Domiphen Bromide *(BAN, USAN, rINN)*

Bromuro de domifeno; Domifeenibromidi; Domifenbromid; Domiphène, Bromure de; Domipheni Bromidum; NSC-39415; PDDB; Phenododecinium Bromide. Dodecyldimethyl-2-phenoxyethylammonium bromide.

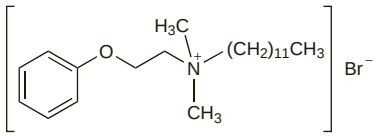
Домифена Бромид

$C_{22}H_{40}BrNO$ = 414.5.

CAS — 13900-14-6 (domiphen); 538-71-6 (domiphen bromide).

ATC — A01AB06.

ATC Vet — QA01AB06.



Pharmacopoeias. In *Br. Chin.* includes the monohydrate.

BP 2008 (Domiphen Bromide). Colourless or faintly yellow, crystalline flakes. Freely soluble in water and in alcohol; soluble in acetone.

Incompatibility. Domiphen bromide is incompatible with soaps and other anionic surfactants.

Profile

Domiphen bromide is a quaternary ammonium antiseptic with actions and uses similar to those of other cationic surfactants (see Cetrimide, p.1634). Preparations containing domiphen bromide are used in the treatment of minor infections of the mouth and throat.

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Antiseptique Pastilles; Bronchodex Pastilles; ***Ital.:*** Bradoral; ***Malaysia:*** Domidin; ***Port.:*** Neobradoral.

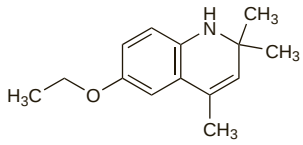
Multi-ingredient: ***Austria:*** Bepanthen; Bradosol; ***Canad.:*** Nupercainal; ***Chile:*** Oralfresh Menta; ***Fr.:*** Fluoselgine; ***Ital.:*** Inalar; ***Pol.:*** Viosept.

Ethoxyquin

Etoxiquina. 6-Ethoxy-1,2-dihydro-2,2,4-trimethylquinoline.

$C_{14}H_{19}NO$ = 217.3.

CAS — 91-53-2.



Profile

Ethoxyquin has been used as an antoxidant for the prevention of common scald of apples and pears during storage and as an additive to animal feeds. Concern has been expressed over the toxicity of ethoxyquin and its residues on foodstuffs and its use is limited or restricted in some countries.

Ethylene Oxide

Dimethylene oxide; Epoxietano; 1,2-Epoxyethane; Etylenu tlenek; Óxido de etileno; Oxirane; Oxirano; Oxirano.

Окись Этилена; Этиленоксид

C_2H_4O = 44.05.

CAS — 75-21-8.

Description. Ethylene oxide is a colourless flammable gas at room temperature and atmospheric pressure.

Stability. Mixtures of ethylene oxide with oxygen or air are explosive but the risk can be reduced by the addition of carbon dioxide or fluorocarbons.

Adverse Effects and Precautions

Ethylene oxide irritates the eyes and respiratory tract and may also cause nausea and vomiting, diarrhoea, headache, vertigo, CNS depression, dyspnoea, and pulmonary oedema. Liver and kidney damage and haemolysis may occur. Fatalities have occurred. Excessive exposure of the skin to liquid or solution causes burns, blistering, irritation, and dermatitis; percutaneous absorption may lead to systemic effects.

Many materials including plastics and rubber adsorb ethylene oxide. If such materials are being sterilised with ethylene oxide all traces of the gas must be removed before the materials can be used; removal may be by ventilation or more active means. Hypersensitivity reactions, including anaphylaxis, have been associated with ethylene oxide-contaminated materials. Ethylene oxide may also react with materials being sterilised to produce substances such as ethylene chlorohydrin (with chloride) or ethylene glycol (with water); these may contribute to any toxicity.

Pharmaceutical manufacturers within the EU have been advised to use ethylene oxide only when there is no alternative. Ethylene oxide has been shown to have carcinogenic and mutagenic properties and there is evidence of increased risk of neoplasms following occupational exposure.

◊ Reviews.

1. WHO. Ethylene oxide. *Environmental Health Criteria 55*. Geneva: WHO, 1985. Available at: http://www.inchem.org/documents/ehc/ehc/ehc55.htm (accessed 15/03/06)
2. WHO. Ethylene oxide health and safety guide. *IPCS Health and Safety Guide 16*. Geneva: WHO, 1988. Available at: http://www.inchem.org/documents/hsg/hsg/hsg016.htm (accessed 15/03/06)
3. WHO. Ethylene oxide. *Concise International Chemical Assessment Document 54* Geneva: WHO, 2003. Available at: http://www.who.int/ipcs/publications/cicad/en/cicad54.pdf (accessed 15/03/06)

Carcinogenicity. Exposure of workers to ethylene oxide has been associated with the development of lymphatic and haematopoietic cancer and there is concern that it may be linked to breast cancer. In order to evaluate the carcinogenicity of ethylene oxide the National Institute for Occupational Safety and Health (NIOSH), in the mid 1980s, assembled a cohort of about 18 000 workers exposed to ethylene oxide.[1-3] Results of the initial cohort followed up to 1987 showed no overall excess of haematopoietic cancer, but did find a significant excess of non-Hodgkin's lymphoma among men.[1] Based on limited clinical evidence from humans and from significant evidence in *animal* studies, the International Agency for Research on Cancer concluded in 1994 that there was sufficient evidence to classify ethylene oxide as a definite human carcinogen.[4] A later evaluation[3] of the NIOSH cohort from 1987 to 1998 indicated that, despite 2852 deaths as opposed to 1177 deaths in the earlier study, there was little evidence of cancer excesses for ethylene oxide exposed workers versus the general population, with the exception of bone cancer (6 deaths), and no conclusion could be drawn from this small number. However, exposure-response analyses found statistically significant evidence of an association between increased exposure and some types of haematopoietic cancer (non-Hodgkin's lymphoma and lymphocytic leukaemia), particularly for males.[2,3] There was also some evidence for a positive exposure-response for breast cancer. Follow-up of a cohort of 2876 workers exposed to ethylene oxide in the UK[5] found no statistically significant increase in mortality from cancer overall, or from any specific category of tumour. A study[6] of a cohort of 7576 female workers exposed to ethylene oxide suggested that ethylene oxide was associated with breast cancer. However, the authors indicated weaknesses in the study that could have influenced the findings.

1. Steenland K, *et al.* Mortality among workers exposed to ethylene oxide. *N Engl J Med* 1991; **324:** 1402–7.
2. Stayner L, *et al.* Exposure-response analysis of cancer mortality in a cohort of workers exposed to ethylene oxide. *Am J Epidemiol* 1993; **138:** 787–98.
3. Steenland K, *et al.* Mortality analyses in a cohort of 18 235 ethylene oxide exposed workers: follow up extended from 1987 to 1998. *Occup Environ Med* 2004; **61:** 2–7.
4. IARC/WHO. Some industrial chemicals. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans volume 60* 1994. Available at: http://monographs.iarc.fr/ENG/Monographs/vol60/volume60.pdf (accessed 23/05/06)
5. Coggon D, *et al.* Mortality of workers exposed to ethylene oxide: extended follow up of a British cohort. *Occup Environ Med* 2004; **61:** 358–62.
6. Steenland K, *et al.* Ethylene oxide and breast cancer incidence in a cohort study of 7576 women (United States). *Cancer Causes Control* 2003; **14:** 531–9.

Effects on the nervous system. Four men exposed to ethylene oxide at a concentration of greater than 700 ppm developed neurological disorders. One experienced headaches, nausea, vomiting, and lethargy followed by major motor seizures. The others had headaches, limb numbness and weakness, increased fatigue, trouble with memory and thought processes, and slurred speech. Three also developed cataracts, and one required bilateral cataract extractions.[1] Rash, followed a few months later by hand numbness and weakness, headaches, and cognitive impairment, has been reported[2] in a cluster of 12 surgical nurses and technicians after exposure for 5 months to ethylene oxide-contaminated surgical gowns. Several patients showed signs of peripheral and CNS dysfunction and one patient had signs of axonal injury.

1. Jay WM, *et al.* Possible relationship of ethylene oxide exposure to cataract formation. *Am J Ophthalmol* 1982; **93:** 727–32.
2. Brashear A, *et al.* Ethylene oxide neurotoxicity: a cluster of 12 nurses with peripheral and central nervous system toxicity. *Neurology* 1996; **46:** 992–8.

Hypersensitivity. Anaphylactoid reactions in dialysis patients have resulted from the use of dialysis equipment sterilised with ethylene oxide.[1-3] There have also been reports of hypersensitivity[4] and anaphylactoid[5] reactions in plateletpheresis donors caused by residues of ethylene oxide in components of apheresis kits. The most common adverse reactions reported have been dyspnoea, wheezing, urticaria, flushing, headache, and hypotension, but acute severe bronchospasm, circulatory collapse, cardiac arrest, and death have also occurred. It was noted[6] that where severe, sometimes fatal, anaphylactoid reactions have occurred at the beginning of dialysis, ethylene oxide has almost universally been implicated, although exposure to cuprammonium cellulose (cuprophane) dialysis membranes may also have been involved.

It has been reported that there may be an increased risk of ethylene oxide-induced anaphylactic shock in children undergoing surgery for spina bifida.[7] Such children might be at increased risk of sensitisation and anaphylaxis, and came into frequent contact with ethylene oxide through multiple operations and catheterisations.

Occupational asthma and contact dermatitis have been attributed to residual ethylene oxide in surgical gloves.[8]

1. Bommer J, *et al.* Anaphylactoid reactions in dialysis patients: role of ethylene-oxide. *Lancet* 1985; **ii:** 1382–5.
2. Rumpf KW, *et al.* Association of ethylene-oxide-induced IgE antibodies with symptoms in dialysis patients. *Lancet* 1985; **ii:** 1385–7.
3. Röckel A, *et al.* Ethylene oxide hypersensitivity in dialysis patients. *Lancet* 1986; **i:** 382–3.
4. Leitman SF, *et al.* Allergic reactions in healthy plateletpheresis donors caused by sensitization to ethylene oxide gas. *N Engl J Med* 1986; **315:** 1192–6.
5. Muylle L, *et al.* Anaphylactoid reaction in platelet-pheresis donor with IgE antibodies to ethylene oxide. *Lancet* 1986; **ii:** 1225.
6. Nicholls A. Ethylene oxide and anaphylaxis during haemodialysis. *BMJ* 1986; **292:** 1221–2.
7. Moneret-Vautrin DA, *et al.* High risk of anaphylactic shock during surgery for spina bifida. *Lancet* 1990; **335:** 865–6.
8. Verraes S, Michel O. Occupational asthma induced by ethylene oxide. *Lancet* 1995; **346:** 1434–5.

Pregnancy. A study[1] of female staff responsible for sterilising instruments was carried out in all general hospitals in Finland. The incidence of spontaneous abortion (analysed according to employment at the time of conception and corrected for maternal age, parity, decade of pregnancy, smoking, and consumption of alcohol and coffee) was significantly increased in those exposed to ethylene oxide during pregnancy compared with those not so exposed. This study provoked criticism,[2,3] and the authors conceded that the study was not large enough to compare abortion rates and known ethylene oxide concentrations.[4] A retrospective analysis[5] of 32 dental assistants who had been exposed to ethylene oxide during pregnancy suggested that, after adjusting for age, the risk of spontaneous abortions and preterm or post-term births may have been more than doubled.

1. Hemminki K, *et al.* Spontaneous abortions in hospital staff engaged in sterilising instruments with chemical agents. *BMJ* 1982; **285:** 1461–3.
2. Gordon JE, Meinhardt TJ. Spontaneous abortions in hospital sterilising staff. *BMJ* 1983; **286:** 1976.
3. Austin SG. Spontaneous abortions in hospital sterilising staff. *BMJ* 1983; **286:** 1976.
4. Hemminki K, *et al.* Spontaneous abortions in hospital sterilising staff. *BMJ* 1983; **286:** 1976–7.
5. Rowland AS, *et al.* Ethylene oxide exposure may increase the risk of spontaneous abortion, preterm birth, and postterm birth. *Epidemiology* 1996; **7:** 363–8.

Pharmacokinetics

Ethylene oxide gas is rapidly absorbed through the lungs and distributed throughout the body. Percutaneous absorption can occur from aqueous solutions. It is rapidly metabolised by hydrolysis or conjugation with glutathione.

Uses

Ethylene oxide is a bactericidal and fungicidal gaseous disinfectant that is effective against most micro-organisms, including viruses. It is also sporicidal. It is used for the gaseous sterilisation of heat-labile pharmaceutical and surgical materials that cannot be sterilised by other means.

Ethylene oxide forms explosive mixtures with air; this may be overcome by using mixtures containing 10% ethylene oxide in carbon dioxide, or by removing at least 95% of the air from the apparatus before admitting either ethylene oxide or a mixture of 90% ethylene oxide in carbon dioxide. Alternatively, non-flammable

mixtures of dichlorodifluoromethane and trichlorofluoromethane with 9 to 12% w/w of ethylene oxide have been employed, but restrictions on the release of fluorocarbons or CFCs limit their use.

Effective sterilisation by ethylene oxide depends on exposure time, temperature, humidity, the amount and type of microbial contamination, and the partial pressure of the ethylene oxide in the exposure chamber. Concentrations of between 400 and 1000 mg/litre are usually used for sterilisation and the process time may vary from 30 minutes to 10 hours. The material being sterilised must be permeable to ethylene oxide if occluded micro-organisms are present. The bactericidal action is accelerated by increase of temperature; the average temperature used is between 40° and 50°.

Moisture is essential for sterilisation by ethylene oxide. In practice, dry micro-organisms need to be rehydrated before ethylene oxide can be effective; humidification is normally carried out under vacuum prior to introduction of ethylene oxide. Relative humidities of 40 to 60% are used.

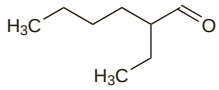
Control of physical factors does not assure sterility, and the process should be monitored usually by using standardised suspensions of aerobic spores such as those of *Bacillus subtilis* var. *niger*.

Ethylhexanal

2-Ethylcaproaldehyde; 2-Ethylhexylaldehyde; Octylaldehyde. 2-Ethylhexanal.

$C_8H_{16}O$ = 128.2.

CAS — 123-05-7.



Profile

Ethylhexanal is an aldehyde disinfectant used for instrument disinfection.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ger.:*** Buraton 10 F; Helipur H plus N; Lysetol FF†; Sekucid konz†.

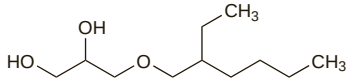
Ethylhexylglycerin

Octoxyglycerin. 3-[(2-Ethylhexyl)oxy]-1,2-propanediol.

Этилгексилглицерин

$C_{11}H_{24}O_3$ = 204.3.

CAS — 70445-33-9.



Profile

Ethylhexylglycerin is a disinfectant used in a concentration of 0.3% in topical deodorant preparations. It is also used in products for disinfection of the hands.

◊ References.

1. Stausbøl-Grøn B, Andersen KE. Allergic contact dermatitis to ethylhexylglycerin in a cream. *Contact Dermatitis* 2007; **57:** 193–4.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Effidrate†; ***Chile:*** Uriage Desodorante Tri-Actif.

Formaldehyde

Formaldehid; Formaldehído; Formaldehyd.

Формальдегид

CH_2O = 30.03.

CAS — 50-00-0.

ATC Vet — QP53AX19.

Formaldehyde Solution

Formaldehído, solución de; Formaldehido tirpalas; Formaldehidoldat; Formaldehyd roztok; Formaldéhyde, solution de; Formaldehydi solutio; Formaldehydiliuos; Formaldehydlösning; Formaldehydu roztwór.

NOTE. The names formalin and formol have been used for formaldehyde solution but in some countries they are trade marks.

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

Ph. Eur. 6.2 (Formaldehyde Solution (35 per cent); Formaldehyde Solution BP 2008). It contains 34.5 to 38.0% w/w of formaldehyde with methyl alcohol as a stabiliser. It is a clear, colourless, liquid. Miscible with water and with alcohol. It may be cloudy after storage. Store at a temperature between 15° and 25°. Protect from light.

USP 31 (Formaldehyde Solution). It contains not less than 34.5% w/w of formaldehyde with 9 to 15% methyl alcohol added to prevent polymerisation. It is a clear, colourless, or practically colourless liquid with a pungent, irritating odour. Miscible with water and with alcohol. Store at a temperature above 15° in airtight containers. It may become cloudy on standing due to the separation of paraformaldehyde, especially if the solution is kept in a cold place; the cloudiness disappears on warming.

Strength of solutions. Formaldehyde solution is sometimes known simply as formaldehyde and this has led to confusion in interpreting the strength and the form in which formaldehyde is being used. In practice formaldehyde is available as formaldehyde solution which is diluted before use, the percentage strength being expressed in terms of formaldehyde solution rather than formaldehyde. For example, in the UK, formaldehyde solution 3% consists of 3 volumes of Formaldehyde Solution (35 Per Cent) (Ph. Eur. 6.2) diluted to 100 volumes with water and thus contains 1.04 to 1.14% w/w of formaldehyde; it is ***not*** prepared by diluting Formaldehyde Solution (35 Per Cent) (Ph. Eur. 6.2) to arrive at a solution containing 3% w/w of formaldehyde.

Incompatibility. Formaldehyde reacts with protein and this may diminish its antimicrobial activity.

Adverse Effects and Precautions

Concentrated formaldehyde solutions applied to the skin cause whitening and hardening. Contact dermatitis and sensitivity reactions have occurred after the use of conventional concentrations and after contact with residual formaldehyde in resins.

Ingestion of formaldehyde solution causes intense burning pain in the mouth, throat, chest, and stomach, with inflammation, ulceration, and necrosis of mucous membranes. There may be nausea, vomiting, haematemesis, blood-stained diarrhoea, haematuria, and anuria; metabolic acidosis, vertigo, convulsions, loss of consciousness, and circulatory and respiratory failure may occur. Death has occurred after the ingestion of the equivalent of about 30 mL of formaldehyde solution. If the patient survives 48 hours, recovery is probable. Formaldehyde vapour is irritant to the eyes, nose, and upper respiratory tract, and may cause coughing, dysphagia, spasm and oedema of the larynx, bronchitis, pneumonia, and rarely, pulmonary oedema. Asthma-like symptoms have been reported after repeated exposure.

◊ General references.

1. Health and Safety Executive. Formaldehyde. *Toxicity Review 2.* London: HMSO, 1981.
2. WHO. Formaldehyde. *Environmental Health Criteria 89.* Geneva: WHO, 1989. Available at: http://www.inchem.org/documents/ehc/ehc/ehc89.htm (accessed 15/03/06)
3. WHO. Formaldehyde health and safety guide. *IPCS Health and Safety Guide 57.* Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg057.htm (accessed 15/03/06)
4. WHO. Formaldehyde. *Concise International Chemical Assessment Document 40* Geneva: WHO, 2002. Available at: http://whqlibdoc.who.int/hq/2002/a73769.pdf (accessed 15/03/06)

Abuse. References to the abuse of embalming fluid (the primary ingredient of which is formaldehyde), usually in the form of marijuana treated with embalming fluid and in some cases phencyclidine, a mixture known as 'fry'.[1-4]

1. Holland JA, *et al.* Embalming fluid-soaked marijuana: new high or new guise for PCP? *J Psychoactive Drugs* 1998; **30:** 215–9.
2. Peters RJ, *et al.* Beliefs and social norms about cigarettes or marijuana sticks laced with embalming fluid and phencyclidine (PCP): why youth use "fry". *Subst Use Misuse* 2005; **40:** 563–71.
3. Singer M, *et al.* Dust in the wind: the growing use of embalming fluid among youth in Hartford, CT. *Subst Use Misuse* 2005; **40:** 1035–50.
4. Singer M, *et al.* When the drug of choice is a drug of confusion: embalming fluid use in inner city Hartford, CT. *J Ethn Subst Abuse* 2005; **4:** 73–96.

Carcinogenicity. There is controversy as to the risk formaldehyde presents as a carcinogen. Studies on the occupational exposure of medical personnel and industrial workers[1-3] to formaldehyde have generally concluded that although the risk is small or non-existent, the possibility that formaldehyde is a human carcinogen cannot be excluded. Reanalyses of some studies have led to different interpretations of the results, with some workers concluding that the risk of cancer from formaldehyde is greater than originally thought.[4] Analysis of mortality data[5] for a cohort of 25619 workers exposed to formaldehyde in the USA found some evidence of an association with nasopharyngeal cancer and possibly cancers at other upper respiratory-tract sites. Based on the results of this large cohort study and supported by evidence from other epidemiological and *animal* studies, the International Agency for Research on Cancer (IARC) concluded,[6] in 2004, that occupational exposure to formaldehyde does cause nasopharyngeal cancer. Furthermore, they found strong, but not sufficient, evidence to establish a causal link with leukaemia and limited evidence to suggest it causes sinonasal cancer. IARC has concluded that formaldehyde is a definite human carcinogen.[6]

1. Gérin M, *et al.* Cancer risks due to occupational exposure to formaldehyde: results of a multi-site case-control study in Montreal. *Int J Cancer* 1989; **44:** 53–8.
2. Blair A, *et al.* Mortality from lung cancer among workers employed in formaldehyde industries. *Am J Ind Med* 1990; **17:** 683–99.
3. Coggon D, *et al.* Extended follow-up of a cohort of British chemical workers exposed to formaldehyde. *J Natl Cancer Inst* 2003; **95:** 1608–15.
4. Sterling TD, Weinkam JJ. Mortality from respiratory cancers (including lung cancer) among workers employed in formaldehyde industries. *Am J Ind Med* 1994; **25:** 593–602.
5. Hauptmann M, *et al.* Mortality from solid cancers among workers in formaldehyde industries. *Am J Epidemiol* 2004; **159:** 1117–30.
6. IARC/WHO. Formaldehyde, 2-butoxyethanol and 1-*tert*-butoxy-2-propanol. *IARC monographs on the evaluation of carcinogenic risks to humans volume 88* 2004. Available at: http://monographs.iarc.fr/ENG/Monographs/vol88/volume88.pdf (accessed 23/05/06)

Effects on the blood. Haemolysis during chronic haemodialysis was due to formaldehyde eluted from filters.[1]

1. Orringer EP, Mattern WD. Formaldehyde-induced hemolysis during chronic hemodialysis. *N Engl J Med* 1976; **294:** 1416–20.

Effects on the urinary tract. Adverse effects have resulted from intravesical instillation of formaldehyde solutions, ranging in strength from 1 to 10%, in the treatment of haemorrhagic cystitis. They include dysuria, suprapubic pain, ureteric and bladder fibrosis, hydronephrosis, vesicoureteral reflux, bilateral ureteral obstruction, papillary necrosis, bladder rupture, and acute tubular necrosis. Intraperitoneal spillage through a fistula, leading to adverse systemic effects, has also occurred.[1] Fatalities have resulted from cardiac arrest and acute renal failure.[1-3] See also Haemorrhagic Cystitis under Uses, below.

There has also been a report[4] of 4 patients exposed to high levels of atmospheric formaldehyde who developed membranous nephropathy, suggesting that there may be genetic susceptibility for this effect.

1. Capen CV, *et al.* Intraperitoneal spillage of formalin after intravesical instillation. *Urology* 1982; **19:** 599–601.
2. Melekos M, Lalos J. Intravesical instillation of formalin and its complications. *Urology* 1983; **21:** 331–2.
3. Sarnak MJ, *et al.* Intravesicular formaldehyde instillation and renal complications. *Clin Nephrol* 1999; **51:** 122–5.
4. Breysse P, *et al.* Membranous nephropathy and formaldehyde exposure. *Ann Intern Med* 1994; **120:** 396–7.

Hypersensitivity. Hypersensitivity to formaldehyde has had several manifestations. Effects on the skin have included acute exacerbation of eczema after injection of hepatitis B vaccine containing formaldehyde up to 20 micrograms/mL.[1] In another case, formaldehyde sensitivity was characterised by pruritus, burning, and redness within minutes of exposure to sunlight.[2] Painful, enlarged, and haemorrhagic gingival margins have occurred after the use of a toothpaste containing a solution of formaldehyde.[3] There is conflicting evidence of the respiratory effects of formaldehyde: although a low concentration has been reported not to trigger an asthma attack in patients with severe bronchial hyperresponsiveness,[4] occupational asthma has been documented.[5] More severe manifestations of hypersensitivity include 7 cases of shock of possible toxic or anaphylactic aetiology that occurred after the use of formaldehyde solutions during surgical removal of hydatid cysts.[6]

For mention of an allergic response to root canal paste containing paraformaldehyde, see p.1655.

1. Ring J. Exacerbation of eczema by formalin-containing hepatitis B vaccine in formaldehyde-allergic patients. *Lancet* 1986; **ii:** 522–3.
2. Shelley WB. Immediate sunburn-like reaction in a patient with formaldehyde photosensitivity. *Arch Dermatol* 1982; **118:** 117–18.
3. Laws IM. Toothpaste formulations. *Br Dent J* 1984; **156:** 240.
4. Harving H, *et al.* Low concentrations of formaldehyde in bronchial asthma: a study of exposure under controlled conditions. *BMJ* 1986; **293:** 310.