexahydroindan: see Bicyclo(4.3.0)nonane								
Hexanal		19.82	1.061	0	781	-	100.2	1 3 0 66-25-1
Hexane	11.51	0.616	0	*600*	*600*	86.2	69	110-54-3
2,5-Hexanedione	23.25	1.242	1	890	894	114.1	188	110-13-4
1-Hexanol	22.12	1.184	0	852	860	102.2	157	111-27-3
2-Hexanol	19.95	1.068	0	784	786	102.2	140	626-93-7
2-Hexanone	19.45	1.041	0	771	787	100.2	127	591-78-6
3-Hexanone	19.33	1.035	0	768	781	100.2	124	589-38-8
1-Hexene	10.89	0.583	0	587	-	84.2	64	592-41-6

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Hexyl acetate	25.83	1.383	0	992	-	144.2	170	142-92-7
Hexyl formate	23.84	1.276	0	911	-	130.2	155	629-33-4
4-Hydroxy-4-methyl-2-pentanone	21.17	1.131	1	820	821	116.2	168	123-42-2
1-Iodobutane	20.91	1.117	2	811	840	184.0	130	542-69-8
Iodoethane	11.55	0.617	2	601	680	156.0	72	75-03-6
Iodomethane	7.13	0.381	2	509	515	142.0	43	74-88-4
1-Iodopropane	16.90	0.903	2	705	785	170.0	102	107-08-4
Isoamyl ... : see Isopentyl ...								
Isobutane	3.61	0.193	0	354	370	58.1	-12	75-28-5
Isobutanol: see 2-Methyl-1-propanol								
Isobutyl acetate	19.00	1.017	0	759	754	116.2	118	110-19-0
Isobutylamine	10.95	0.586	0	588	-	73.1	69	78-81-9
Isobutyl nitrite	10.37	0.555	2	576	-	103.1	67	542-56-3
Isoflurane	5.52	0.295	2	454	-	184.5	49	26675-46-7
Isooctane	16.31	0.873	0	692	725	114.2	99	540-84-1
Isopentyl acetate	22.34	1.196	0	859	884	130.2	142	123-92-2
Isopentyl alcohol: see 3-Methyl-1-butanol								
Isopentylamine	16.42	0.879	0	695	-	87.2	95	107-85-7
Isopentyl nitrite (“amyl nitrite”)	15.87	0.848	2	684	680	117.2	98	110-46-3
Isoprene	6.91	0.370	0	504	-	68.1	34	78-79-5
Isopropanol: see 2-Propanol								
Isopropyl acetate	14.10	0.755	0	650	648	102.1	89	108-21-4
Isopropylacetone: see Methyl isobutyl ketone								
Isopropyl formate	9.55	0.511	0	559	567	88.1	68	625-55-8
Isopropyl nitrate	14.84	0.793	2	664	693	105.1	103	1712-64-7
Isovaleraldehyde: see 3-Methylbutanal								
Limonene	25.69	1.375	0	986	1053	136.2	177	138-86-3
MEK: see Butanone								
Meparfynol: see 3-Methylpent-1-yn-3-ol								
2-Mercaptoethanol	17.63	0.942	1	724	795	78.1	158	60-24-2
Methane	2.52	0.135	0	*100*	*100*	16.0	-161	74-82-8
Methanol	3.60	0.192	0	353	491	32.0	65	67-56-1
2-Methoxyethanol	12.38	0.663	0	617	616	76.1	124	109-86-4
Methoxyflurane	17.04	0.910	2	617	701	165.0	105	76-38-0
Methyl acetate	7.30	0.391	0	512	513	74.1	57	79-20-9
Methylal	7.08	0.379	0	508	505	76.1	42	109-87-5
Methyl bromide: see Bromomethane								
2-Methylbuta-1,3-diene: see Isoprene								
3-Methylbutanal	13.43	0.719	0	637	-	86.1	93	590-86-3
2-Methyl-1-butanol	17.63	0.944	0	724	-	88.2	128	137-32-6
2-Methyl-2-butanol	12.96	0.694	0	628	636	88.2	103	75-85-4
3-Methyl-1-butanol	17.45	0.934	0	719	720	88.2	132	123-51-3
3-Methyl-2-butanone: see Methyl isopropyl ketone								

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Methyl *tert.*-butyl ether	9.60	0.514	0	560	-	88.2	55	1634-04-4
Methyl butyl ketone: see 2-Hexanone								
Methyl butyrate	16.94	0.907	0	706	723	102.1	102	623-42-7
Methyl cellosolve: see 2-Methoxyethanol								
Methylchloroform: see 1,1,1-Trichloroethane								
Methyl cyanide: see Acetonitrile								
Methylcyclohexane	17.82	0.954	0	729	748	98.2	101	108-87-2
Methylcyclopentane	13.11	0.702	0	631	650	84.2	73	96-37-7
Methyl cyclopropyl ketone	16.85	0.902	0	704	730	84.1	114	765-43-5
Methyl disulphide	18.07	0.965	1	735	-	94.2	110	624-92-0
Methylene chloride: see Dichloromethane								
Methyl ethyl ketone: see Butanone								
Methyl formate	4.28	0.229	0	407	499	60.1	32	107-31-3
6-Methylhept-5-en-2-one	25.24	1.351	0	968	-	126.2	58	110-93-0
2-Methyl-1-hexene	16.05	0.859	0	687	725	98.2	92	6094-02-6
Methyl hexanoate	25.50	1.365	0	978	-	130.2	151	106-70-7
Methyl iodide: see Iodomethane								
Methyl isobutyl ketone	17.60	0.942	1	723	724	100.2	118	108-10-1
Methyl isopropyl ketone	13.71	0.734	1	642	650	86.0	93	563-80-4
Methyl methacrylate	16.48	0.882	0	696	699	100.1	100	80-62-6
2-Methylpentane	9.90	0.530	0	566	610	86.2	60	107-83-5
3-Methylpentane	10.61	0.568	0	581	-	86.2	64	96-14-0
2-Methyl-2-pentanol	17.45	0.934	0	719	725	102.2	124	590-36-3
4-Methyl-2-pentanone: see Methyl isobutyl ketone								
Methylpentynol: see 3-Methylpent-1-yn-3-ol								
3-Methylpent-1-yn-3-ol	16.42	0.879	0	695	715	98.1	121	77-75-8
2-Methylpropanal	8.46	0.453	0	536	-	72.1	64	74-84-2
2-Methylpropane: see Isobutane								
2-Methyl-1-propanol	12.22	0.654	0	614	619	74.1	108	78-83-1
2-Methyl-2-propanol	7.14	0.382	0	509	512	74.1	82	75-65-0
Methyl propionate	12.33	0.660	0	616	639	88.1	80	554-12-1
2-Methylpropylamine: see Isobutylamine								
Methyl propyl ketone: see 2-Pentanone								
1-Methylpyrrole	17.56	0.940	0	722	715	81.1	111	96-54-8
Methyl sulphide	7.12	0.381	0	508	-	62.1	36	75-18-3
MIBK: see Methyl isobutyl ketone								
Monochloroethane	4.77	0.255	2	426	447	64.5	12	75-00-3
Morpholine	19.77	1.056	1	779	800	87.1	129	110-91-8
MTBE: see Methyl *tert.*-butyl ether								
Neopentane: see 2,2-Dimethylpropane								
Nitroethane	12.47	0.666	2	618	655	75.1	115	79-24-3
Nitromethane	7.98	0.427	1	526	565	61.0	101	75-52-5
1-Nitropropane	17.00	0.907	2	708	725	89.1	132	108-03-2
2-Nitropropane	15.27	0.816	2	672	685	89.1	120	79-46-9

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Nitrous oxide	2.66	0.142	2	182	-	44.0	-88	10024-97-2
Nonane	23.56	1.261	0	*900*	*900*	128.3	151	111-84-2
Octanal	25.70	1.376	0	986	990	128.2	68	124-13-0
Octane	20.57	1.101	0	*800*	*800*	114.2	126	111-65-9
2-Octanol	25.65	1.373	0	984	-	130.2	179	123-93-6
2-Octanone	25.39	1.359	0	974	-	128.2	173	111-13-7
3-Octanone	25.29	1.354	0	970	-	128.2	169	106-68-3
4-Octanone	24.99	1.338	0	958	-	128.2	164	
1-Octene	20.17	1.080	0	790	790	112.2	122	111-66-0
2-Octyne	22.57	1.208	0	867	870	110.2	138	
Paraldehyde	19.28	1.032	0	767	771	132.2	124	123-63-7
2,3-Pentanedione	15.37	0.821	1	674	681	100.1	115	600-14-6
2,4-Pentanedione	19.17	1.026	0	764	790	100.1	141	123-54-6
Pentanal	15.50	0.830	0	677	-	86.1	103	110-62-3
Pentane	6.72	0.360	0	*500*	*500*	72.2	36	109-66-0
1-Pentanol	18.74	1.003	0	753	763	88.2	138	71-41-0
2-Pentanone	15.07	0.807	1	669	680	86.1	102	107-87-9
3-Pentanone	15.58	0.834	1	678	683	86.1	102	96-22-0
1-Pentene	6.28	0.336	0	483	-	70.1	30	109-67-1
Pentyl acetate	23.31	1.248	0	892	-	130.2	149	628-63-7
Pentyl formate	20.87	1.117	0	810	772	116.1	132	638-49-3
tert.-Pentyl alcohol: see 2-Methyl-2-butanol								
Perchloroethylene: see Tetrachloroethylene								
Perfluoropropane	6.08	0.325	2	476	-	188.0	-39	76-19-7
Phenylamine: see Aniline								
alpha-Pinene	24.81	1.328	0	950	942	136.2	156	80-56-8
Piperidine	18.81	1.007	1	755	782	85.2	106	110-89-4
Propanal	5.77	0.309	0	464	-	58.1	49	123-38-6
Propane	3.05	0.163	0	*300*	*300*	44.1	-42	74-98-6
1,2-Propanediol[2]	17.09	0.915	0	710	745	76.1	187	57-55-6
1,3-Propanediol[2]	20.29	1.086	0	793	820	76.1	214	504-63-2
1-Propanol	8.61	0.461	0	539	571	60.1	97	71-23-8
2-Propanol	6.04	0.323	0	474	530	60.1	83	67-63-0
Propanone: see Acetone								
Propionaldehyde: see Propanal								
Propionitrile	8.57	0.459	0	539	580	55.1	97	107-12-1
Propyl acetate	16.51	0.884	0	696	696	102.1	102	109-60-4
Propylamine	7.60	0.407	0	518	-	59.1	49	107-10-8
Propyl bromide: see 1-Bromopropane								
Propyl chloride: see 1-Chloropropane								
Propylene	2.99	0.160	0	283	310	42.1	-48	115-07-1
Propyl formate	11.84	0.634	0	606	603	88.1	81	110-74-7
Propyl iodide: see 1-Iodopropane								
Pyridine	17.65	0.945	0	725	725	79.1	115	110-86-1
Pyrrole	17.97	0.962	0	733	755	67.1	130	109-97-7
Pyrrolidine	15.21	0.814	0	671	695	71.1	89	123-75-1

(a) Alphabetical order (continued)

Compound	RT	RRT	ECD	Retention Index Calc	Retention Index Lit	FM	BPt	CAS No
Styrene	23.18	1.241	0	887	890	104.1	145	100-42-5
Sevoflurane	4.32	0.231	1	409	-	200.1	24	28523-86-6
Sulphur hexafluoride	2.58	0.138	2	135	-	146.1	-64	2551-62-4
1,1,2,2-Tetrabromoethane 79-27-6		25.50	1.362	2	978	-	345.7	2 2 9
1,1,1,2-Tetrachloroethane	21.85	1.167	2	843	870	167.9	131	630-20-6
1,1,2,2-Tetrachloroethane	23.33	1.246	2	892	905	167.9	146	79-34-5
Tetrachloroethylene	20.89	1.116	2	811	807	165.9	121	127-18-4
Tetrachloromethane: see Carbon tetrachloride								
1,1,1,2-Tetrafluoroethane	2.76	0.148	1	219	-	102.0	-27	811-97-2
Tetrahydrofuran	12.31	0.659	0	615	638	72.1	66	109-99-9
THF: see Tetrahydrofuran								
Toluene	19.14	1.025	0	763	768	92.1	111	108-88-3
Tribromomethane: see Bromoform								
1,1,1-Trichloroethane	13.56	0.724	2	639	634	133.4	74	71-55-6
1,1,2-Trichloroethane	18.72	1.000	2	752	727	133.4	113	79-00-5
2,2,2-Trichloroethanol	22.29	1.191	2	858	859	149.4	151	115-20-8
Trichloroethylene	16.25	0.868	2	691	710	131.4	87	79-01-6
Trichloromethane: see Chloroform								
1,1,1-Trichloro-2-methyl-2-propanol: see Chlorobutanol								
1,2,3-Trichloropropane	23.53	1.257	2	899	910	147.4	156	96-18-4
1,1,1-Trichloro-2-propanol	23.85	1.274	2	912	920	163.4	162	76-00-6
1,1,1-Trichlorotrifluoroethane	8.01	0.428	2	527	530	187.4	46	354-58-5
1,1,2-Trichlorotrifluoroethane	7.96	0.425	2	526	555	187.4	48	76-13-1
Triethylamine	15.84	0.848	0	684	-	101.2	90	121-44-8
2,2,2-Trifluoroethanol	5.17	0.276	1	441	580	100.0	75	75-89-8
2,2,2-Trifluoroethyl chloride: see 2-Chloro-1,1,1-trifluoroethane								
Trifluoromethyl bromide: see Bromotrifluoromethane								
Trimethylene: see Cyclopropane								
2,2,4-Trimethylpentane: see Isooctane								
Valeraldehyde: see Pentanal								
gamma-Valerolactone	23.98	1.281	1	917	921	100.1	218	108-29-2
Vinyl chloride	6.10	0.326	2	476	440	62.5	-14	75-01-4
Vinylidine chloride	7.24	0.387	2	511	515	97.0	32	75-35-4
meta-Xylene	22.62	1.211	0	869	871	106.2	138	108-38-3
ortho-Xylene	23.32	1.250	0	892	895	106.2	144	95-47-6
para-Xylene	22.66	1.213	0	870	870	106.2	138	106-42-3

(b) Retention time order

Compound	RT	RRT	ECD
Methane	2.52	0.135	0
Sulphur hexafluoride	2.58	0.138	2
Acetylene	2.63	0.141	0
Ethylene	2.63	0.141	0
Nitrous oxide	2.66	0.142	2
Ethane	2.69	0.144	0
1,1,1,2-Tetrafluoroethane	2.76	0.148	1
Bromotrifluoromethane	2.77	0.148	2
1,1-Difluoroethane	2.84	0.152	1
Formaldehyde	2.85	0.153	0
Chlorodifluoromethane	2.90	0.155	1
Propylene	2.99	0.160	0
Propane	3.05	0.163	0
Dichlorodifluoromethane	3.18	0.170	2
Dimethyl ether	3.34	0.179	0
2-Chloro-1,1-difluoroethane	3.41	0.182	1
2-Chloro-1,1-difluoroethylene	3.46	0.185	2
Acetaldehyde	3.59	0.192	0
1,2-Dichlorotetrafluoroethane	3.59	0.192	2
Methanol	3.60	0.192	0
Isobutane	3.61	0.193	0
2-Chloro-1,1,1-trifluoroethane	3.73	0.199	2
1-Butene	3.94	0.211	0
1,3-Butadiene	4.04	0.215	0
Bromochlorodifluoromethane	4.07	0.217	2
Butane	4.09	0.219	0
Ethylene oxide	4.22	0.226	0
Methyl formate	4.28	0.229	0
Ethylamine	4.30	0.230	0
2,2-Dimethylpropane	4.32	0.231	0
Sevoflurane	4.32	0.231	1
Bromomethane	4.47	0.239	2
Monochloroethane	4.77	0.255	2
Ethanol	4.80	0.257	0
2,2,2-Trifluoroethanol	5.17	0.276	1
Acetonitrile	5.22	0.279	0
Isoflurane	5.52	0.295	2
Acetone	5.66	0.303	1
Propanal	5.77	0.309	0
2-Propanol	6.04	0.323	0
Perfluoropropane	6.08	0.325	2
Vinyl chloride	6.10	0.326	2
Dibromodifluoromethane	6.12	0.327	2
Fluorotrichloromethane	6.13	0.327	2
Enflurane	6.14	0.328	2
Cyanogen bromide	6.25	0.334	2
1-Pentene	6.28	0.336	0
Acrylonitrile	6.50	0.348	0
Diethyl ether	6.69	0.358	0
Pentane	6.72	0.360	0

(b) Retention time order (continued)

Compound	RT	RRT	ECD
Ethyl formate	6.82	0.365	0
Isoprene	6.91	0.370	0
Methylal	7.08	0.379	0
Methyl sulphide	7.12	0.381	0
Iodomethane	7.13	0.381	2
2-Methyl-2-propanol	7.14	0.382	0
Vinylidine chloride	7.24	0.387	2
1,1-Dichloroethylene	7.28	0.389	2
Methyl acetate	7.30	0.391	0
Dichloromethane	7.45	0.398	2
Propylamine	7.60	0.407	0
1,1,2-Trichlorotrifluoroethane	7.96	0.425	2
Nitromethane	7.98	0.427	1
1,1,1-Trichlorotrifluoroethane	8.01	0.428	2
Carbon disulphide	8.03	0.429	1
Cyclopropane	8.29	0.444	0
1-Chloropropane	8.31	0.444	1
2-Methylpropanal	8.46	0.453	0
Propionitrile	8.57	0.459	0
1-Propanol	8.61	0.461	0
Halothane	8.76	0.468	2
1,2-Dichloroethylene (both isomers)	9.19	0.491	2
2,2,3,3,4,4,4-Heptafluoro-1-butanol	9.25	0.494	2
Diethylamine	9.53	0.510	0
Isopropyl formate	9.55	0.511	0
1,1-Dichloroethane	9.57	0.511	2
Methyl *tert.*-butyl ether	9.60	0.514	0
2,3-Butanedione	9.72	0.519	2
2-Methylpentane	9.90	0.530	0
Butanal	9.98	0.534	0
Butanone	10.18	0.545	1
Isobutyl nitrite	10.37	0.555	2
3-Methylpentane	10.61	0.568	0
1,2-Epoxybutane	10.63	0.569	0
2-Butanol	10.80	0.578	0
1-Hexene	10.89	0.583	0
Isobutylamine	10.95	0.586	0
1,3-Dioxolane	11.13	0.596	0
Bromochloromethane	11.40	0.609	2
Ethyl acetate	11.42	0.611	0
Diisopropyl ether	11.43	0.612	0
Hexane	11.51	0.616	0
Iodoethane	11.55	0.617	2
Chloroform	11.65	0.622	2
Propyl formate	11.84	0.634	0
2-Methyl-1-propanol	12.22	0.654	0
1-Bromopropane	12.24	0.654	2
Tetrahydrofuran	12.31	0.659	0
Methyl propionate	12.33	0.660	0

(b) Retention time order (continued)

Compound	RT	RRT	ECD
2-Methoxyethanol	12.38	0.663	0
Butyl nitrite	12.41	0.663	2
Nitroethane	12.47	0.666	2
2-Methyl-2-butanol	12.96	0.694	0
1,2-Dichloroethane	13.09	0.699	2
Methylcyclopentane	13.11	0.702	0
3-Methylbutanal	13.43	0.719	0
1,1,1-Trichloroethane	13.56	0.724	2
2-Chloroethanol	13.57	0.725	2
1-Chlorobutane	13.64	0.730	2
Methyl isopropyl ketone	13.71	0.734	1
Ethanolamine[2]	13.75	0.736	0
1-Butanol	14.08	0.754	0
Isopropyl acetate	14.10	0.755	0
Benzene	14.39	0.770	0
Carbon tetrachloride	14.70	0.785	2
Isopropyl nitrate	14.84	0.793	2
Cyclohexane	14.91	0.798	0
2-Pentanone	15.07	0.807	1
Ethylene glycol[2]	15.15	0.811	0
Pyrrolidine	15.21	0.814	0
2-Nitropropane	15.27	0.816	2
2,3-Pentanedione	15.37	0.821	1
Pentanal	15.50	0.830	0
3-Pentanone	15.58	0.834	1
Cyclohexene	15.69	0.840	0
Dibromomethane	15.80	0.844	2
Triethylamine	15.84	0.848	0
1,2-Dichloropropane	15.87	0.848	1
Isopentyl nitrite (“amyl nitrite”)	15.87	0.848	2
2-Methyl-1-hexene	16.05	0.859	0
Bromodichloromethane	16.16	0.863	2
Dioxane	16.16	0.865	0
1-Heptene	16.18	0.866	0
Trichloroethylene	16.25	0.868	2
Iso-octane	16.31	0.873	0
2-Ethoxyethanol	16.38	0.877	0
1-Chloro-2,3-epoxypropane	16.42	0.877	2
Ethyl propionate	16.42	0.879	0
Isopentylamine	16.42	0.879	0
3-Methylpent-1-yn-3-ol	16.42	0.879	0
Methyl methacrylate	16.48	0.882	0
Propyl acetate	16.51	0.884	0
2,5-Dimethylfuran	16.53	0.885	1
Chloral hydrate	16.60	0.887	2
Heptane	16.70	0.894	0
1,1-Difluorotetrachloroethane	16.77	0.896	2
Methyl cyclopropyl ketone	16.85	0.902	0
1,2-Difluorotetrachloroethane	16.90	0.903	2

(b) Retention time order (continued)

Compound	RT	RRT	ECD
1-Iodopropane	16.90	0.903	2
Methyl butyrate	16.94	0.907	0
1-Nitropropane	17.00	0.907	2
Butyl formate	17.02	0.911	0
Methoxyflurane	17.04	0.910	2
1,2-Propanediol[2]	17.09	0.915	0
3-Methyl-1-butanol	17.45	0.934	0
2-Methyl-2-pentanol	17.45	0.934	0
1-Methylpyrrole	17.56	0.940	0
Methyl isobutyl ketone	17.60	0.942	1
2-Mercaptoethanol	17.63	0.942	1
2-Methyl-1-butanol	17.63	0.944	0
Bromoacetonitrile	17.65	0.943	2
Pyridine	17.65	0.945	0
Methylcyclohexane	17.82	0.954	0
Pyrrole	17.97	0.962	0
Methyl disulphide	18.07	0.965	1
N,N-Dimethylformamide	18.47	0.989	0
1,1,2-Trichloroethane	18.72	1.000	2
1-Pentanol	18.74	1.003	0
Piperidine	18.81	1.007	1
Bromotrichloromethane	18.98	1.014	2
Isobutyl acetate	19.00	1.017	0
Toluene	19.14	1.025	0
2,4-Pentanedione	19.17	1.026	0
1,3-Dichloropropane	19.20	1.026	2
Paraldehyde	19.28	1.032	0
3-Hexanone	19.33	1.035	0
2-Hexanone	19.45	1.041	0
1-Bromo-2,3-epoxypropane	19.54	1.044	2
Morpholine	19.77	1.056	1
Hexanal	19.82	1.061	0
2-Hexanol	19.95	1.068	0
Dimethyl sulphoxide	19.97	1.069	0
1-Octene	20.17	1.080	0
1,2-Dibromoethane	20.20	1.079	2
1,3-Propanediol[2]	20.29	1.086	0
Butyl acetate	20.36	1.090	0
Octane	20.57	1.101	0
Furfural	20.74	1.108	1
Pentyl formate	20.87	1.117	0
Tetrachloroethylene	20.89	1.116	2
1-Iodobutane	20.91	1.117	2
4-Hydroxy-4-methyl-2-pentanone	21.17	1.131	1
N,N-Dimethylacetamide	21.61	1.157	0
1,1,1,2-Tetrachloroethane	21.85	1.167	2
Chlorobenzene	21.90	1.170	1
1-Hexanol	22.12	1.184	0
4-Heptanone	22.27	1.192	0
2,2,2-Trichloroethanol	22.29	1.191	2
Allyl isothiocyanate	22.31	1.192	2

(b) Retention time order (continued)

Compound	RT	RRT	ECD
Isopentyl acetate	22.34	1.196	0
Ethylbenzene	22.38	1.198	0
2-Octyne	22.57	1.208	0
Allyl glycidyl ether	22.62	1.211	0
2,6-Dimethylpyridine	22.62	1.211	0
3-Heptanone	22.62	1.211	0
meta-Xylene	22.62	1.211	0
para-Xylene	22.66	1.213	0
4-Ethylmorpholine	22.68	1.214	0
1,3-Dichloro-2-propanol	22.74	1.215	2
Cyclohexanol	22.77	1.219	0
2-Heptanone	22.79	1.220	0
Bromoform	22.82	1.219	2
2-Ethoxyethyl acetate	22.83	1.222	0
Cyclohexanone	22.90	1.226	1
Heptanal	23.05	1.234	0
Styrene	23.18	1.241	0
2,5-Hexanedione	23.25	1.242	1
Pentyl acetate	23.31	1.248	0
ortho-Xylene	23.32	1.250	0
1,1,2,2-Tetrachloroethane	23.33	1.246	2
2-Butoxyethanol	23.39	1.244	0
1,2,3-Trichloropropane	23.53	1.257	2
Nonane	23.56	1.261	0
Hexyl formate	23.84	1.276	0
1,1,1-Trichloro-2-propanol	23.85	1.274	2
gamma-Valerolactone	23.98	1.281	1
Cumene	24.19	1.295	0
Bromobenzene	24.45	1.306	2
Benzaldehyde	24.75	1.325	0
alpha-Pinene	24.81	1.328	0
1-Heptanol	24.88	1.332	0
1-Chloro-2-methylbenzene	24.96	1.336	1
4-Octanone	24.99	1.338	0
1-Chloro-3-methylbenzene	25.03	1.337	1
1-Chloro-4-methylbenzene	25.05	1.343	1
Aniline	25.13	1.345	0
Benzonitrile	25.16	1.347	0
6-Methylhept-5-en-2-one	25.24	1.351	0
3-Octanone	25.29	1.354	0
2-Octanone	25.39	1.359	0
Chlorobutanol	25.44	1.359	2
Bicyclo(4.3.0)nonane	25.48	1.364	0
Methyl hexanoate	25.50	1.365	0
1,1,2,2-Tetrabromoethane	25.50	1.362	2
2-Octanol	25.65	1.373	0
Limonene	25.69	1.375	0
Octanal	25.70	1.376	0
2-Chlorophenol	25.83	1.380	2
Hexyl acetate	25.83	1.383	0

Notes

RT	Retention time (min)
RRT	Retention time relative to 1,1,2-trichloroethane (on the ECD channel for compounds responding on that channel)
ECD	Relative ECD response (0 = nil, 1 = poor, 2 = good)
Retention index	calc = calculated on the SPB-1 system lit = literature value on SE 30/OV-1/OV-101 (Ramsey & Flanagan 1982; Ardrey et al. 1985)
FM	Formula mass
BPt	Boiling point (°C, atmospheric pressure)
CAS No	Chemical Abstracts Registry number
1	BPt at 24 mm Hg pressure
2	Compounds injected as liquids