

OVERVIEW

FORMALDEHYDE

AND ITS HEALTH EFFECTS

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INTRODUCTION

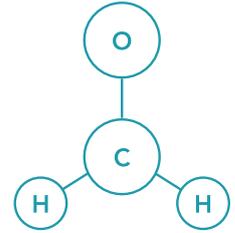
At BiopSafe, providing awareness of the health risks associated with exposure to formaldehyde is of utmost importance to us. The purpose of this publication is to help provide an overview of what formaldehyde is, how and where it is used, explain the possible risks associated with formaldehyde exposure and possible ways to evade it. Should you wish to do further research, a reference list is also provided.

WHAT IS FORMALDEHYDE?

Formaldehyde is a naturally occurring organic compound. It is a colourless, strong-smelling gas.¹

Formaldehyde can be present in several forms.

- Gas, which is the natural stage.
- Solid as paraformaldehyde, which is a waxy solid polymer.
- Liquid formaldehyde in a solution with methanol named Formalin.
- Within materials that can release formaldehyde gas, like insulation, carpeting, plywood and as a by-product of some combustion processes.



WHAT IS FORMALDEHYDE USED FOR?

Formaldehyde is used in many products, including fertiliser, paper, plywood, industrial resins, and building materials. It is also used in household products, such as antiseptics, medicines, and cosmetics, as well as in dyes, textiles, disinfectants, and as preservatives in mortuaries and medical laboratories.^{1,2}

FORMALDEHYDE FOR LABORATORY USE

Formaldehyde is often stabilised in a neutralised, aqueous methanol solution called formalin. A 100% formalin solution is prepared by bubbling formaldehyde gas through water until saturated. Formalin is 40% formaldehyde by volume (37% formaldehyde by weight) and methanol in water. Formalin is commonly used as a preservative in medical laboratories as well as mortuaries in a 10% formalin solution (4% formaldehyde).

In medical laboratories, formalin or formaldehyde is used for tissue fixation.² Biopsies are fixated using 4% formaldehyde immediately after excision in order to preserve the sample for subsequent analysis. The purpose of the fixation is to stop the autolytic changes in the biopsy, thus preserving the morphological characteristics of the tissue. Consequently, the necessary analysis can be performed on the tissue without histopathological changes.

EXPOSURE TO FORMALDEHYDE

We are all exposed to formaldehyde, primarily by inhaling formaldehyde gas or vapour from the air, (in low concentrations), or by absorbing formaldehyde liquids through the skin.^{2,3}

Formaldehyde is an occupational indoor air pollutant because it volatilises quickly and is emitted into the working environment. Workers who produce formaldehyde or products containing formaldehyde and healthcare workers in contact with formaldehyde are at greater risk than others because they are exposed to higher amounts of formaldehyde daily, either through inhalation or direct contact with the skin.³



Exposure may cause severe allergic reactions of the skin, eyes and respiratory tract.

Measurements of naturally occurring formaldehyde levels in indoor air range from 0.02–4 ppm. For outdoor air it ranges from 0.0002 to 0.006 ppm in the countryside and suburban areas and 0.001 to 0.02 ppm in urban areas.²² However, already at low formaldehyde concentrations (0.1 to 0.5 ppm), increased nasal and eye irritation, neurological effects, and increased risk of asthma and allergy have been observed.²² Eczema and changes in lung function have been observed at 0.6 to 1.9 ppm.²² Airborne formaldehyde concentrations above 0.1 ppm can cause respiratory tract irritation. The severity of irritation intensifies as concentrations increase.³

Low-dose acute exposure can often be detected by smell. It can be highly irritating to the eyes, nose, and throat, making those exposed cough and wheeze. Allergic reactions to the skin, eyes, and respiratory tract may also appear. Long-term exposure to low levels of formaldehyde in the air or on the skin can cause asthma-like respiratory problems and skin irritation, such as dermatitis and itching. Higher doses may cause severe mucous membrane irritation and changes in lung function.^{3,5}

Working with formaldehyde could increase your chances of having fertility problems or miscarriage.²⁶ The association between miscarriage and plasma formaldehyde levels were also found in a Chinese study of pregnant women.²⁷

FORMALDEHYDE EXPOSURE STUDIES:

A controlled-exposure study reported that healthy young subjects exposed to formaldehyde at 0.25, 0.42, 0.83, or 1.6 ppm for five hours per day for four days experienced slight discomfort over the increasing formaldehyde concentrations. More specifically, the subjects complained of conjunctival irritation and dryness of the nose and throat.⁶

Another study reported that subjects exposed to formaldehyde at increasing concentrations from 0.03 to 3.2 ppm for a total of 35 min, or to 0.03 to 4 ppm for 1.5 min showed responses like eye-, nose-, and throat irritation, odour, a “desire to leave the room,” and an increased eye-blinking rate appearing at 1.2 ppm.⁷

Several studies have shown that formaldehyde contact with the skin may cause primary irritation or allergic dermatitis.^{8,9} Eczematous sensitivity to formalin in nurses who handled thermometers immersed in a 10% formaldehyde solution has also been reported.¹⁰

Formaldehyde has been reported to cause irritation and dryness of the nose and throat as well as olfactory fatigue. A survey of six funeral homes that used formaldehyde and paraformaldehyde in the embalming process showed an average airborne concentration in the embalming rooms at 0.25-1.39 ppm. The investigations noted eye and upper respiratory tract irritation among some employees.¹¹

A recent study has found an association between formaldehyde exposure and the development of amyotrophic lateral sclerosis (ALS) and brain cancer. They reported a meta-relative risk (meta-RR) was increased by 78% for ALS development following high exposures to formaldehyde. Similarly, the meta-RR for brain cancer was increased by 71% among highly exposed individuals.²⁵



Working with formaldehyde could increase your chances of having fertility problems or miscarriage.

THE NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)

FORMALDEHYDE AND RISK OF CANCER

Formaldehyde was first listed in the Second Annual Report on Carcinogens in 1981¹² as reasonably anticipated to be a human carcinogen based on evidence from studies in experimental animals. Based on additional cancer studies in humans¹³, the listing status was changed to known to be a human carcinogen in the fifteenth Report on Carcinogens (2011).¹⁴ Formaldehyde is now classified as a category 1b carcinogen (IARC regulations 605/2014).

Several international organisations have established legal or recommended standards for using formaldehyde in the workplace to protect workers from the acute and chronic health effects of formaldehyde exposure.

FORMALDEHYDE CANCER STUDIES:

A comprehensive study¹⁵ of 25,619 U.S. factory workers exposed to formaldehyde was followed for 28 years. The authors found that the relative risks for leukaemia, particularly myeloid leukaemia, increased with formaldehyde exposure. The study showed that workers exposed to low levels of formaldehyde (0.1–1.9 ppm) showed an increased relative risk of 2.43 for myeloid leukaemia compared to a relative risk of 3.46 for workers exposed to higher peak levels (2.0–3.9 ppm and >4.0 ppm).

A follow-up study, also using a large cohort of formaldehyde-exposed workers, showed that the relative risks for nasopharyngeal cancer increased with average exposure intensity and duration of exposure to formaldehyde. In this cohort of formaldehyde-industry workers, an exposure-response relation with mortality from nasopharyngeal cancer was found.¹⁶

Another study investigated the association of mortality of anatomists, pathologists, and funeral industry workers and their exposure levels to formaldehyde to address cancer risk in the funeral industry. It showed that the duration of embalming practice and related formaldehyde exposures in the funeral industry was associated with a significantly increased risk for mortality from myeloid leukaemia.¹⁷

A case-control study¹⁸ showed evidence that formaldehyde causes an increased risk of nasopharyngeal cancer for individuals exposed to formaldehyde. An earlier study showed a relative risk with high formaldehyde exposure for oro-, hypopharynx, and nasopharynx cancer.¹⁹ Similar results were found by Roush et al. 1987.²⁰

EXPOSURE LIMITS

Formaldehyde is a known carcinogen and a sensitiser, which can potentially cause cancer and allergic reactions. Exposure in the general population is mainly from breathing air containing off-gassed formaldehyde from consumer articles. However, there are also naturally occurring sources of formaldehyde, and exposure can occur by eating apples and walking in a pine forest.

Due to the potential health risks associated with formaldehyde from consumer articles, the European Union (EU) has implemented a Restriction on using formaldehyde under the Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) Regulation (Regulation (EC) No 1907/2006). By restricting the emission of formaldehyde from articles, the EU aims to minimise the exposure of consumers to this hazardous substance.

Most countries have regulations for the exposure of formaldehyde. For example, according to Annex III of Directive 2004/37/EC (CMRD), employers must minimise workers' exposure to formaldehyde where possible. Wherever possible, formaldehyde therefore needs to be in closed systems. The directive further says, "Where a closed system is not technically possible, the employer shall ensure that the level of exposure of workers is reduced to as low a level as is technically possible". The employer must arrange for medical surveillance of workers exposed to the substances.

The table below shows formaldehyde's Long-Term Exposure Limit (LTEL) Values and Short-Term Exposure Limit (STEL) values.

Long-term Exposure Limit (LTEL), (ppm)	Occupational exposure limits/Short-term Exposure Limit (STEL), (ppm)**	Reference
0.3	0.6	EU
0.016	0.1	NIOSH
2*	0.75	OSHA

* The maximum exposure allowed for 15 minutes

** Measured as an 8-hour time-weighted average



Where a closed [biopsy] system is not technically possible, the employer shall ensure that the level of exposure of workers is reduced to as low a level as is technically possible.

ANNEX III OF DIRECTIVE 2004/37/EC (CMRD)

A study has shown that lab technicians and healthcare workers exceed the maximum daily exposure limits.²¹ The time-weighted average (TWA) exposure to formaldehyde ranged from 0.07-2.94 parts per million (ppm) during dissecting operations. More than 94% ty exposed to formaldehyde at higher than the ceiling value of 0.3 ppm.

From July 2023, a new regulation for exposure limits of formaldehyde from REACH is valid. The new rules establish an emission limit of 0.062 mg/m³ of formaldehyde into indoor air for wood-based articles and furniture, and a limit of 0.08 mg/m³ will apply to all other articles such as textile, leather, plastic, construction materials or electronic products.

HOW TO REDUCE FORMALDEHYDE EXPOSURE IN BIOPSY PROCEDURES

Formaldehyde is the golden standard in tissue preservation. Formalin preserves proteins and cellular organelles in a stepwise process. It is considered a highly efficient fixative due to its small size, allowing it to permeate cell walls and membranes easily.²³

Although formaldehyde exposure has long been associated with skin, eye, and respiratory tract irritation, most laboratories continue to use formalin. The main challenge has been finding an equally reliable and inexpensive replacement.

In recent years, however, alternatives to standard open vials have been developed, for instance in the shape of closed systems which keeps the formaldehyde sealed inside the lid. After placing the sample in the container and attaching the top lid, the formaldehyde can then be released from the lid with just a simple touch of the thumb. This procedure reduces contact with formaldehyde during sampling.

**LONG-TERM EXPOSURE TO LOW LEVELS OF FORMALDEHYDE IN THE AIR
OR ON THE SKIN CAN CAUSE ASTHMA-LIKE RESPIRATORY PROBLEMS AS WELL AS
SKIN IRRITATION SUCH AS DERMATITIS AND ITCHING.**

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We are deeply committed to help ensure a safe working environment for medical staff involved in biopsy procedures and to spread awareness of the many health risks associated with exposure to formalin. That is why we invented BiopSafe in 2014, an innovative solution that not only eliminates any exposure to formalin during the procedure but is also fast and easy to use. BiopSafe is part of Axlabs, specialized in solutions for pathology. Today, BiopSafe is used by thousands of healthcare professionals around the world and distributed globally through a dedicated partner network.