Handling. Suitable precautions should be taken to avoid skin contact with dimethylformamide as it can penetrate skin and produce systemic toxicity.

Malignant neoplasms. There have been reports of testicular cancer in men occupationally exposed to dimethylformamide.[1] Such an association could not, however, be substantiated by epidemiological data[2] on 3859 male employees exposed to dimethylformamide between 1950 and 1970 and followed up to 1984. It has been suggested that although dimethylformamide may not itself be carcinogenic, it may increase absorption through the skin of heavy metal carcinogens, possibly including chromates.[3]

1. Levin SM, *et al.* Testicular cancer in leather tanners exposed to dimethylformamide. *Lancet* 1987; **ii:** 1153.
2. Chen JL, Kennedy GL. Dimethylformamide and testicular cancer. *Lancet* 1988; **i:** 55.
3. Ducatman AM. Dimethylformamide, metal dyes, and testicular cancer. *Lancet* 1989; **i:** 911.

Pharmacokinetics
Dimethylformamide is absorbed after inhalation and through intact skin. It is excreted mainly in the urine as metabolites.

Uses
Dimethylformamide is used as an industrial solvent.

Dioxan

Diethylene Dioxide; Diethylene Ether; Dioksan; Dioxane; Dioxano. 1,4-Dioxane.

Диоксан

$C_4H_8O_2$ = 88.11.
CAS — 123-91-1.

NOTE. Do not confuse dioxan and dioxin (p.2295).

Description. Dioxan is a colourless flammable liquid with an ethereal odour. Wt per mL about 1.03 g. B.p. about 101°. Store in airtight containers.

Stability. It is dangerous to distil or evaporate dioxan unless precautions have been taken to remove explosive peroxides.

Adverse Effects, Treatment, and Precautions
Dioxan vapour is irritant to mucous membranes. High concentrations may cause nausea and vomiting, and CNS depression with headache, dizziness, drowsiness, and in severe cases unconsciousness. On repeated exposure, severe hepatic and renal damage, including necrotic changes, can occur and may be fatal. Direct contact with liquid dioxan can result in dermatitis. Dioxan has been shown to be carcinogenic in *animals.*

Treatment consists of removal from exposure and general supportive and symptomatic measures.

Handling. Suitable precautions should be taken to avoid skin contact with dioxan as it can penetrate skin and produce systemic toxicity.

Pharmacokinetics
Dioxan is absorbed after inhalation and through the skin. It is metabolised by oxidation to β-hydroxyethoxy-acetic acid.

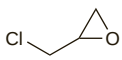
Uses
Dioxan is used as an industrial solvent.

Epichlorohydrin

Epiclorhidrina. 1-Chloro-2,3-epoxypropane.

Эпихлоргидрин

C_3H_5ClO = 92.52.
CAS — 106-89-8.



Description. Epichlorohydrin is a colourless, flammable liquid. Wt per mL about 1.18 g. B.p. 115° to 118°. Store in airtight containers.

Stability. The vapour of epichlorohydrin forms explosive mixtures with air. Harmful gases including phosgene are liberated on heating of epichlorohydrin.

Adverse Effects and Precautions
Epichlorohydrin is irritant. It has been shown to be carcinogenic in *animals*.

◊ References to the toxicity of epichlorohydrin.

1. WHO. Epichlorohydrin. *Environmental Health Criteria 33*. Geneva: WHO, 1984. Available at: http://www.inchem.org/documents/ehc/ehc/ehc33.htm (accessed 30/06/04)
2. WHO. Epichlorohydrin health and safety guide. *IPCS Health and Safety Guide 8.* Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/hsg/hsg/hsg008.htm (accessed 30/06/04)
3. Health and Safety Executive. Ammonia, 1-chloro-2,3-epoxypropane (epichlorohydrin), carcinogenicity of cadmium and its compounds. *Toxicity Review 24.* London: HMSO, 1991.
4. Kolman A, *et al.* Genotoxic effects of ethylene oxide, propylene oxide and epichlorohydrin in humans: update review (1990–2001). *Mutat Res* 2002; **512:** 173–94.

Handling. Suitable precautions should be taken to avoid skin contact with epichlorohydrin as it can penetrate skin and produce systemic toxicity.

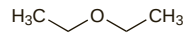
Uses
Epichlorohydrin is used as an industrial solvent.

Solvent Ether

Aether; Aether Aethylicus; Aether Solvens; Diethyl Ether; Eetteri; Éter; Eter; Éter disolvente; Eteris; Éther; Ether; Éther rectifié; Ethyl Ether; Ethyl Oxide.

Диэтиловый Эфир; Этиловый Эфир

$(C_2H_5)_2O$ = 74.12.
CAS — 60-29-7.



NOTE. Solvent ether is not intended for anaesthesia; only ether of a suitable quality (see p.1783) should be so used.

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US.*

Ph. Eur. 6.2 (Ether). A colourless, clear, volatile, highly flammable liquid. It may contain a suitable non-volatile antoxidant at a suitable concentration. Relative density 0.714 to 0.716. Distillation range 34° to 35°. Soluble in water; miscible with alcohol, with dichloromethane, and with fatty oils. Store at 8° to 15° in airtight containers. Protect from light.

USP 31 (Ether). A colourless, mobile, volatile, flammable liquid, having a characteristic sweet, pungent odour. It is slowly oxidised by the action of air and light, with the formation of peroxides. B.p. about 35°. Sp. gr. 0.713 to 0.716. Soluble 1 in 12 of water; miscible with alcohol, with chloroform, with dichloromethane, with petroleum spirit, with benzene, and with fixed and volatile oils; soluble in hydrochloric acid. Store in partly filled airtight containers at a temperature not exceeding 30° and remote from fire. Protect from light.

Stability. Though ether is one of the lightest of liquids, its vapour is very heavy, being 2⁄ times heavier than air.

Ether is very volatile and flammable and mixtures of its vapour with oxygen, nitrous oxide, or air at certain concentrations are explosive. It should not be used in the presence of an open flame or any electrical apparatus liable to produce a spark; precautions should be taken against the production of static electrical discharge. Explosive peroxides are generated by the atmospheric oxidation of solvent ether and it is dangerous to distil a sample which contains peroxides.

Adverse Effects
As for Anaesthetic Ether, p.1783. Ingestion of 30 to 60 mL may be fatal.

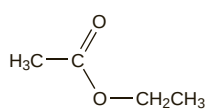
Uses
Solvent ether is widely used as a pharmaceutical and industrial solvent, and is used as an extraction solvent in food processing.

Ethyl Acetate

Acetato de etilo; Acetic Ether; Aethylis Acetas; Aethylium Aceticum; Ethyl Ethanoate; Ethyl-acetát; Éthyle, acétate d'; Ethylis acetas; Etil-acetát; Etilacetatas; Etylacetat; Etylu octan; Etyyliasetaatti.

Этилацетат

$C_4H_8O_2$ = 88.11.
CAS — 141-78-6.



Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*

Ph. Eur. 6.2 (Ethyl Acetate). A colourless, clear, volatile liquid. Relative density 0.898 to 0.902. B.p. 76° to 78°. Soluble in water; miscible with alcohol, with acetone, and with dichloromethane. Store at a temperature not exceeding 30°. Protect from light.

USNF 26 (Ethyl Acetate). A transparent, colourless, flammable liquid having a fragrant, refreshing, slightly acetous odour. Sp. gr. 0.894 to 0.898. Soluble in water; miscible with alcohol, with ether, and with fixed and volatile oils. Store in airtight containers at a temperature not exceeding 40°.

Adverse Effects
Ethyl acetate is irritant to mucous membranes. High concentrations may cause CNS depression. Ethyl acetate may be implicated in volatile substance abuse (p.2019).

◊ For discussion of neurotoxicity after occupational exposure to solvents and the absence of such an effect with ethyl acetate, see under Toluene, p.2026.

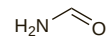
Uses
Ethyl acetate is used as a flavour and solvent in pharmaceutical preparations. It is also used in industry as a solvent and as an extraction solvent in food processing.

Formamide

Carbamaldehyde; Formamid; Formamida; Methanamide.

Формамид

CH_3NO = 45.04.
CAS — 75-12-7.



Description. Formamide is a colourless, oily liquid. B.p. 210°. Wt per mL, about 1.13 g.

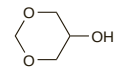
Profile
Formamide is used as an industrial solvent. It is reported to be irritant.

Glycerol Formal

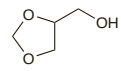
Glycérol formal; Glycerol-formalum. A mixture of the two isomers 4-hydroxymethyl-1,3-dioxolane and 5-hydroxy-1,3-dioxane present in a constant ratio of 40:60 respectively.

Глицерол Формаль

$C_4H_8O_3$ = 104.1.
CAS — 4740-78-7 (5-hydroxy-1,3-dioxane); 5464-28-8 (4-hydroxymethyl-1,3-dioxolane).



(5-hydroxy-1,3-dioxane)



(4-hydroxymethyl-1,3-dioxolane)

Profile
Glycerol formal is used as a pharmaceutical solvent.

Glycofurol

Glicofurol; Glycofural; Glycofurol 75; Tetrahydrofurfuryl Alcohol Polyethylene Glycol Ether. α-(Tetrahydrofuranyl)-ω-hydroxypoly(oxyethylene).

Гликофурфурол

$C_5H_9O.(C_2H_4O)_n.OH$.
CAS — 9004-76-6; 31692-85-0.

Description. Glycofurol is a clear, colourless, almost odourless liquid. Wt per mL about 1.08 g. B.p. 80° to 100°. Incompatible with oxidising agents. Store under nitrogen in airtight containers. Protect from light.

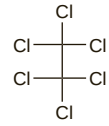
Profile
Glycofurol is used as a pharmaceutical solvent for injections.

Hexachloroethane

Hexacloroetano.

Гексахлорэтан

C_2Cl_6 = 236.7.
CAS — 67-72-1.



Profile
Hexachloroethane is a chlorinated hydrocarbon used in industry as a solvent. Eye irritation and photophobia have resulted from industrial exposure to the vapour. It was formerly used in veterinary medicine as an anthelmintic, but has been superseded by less toxic drugs.

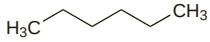
n-Hexane

n-Hexano.

н-Гексан

C_6H_{14} = 86.18.

CAS — 110-54-3.



Description. *n*-Hexane is a colourless, flammable, volatile liquid with a faint odour. Wt per mL about 0.66 g. B.p. about 69°. Store in airtight containers.

Adverse Effects

n-Hexane is irritant. Acute exposure to the vapour may result in CNS depression with headache, drowsiness, dizziness, and in severe cases unconsciousness. Chronic occupational exposure and abuse of *n*-hexane have been associated with the development of peripheral neuropathies. *n*-Hexane is a constituent of some adhesives and may be implicated in volatile substance abuse (p.2019). Some adverse effects of petrol have been attributed to its content of *n*-hexane.

◊ References.

1. Health and Safety Executive. *n*-Hexane. *Toxicity Review 18*. London: HMSO, 1987.
2. WHO. *n*-Hexane. *Environmental Health Criteria 122*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/ehc/ehc/ehc122.htm (accessed 30/06/04)
3. WHO. *n*-Hexane health and safety guide. *IPCS Health and Safety Guide 59*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg059.htm (accessed 30/06/04)

Effects on the nervous system. There have been many reports of peripheral neuropathy attributed to the abuse of, and occupational exposure to, *n*-hexane, although symptoms tend to be milder in the latter.[1] Tetraplegia has occurred in severe cases. There is typically a clinical deterioration several weeks after exposure followed by a slow recovery which, in severe cases, may not be complete. It has been suggested that methyl ethyl ketone potentiates the peripheral neuropathy induced by *n*-hexane. Occupational exposure to *n*-hexane has also been associated with cranial nerve neuropathy.

Parkinsonism in a leather worker, possibly associated with exposure to solvents, mainly *n*-hexane, has been noted.[2]

For further discussion of neurotoxicity after occupational exposure to solvents including *n*-hexane, see under Toluene, p.2026.

1. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989; **8:** 293–300.
2. Pezzoli G, *et al.* Parkinsonism due to n-hexane exposure. *Lancet* 1989; **ii:** 874.

Pharmacokinetics

n-Hexane is absorbed after inhalation and to a limited extent through the skin. Oxidative metabolites, including 2,5-hexanedione are excreted in the urine largely as conjugates. Some unchanged *n*-hexane is excreted via the lungs.

Uses

n-Hexane is widely used as an industrial solvent, as a solvent in glues, and as an extraction solvent in food processing.

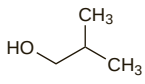
Isobutyl Alcohol

Alcohol isobutílico; Isobutanol.

Изобутиловый Спирт

$C_4H_{10}O$ = 74.12.

CAS — 78-83-1.



Profile

Isobutyl alcohol is used as an industrial solvent. It is also used as an anaesthetic in the American lobster, *Homarus americanus*.

◊ References.

1. WHO. Butanols—four isomers: 1-butanol, 2-butanol, tert-butanol, isobutanol. *Environmental Health Criteria 65*. Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/ehc/ehc/ehc65.htm (accessed 30/06/04)
2. WHO. Isobutanol health and safety guide. *IPCS Health and Safety Guide 9*. Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/hsg/hsg/hsg009.htm (accessed 30/06/04)

Kerosene

Kerosine; 'Paraffin'; Queroseno.

Керосин

CAS — 8008-20-6.

Description. Kerosene is a mixture of hydrocarbons, chiefly members of the alkane series, distilled from petroleum. It is a clear, colourless liquid with a characteristic odour. Sp. gr. about 0.8 g. B.p. 180° to 300°. An odourless grade is available. Store in airtight containers.

Adverse Effects

The chief danger from ingestion of kerosene is pneumonitis and attendant pulmonary complications resulting from aspiration. Spontaneous or induced vomiting increases the risk of aspiration. Ingestion of kerosene results in a burning sensation in the mouth and throat, gastrointestinal disturbances, and possibly cough, dyspnoea, and transient cyanosis. There may be excitation followed by CNS depression, with weakness, dizziness, drowsiness, confusion, incoordination, and restlessness progressing to convulsions, coma, and respiratory depression in severe cases. Cardiac arrhythmias have been reported.

The course of poisoning from inhalation is similar to that following ingestion although CNS and cardiac effects are more likely. Kerosene is irritant.

Abuse. A case of volatile substance abuse (p.2019) involving inhalation and ingestion of kerosene has been reported.[1]

1. Das PS, *et al.* Kerosene abuse by inhalation and ingestion. *Am J Psychiatry* 1992; **149:** 710.

Treatment of Adverse Effects

Treatment of kerosene poisoning is supportive and symptomatic. Every precaution should be taken to avoid aspiration of kerosene into the lungs. The UK National Poisons Information Service considers that gastric lavage should not be used. If large amounts have been taken or there is concern about another toxin, gastric aspiration may be considered if it can be carried out within 1 hour of ingestion and the airway can be protected. Adrenaline and other sympathomimetics should also be avoided because of the risk of precipitating cardiac arrhythmias.

Uses

Kerosene is used as a degreaser and cleaner and as an illuminating and fuel oil in kerosene ('paraffin') lamps and stoves. The odourless grade has been used as a solvent in the preparation of some insecticide sprays.

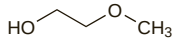
2-Methoxyethanol

Eter monometylowy glikolu etylenowego; Ethylene Glycol Monomethyl Ether; 2-Metoxietanol.

2-Метоксиэтанол

$C_3H_8O_2$ = 76.09.

CAS — 109-86-4.



Description. 2-Methoxyethanol is a clear, colourless to slightly yellow liquid. Wt per mL about 0.96 g. B.p. about 125°. Miscible with water, with alcohol, with acetone, with dimethylformamide, with ether, and with glycerol. Store in airtight containers.

Adverse Effects and Precautions

2-Methoxyethanol is irritant to mucous membranes. Ingestion may result in CNS depression with confusion, weakness, and in severe cases coma and death from respiratory depression. Nausea, metabolic acidosis, and renal damage may also occur. Prolonged industrial exposure to the vapour has been associated with severe effects on the CNS characterised by headache, dizziness, lethargy, weakness, ataxia, tremor, disorientation, mental changes, weight loss, and visual disturbances. Anaemia has also been reported. There has been concern about the potential for reproductive toxicity.

◊ References to the toxicity of 2-methoxyethanol and other glycol ethers.

1. Health and Safety Executive. Glycol ethers. *Toxicity Review 10*. London: HMSO, 1985.
2. WHO. 2-Methoxyethanol, 2-ethoxyethanol, and their acetates. *Environmental Health Criteria 115*. Geneva: WHO, 1990. Available at: http://www.inchem.org/documents/ehc/ehc/ehc115.htm (accessed 30/06/04)
3. Browning RG, Curry SC. Clinical toxicology of ethylene glycol monoalkyl ethers. *Hum Exp Toxicol* 1994; **13:** 325–35.
4. Johanson G. Toxicity review of ethylene glycol monomethyl ether and its acetate ester. *Crit Rev Toxicol* 2000; **30:** 307–45.
5. Bagchi G, Waxman DJ. Toxicity of ethylene glycol monomethyl ether: impact on testicular gene expression. *Int J Androl* 2008; **31:** 269–74.

Handling. Suitable precautions should be taken to avoid skin contact with 2-methoxyethanol as it can penetrate skin and produce systemic toxicity.

Uses

2-Methoxyethanol is used as an industrial solvent.

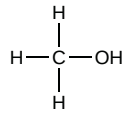
Methyl Alcohol

Metanol; Metanoli; Metanolis; Méthanol; Methanol; Methanolum.

Метиловый Спирт

CH_3OH = 32.04.

CAS — 67-56-1.



Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*.

Ph. Eur. 6.2 (Methanol). A colourless, clear, volatile, hygroscopic liquid. It is flammable. B.p. about 64°. Relative density 0.791 to 0.793. Miscible with water and with dichloromethane. Store in airtight containers.

The BP 2008 gives Methyl Alcohol as an approved synonym.

USNF 26 (Methyl Alcohol). A clear, colourless, flammable liquid having a characteristic odour. Miscible with water, with alcohol, with ether, with benzene, and with most other organic solvents. Store in airtight containers remote from heat, sparks, and open flames.

Adverse Effects

Immediate signs of acute poisoning after ingestion of methyl alcohol resemble those of ethanol (alcohol; ethyl alcohol) intoxication (see p.1625), but are milder. Characteristic symptoms of methyl alcohol poisoning are caused by toxic metabolites and develop after a latent period of about 12 to 24 hours, or longer if taken with ethanol. The outstanding features of poisoning are metabolic acidosis with rapid, shallow breathing, visual disturbances which often proceed to irreversible blindness, and severe abdominal pain. Other symptoms include headache, gastrointestinal disturbances, pain in the back and extremities, and coma which in severe cases may result in death due to respiratory failure or, rarely, to circulatory collapse. Mania and convulsions occasionally occur. Individual response to methyl alcohol varies widely. Ingestion of 30 mL is considered to be potentially fatal.

Absorption of methyl alcohol through the skin or inhalation of the vapour may also lead to toxic systemic effects.

◊ References to the adverse effects of methyl alcohol.

1. Jacobsen D, McMartin KE. Methanol and ethylene glycol poisonings: mechanism of toxicity, clinical course, diagnosis and treatment. *Med Toxicol* 1986; **1:** 309–34.
2. Anderson TJ, *et al.* Neurologic sequelae of methanol poisoning. *Can Med Assoc J* 1987; **136:** 1177–9.
3. Cavalli A, *et al.* Severe reversible cardiac failure associated with methanol intoxication. *Postgrad Med J* 1987; **63:** 867–8.
4. Shapiro L, *et al.* Unusual case of methanol poisoning. *Lancet* 1993; **341:** 112.
5. Medinsky MA, Dorman DC. Recent developments in methanol toxicity. *Toxicol Lett* 1995; **82–83:** 707–11.
6. McKellar MJ, *et al.* Acute ocular methanol toxicity: clinical and electrophysiological features. *Aust N Z J Ophthalmol* 1997; **25:** 225–30.
7. Williams GF, *et al.* Methanol poisoning: a review and case study of four patients from central Australia. *Aust Crit Care* 1997; **10:** 113–18.
8. Shelby M, *et al.* NTP-CERHR expert panel report on the reproductive and developmental toxicity of methanol. *Reprod Toxicol* 2004; **18:** 303–90.
9. Hantson PE. Intoxication aiguë par le méthanol : physiopathologie, pronostic et traitement. *Bull Mem Acad R Med Belg* 2006; **161:** 425–34.

Handling. Suitable precautions should be taken to avoid skin contact with methyl alcohol as it can penetrate skin and produce systemic toxicity.

Treatment of Adverse Effects

Gastric aspiration may be considered if the patient presents within 1 hour of ingesting methyl alcohol. Activated charcoal is probably of little use as it does not absorb significant amounts of methyl alcohol. Metabolic acidosis (p.1667) should be corrected immediately with intravenous sodium bicarbonate. If significant amounts of methyl alcohol have been ingested, early treatment with an antidote (ethanol or fomepizole) is recommended. Ethanol delays the oxidation of methyl alcohol to its toxic metabolites formaldehyde and formic acid; dosage is adjusted to achieve and maintain a blood-ethanol concentration of 1 to 1.5 mg/mL. An **oral** dose for a 70-kg adult of about 150 mL of an ethanolic solution containing 40% v/v of C_2H_5OH has been suggested. Alcoholic spirits (such as whisky, gin, or vodka) may often be of the suitable strength. If required, an ethanolic **infusion** containing 10% v/v of C_2H_5OH may then be given as maintenance for which the following doses have been used:

- for an average adult, 1.38 mL/kg per hour
- for a non-drinker or child, 0.83 mL/kg per hour
- for a chronic drinker, 1.96 mL/kg per hour

The infusion should be continued until methyl alcohol concentrations are undetectable, or fall below 50 micrograms/mL with resolution of systemic toxicity.

Fomepizole (p.1446), an inhibitor of alcohol dehydrogenase, is also used; it inhibits the metabolism of methyl alcohol to its toxic metabolites.