



European
Biosafety
Network

WHITE PAPER

**FORMALIN AND FORMALDEHYDE IN HEALTHCARE:
OCCUPATIONAL RISKS, REGULATORY
OBLIGATIONS, AND CLOSED-SYSTEM SOLUTIONS**

Author: Josh Cobb, Secretary, European Biosafety Network

Published: April 2026

Contents	
Executive Summary	3
Formalin & Formaldehyde’s role in healthcare	4
Occupational risks to healthcare workers	5
The Regulatory & Legal Landscape in Europe & UK	5
Cancer Risks Associated with Formaldehyde	8
Exposure Control in Occupational Settings	11
Health Effects at Low Dose	12
Evidence for Closed-System Interventions	14
Evaluating Closed-System Solutions	15
Conclusion	18
Bibliography	19

Executive Summary

Formalin, the liquid form of formaldehyde used to preserve tissue samples, remains essential to diagnostic pathology. It is also a volatile, toxic substance classified as a Category 1B carcinogen under both EU and UK regulations. Its unmatched performance as a tissue fixative means that formalin will continue to be used in healthcare settings for the foreseeable future. However, its hazardous properties place clear legal obligations on every employer whose staff handle it.

This white paper examines the evidence on formaldehyde exposure in healthcare settings and its implications for worker safety and regulatory compliance. It draws on occupational health research, regulatory analysis, and clinical implementation data to assess the scale of the problem and the effectiveness of available solutions.

The findings are clear. Healthcare workers who handle formalin regularly, including operating theatre nurses, pathology technicians, and laboratory staff, may be exposed to formaldehyde vapour at concentrations that cause measurable harm. Reported symptoms include eye and respiratory irritation, headaches, allergic rhinitis, asthma, and contact dermatitis (ATSDR, 2010), and these symptoms are significantly more prevalent among exposed workers than among the general population. At higher or prolonged exposures, formaldehyde's classification as a carcinogen is supported by epidemiological evidence linking occupational exposure to cancers of the upper respiratory tract (Protano et al., 2022).

European and UK law establishes a hierarchy of control that prioritises elimination of exposure at source. The EU Carcinogens, Mutagens and Reprotoxic Substances Directive (CMRD), updated in 2022, explicitly requires the use of closed systems to protect workers from carcinogenic substances wherever technically feasible. The UK Control of Substances Hazardous to Health (COSHH) Regulations impose equivalent duties. Understanding this landscape is essential for nurse managers and department heads.

Closed-system specimen containers meet these regulatory requirements by encapsulating formalin and preventing vapour release during handling. Evidence from a twenty-year monitoring programme at Careggi University Hospital in Italy demonstrates that adoption of closed systems can reduce airborne formaldehyde concentrations by over 90%, achieving exposure levels that are effectively negligible from an occupational health perspective (Dugheri et al., 2020).

The most effective design uses containers in which formalin is stored in a sealed reservoir within the lid and released only after the specimen has been secured inside the container. This design prevents vapour release at the point of specimen collection and during routine handling. Such systems have been validated in clinical settings across Europe, the Americas, and Australasia, and integrate with existing workflows, requiring low capital expenditure and no specialist training.

For healthcare institutions still using open containers, the availability of proven closed-system alternatives has significant compliance implications. Given current evidence and regulatory expectations, adoption of closed-system specimen handling is not merely advisable but is rapidly becoming the standard of care that employers are legally required to pursue.

The Role of Formalin & Formaldehyde in Healthcare

Formaldehyde is a colourless, volatile gas at room temperature. In healthcare settings, it is mostly used as formalin, an aqueous solution of formaldehyde stabilised with methanol. For tissue fixation, formalin is typically diluted to approximately 4% formaldehyde (commonly referred to as 10% neutral buffered formalin). This formulation provides a reliable balance of stability, reactivity, and practical handling within clinical workflows.

Within histopathology, formalin remains the gold-standard fixative for preserving excised tissue samples for histological examination. Formaldehyde, the active component of formalin, binds to proteins and other cellular components, preventing tissue from breaking down after removal, and preserving its structure so it can be examined accurately under a microscope for diagnosis.

Decades of clinical practice have demonstrated that formalin-fixed tissue provides consistent and reproducible diagnostic outcomes, and alternative fixatives have not yet matched its combination of performance, cost-effectiveness, and compatibility with established laboratory methods. Consequently, formalin is expected to remain an essential component of routine diagnostic pathology for the foreseeable future (OSHA, 2011).

However, formaldehyde's reactivity is a double-edged sword. While these characteristics underpin the reason for its value as a fixative, they also contribute to its hazardous properties.

Formaldehyde is volatile at room temperature, and even small quantities can release detectable vapour. Healthcare workers who work with formaldehyde or formaldehyde-containing products face significantly greater risk than the general population, due to higher levels of exposure through vapours or dermal contact through their daily activities (OSHA, 2011). Measurements show that naturally occurring formaldehyde levels indoors range from 0.02-4 parts per million (ppm), while outdoor levels range from 0.0002 to 0.006 ppm in countryside and suburban areas and 0.001 to 0.02 ppm in urban areas (ATSDR, 2010). By contrast, occupational exposure in pathology laboratories can reach 0.25 to 0.66 ppm during tissue handling and grossing, up to 33 times higher than typical indoor levels and up to eight times the WHO indoor air quality guideline (Yahyaei and Majlesi, 2020).

Occupational Risks to Healthcare Workers

Exposure can occur during a range of routine activities. Operating theatre nurses may be exposed when opening pre-filled specimen containers; pathology technicians during tissue grossing; and laboratory staff when processing fixed samples. Depending on local procedures, ventilation, and control measures, some of these workers may face repeated exposure to formaldehyde vapour during the course of their daily working day.

Formaldehyde volatilises readily at room temperature, creating an inhalation hazard during clinical procedures. Dermal contact constitutes a secondary but important form of exposure, with documented cases of primary irritation and allergic dermatitis among healthcare staff handling 10% formalin solutions. Operating rooms and procedure rooms experience short-term exposure peaks when pre-filled containers are opened, and sometimes left open, at the point of specimen collection (typically the operating theatre) or when spillages occur during sample acquisition (Glass, 1961; Rostenberg et al., 1952).

The health effects begin at very low concentrations. Even at 0.1 to 0.5 ppm, increased nasal and eye irritation, neurological effects, and increased risk of asthma and allergy have been recorded. Eczema and changes in lung function have been observed at 0.6 to 1.9 ppm (ATSDR, 2010). Airborne formaldehyde concentrations above 0.1 ppm cause respiratory tract irritation, with severity intensifying as concentration increases (OSHA, 2011).

These operational realities do not merely represent a health and safety concern; they constitute a breach of legal obligations under European and UK law, both of which classify formaldehyde as a known carcinogen and mandate specific protective controls.

Preliminary evidence has also suggested an association between formaldehyde exposure and adverse reproductive outcomes, including miscarriage (Wang et al., 2017), although further research is needed to confirm these findings.

In a recent Danish documentary (Den Giftige Tvivl, Danish Broadcasting Corporation, February 2026), four former student instructors exposed to formalin in an anatomy dissection lab at the University of Copenhagen developed cancer at a young age; three have died. The diagnoses occurred within a cohort of an estimated 40 to 60 instructors over about ten years, prompting questions about occupational exposure while stopping short of concluding causation.

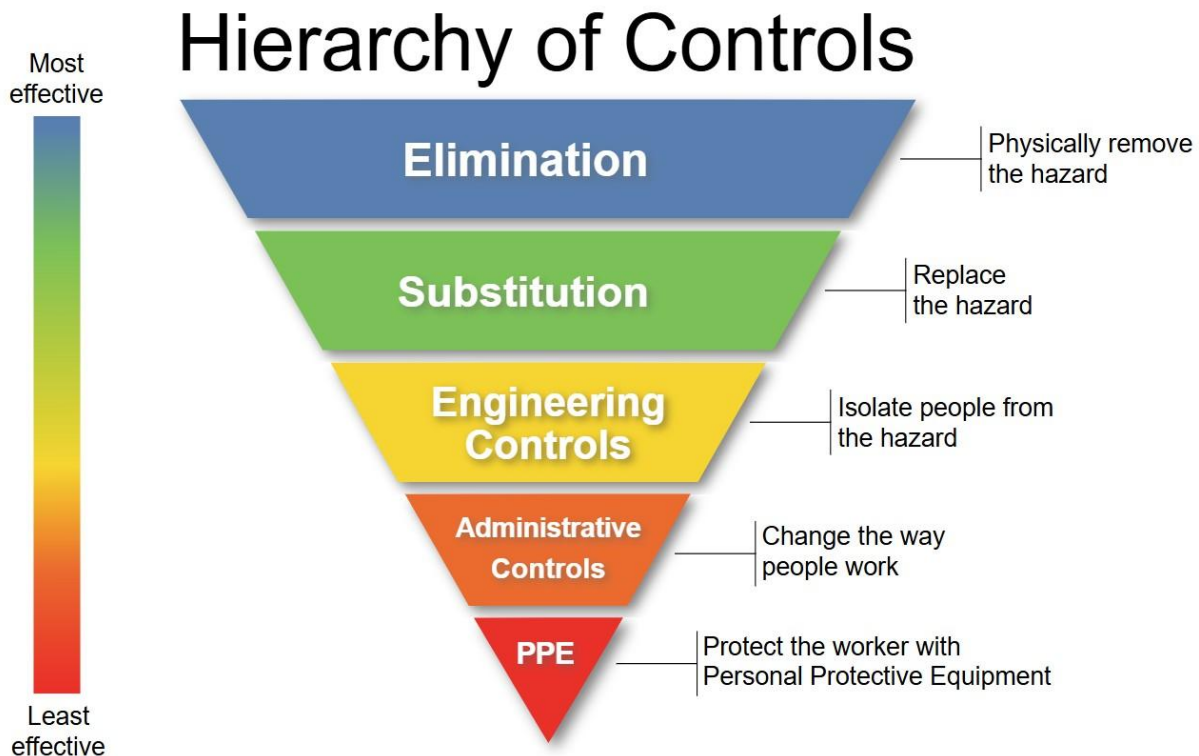
The Regulatory & Legal Landscape in Europe & UK

European and UK regulations establish a clear principle: formaldehyde is a recognised carcinogen, and worker exposure must be prevented or minimised at source.

The European Union

Formaldehyde is classified as Category 1B under the EU CLP Regulation (EC No 1272/2008), bringing it directly under the scope of the Carcinogen, Mutagen and Reprotoxic Substances Directive (CMRD 2004/37/EC; European Commission, 2014). As amended by Directive (EU) 2019/983 and Directive (EU) 2022/431, the CMRD places stringent duties on employers whose staff work with carcinogenic substances.

Following a risk assessment, the directive establishes a hierarchy of controls that prioritises eliminating or substituting the hazardous substance in question. Where elimination or substitution is not technically feasible, as is the case with formalin in current clinical and histopathological practice, the hierarchy requires employers to implement engineering and organisational controls as the next priority, including the use of closed systems. Personal protective equipment (PPE) is a last resort for protection, rather than a primary means of control.



A labelled diagram depicting the hierarchy of controls

For formaldehyde, Annex III of the CMRD requires that work involving carcinogens must be undertaken using closed systems whenever the nature of the work allows.

Where closed systems cannot be applied, exposure must be reduced "to as low a level as is technically possible," a principle consistent with the ALARP (As Low As Reasonably Practicable) framework, and employers must also implement comprehensive risk management measures. This includes mandatory risk assessments, which must be regularly reviewed and updated whenever conditions change, with relevant information made available to the authorities upon request. Risk assessments must identify and evaluate all possible routes of exposure, including inhalation and all forms of skin contact. Where biological limits have been established, health surveillance is mandatory and workers must be informed of this requirement before being assigned to any task involving a risk of exposure (CMRD 2004/37/EC).

The EU Scientific Committee on Occupational Exposure Limits recommends an 8-hour occupational exposure limit of 0.3 ppm and a 15-minute short-term exposure limit of 0.6 ppm (SCOEL, 2016). The World Health Organisation indoor air guideline of 0.1 mg/m³ (approximately 0.08 ppm) over 30 minutes provides a further benchmark frequently used to assess indoor air quality in hospitals, particularly in settings where vulnerable individuals, such as children, the elderly, and people with preexisting asthma or respiratory conditions, may be exposed (WHO, 2010).

Member States are required to establish enforcement mechanisms and penalties, although the nature and scale of said penalties can vary between jurisdictions depending on the Member State, to ensure compliance with the CMRD. Under the Framework Directive 89/391/EEC, which underpins the CMRD, Member States must provide for "adequate penalties" that are "sufficiently dissuasive" for violations of occupational safety and health regulations. The specific enforcement measures and penalty levels vary by Member State, as each country transposes the EU directive into its national law and establishes its own sanctioning procedures. Enforcement typically involves labour inspectorates who conduct workplace audits and can issue warnings, binding orders, and financial penalties. Non-compliance can result in administrative fines, orders to cease non-compliant conduct, mandatory implementation of corrective measures within specified timeframes, and in cases of serious or repeated violations, potential suspension of operating licences or criminal proceedings.

United Kingdom

In the UK, formaldehyde exposure is regulated primarily through the Control of Substances Hazardous to Health (COSHH) Regulations, which establish a legal duty on employers to ensure exposure to hazardous substances "is either prevented or, where this is not reasonably practicable, adequately controlled" (HSE, 2002).

Following Brexit, the UK retained the CLP framework in domestic law under the GB CLP Regulation, which applies in England, Scotland and Wales. Northern Ireland continues to follow the EU CLP Regulation. Formaldehyde remains classified as a Category 1B carcinogen under both regimes, and its handling therefore requires enhanced risk management measures, including strict process controls and ongoing health surveillance (European Commission, 2014)

The HSE's enforceable Workplace Exposure Limit (WEL) for formaldehyde is 2 ppm for both an 8-hour time-weighted average and a 15-minute short-term limit, which is notably higher than the limits adopted in the European Union (HSE, 2020). However, COSHH embeds the principle that exposure to carcinogens must be minimised to the lowest level reasonably practicable (the ALARP principle), meaning that compliance with the numerical limit alone is insufficient if safer engineering controls are available.

COSHH guidance mandates that employers implement closed systems for carcinogenic substances wherever reasonably practicable. Employers must apply the hierarchy of control, beginning with elimination, substitution, and closed or enclosed systems before considering

PPE (HSE, 2002). The regulations also mandate the safe storage, handling and disposal of carcinogens in closed and clearly labelled containers.

While COSHH does not specify the use of closed-system containers when handling biopsies by name, such systems directly fulfil the regulatory requirement to enclose carcinogenic substances and prevent vapour release during handling, transport and disposal. The regulations also emphasise the necessity of local exhaust ventilation, sealed handling systems, and written procedures when working with volatile carcinogens such as formaldehyde (HSE, 2002).



Healthcare workers wearing PPE whilst handling specimen containers

Cancer Risks Associated with Formaldehyde

Studies of workers exposed to formaldehyde over long periods show that cancer risk is highest among those who experience frequent high-concentration exposures or prolonged cumulative contact. The cancers most consistently linked to formaldehyde are those of the nasopharynx and nasal cavities, which is consistent with the fact that inhaled formaldehyde comes into direct contact with the lining of the nose and upper airways. Multiple reviews of the research evidence support this association (Partanen, 1993; Blair et al., 1990). For other cancer types, including lung cancer and blood cancers such as leukaemia, the evidence is weaker and less consistent. However, nasopharyngeal cancer remains the outcome most clearly associated with occupational formaldehyde exposure across the published research.

More recent reviews of the research reinforce this pattern. Although weak or inconsistent associations have been reported for lung cancer and leukaemia, the strongest and most reproducible findings relate to cancers of the nasal cavities and nasopharynx (Protano et al., 2022; Kang et al., 2021). These are the tissues that come into direct contact with inhaled formaldehyde, which helps to explain why they are the most affected.

Formaldehyde is also highly reactive and is toxic primarily at the portal of entry. When inhaled, it directly affects the cells lining the upper airways, where it can damage DNA, disrupt normal cellular processes, and form harmful chemical linkages between DNA and proteins. This damage interferes with the cell's ability to repair itself and is known to play an early role in cancer development. Experimental and occupational studies have documented increased DNA damage, chromosomal alterations, and protein adduct formation in nasal and upper airway tissues of exposed individuals, providing a clear mechanistic explanation for why inhalation exposure specifically drives cancer risk in these regions (Kang et al., 2021).

In contrast, the evidence linking formaldehyde exposure to leukaemia remains inconsistent and controversial. While some cohort and case control studies, particularly among embalmers and funeral industry workers, have reported elevated risks for myeloid leukaemia, many extended follow up analyses have failed to confirm a clear or persistent association. Toxicological and toxicogenomic research suggests possible indirect mechanisms involving oxidative stress and disruption of haematopoietic processes. However, the plausibility of significant distant site effects remains debatable, as inhaled formaldehyde is rapidly metabolised and its toxicity is largely confined to tissues at the portal of entry (Kang et al., 2021). Taken together, the current evidence supports the classification of formaldehyde as a human carcinogen primarily on the basis of upper respiratory tract cancers, while the evidence for leukaemia remains limited and less conclusive.

These findings have direct implications for occupational health practice. Because cancer risk is most clearly associated with high peak exposures rather than low background levels alone, any activity that generates a burst of formaldehyde vapour, such as opening a specimen container or pouring formalin, is a particular concern. Reducing or eliminating these peak exposures is the most effective way to lower cancer risk for healthcare workers.

Asthma & Respiratory Effects

Formaldehyde is a potent respiratory irritant. When present in air at levels above about 0.1 ppm, it can cause watery eyes, burning of the eyes and throat, coughing and wheezing. A strong and consistent body of evidence links formaldehyde exposure with asthma and other respiratory conditions in both occupational and non-occupational settings. Systematic reviews show that people exposed to formaldehyde are more likely to be diagnosed with asthma and to experience worsening respiratory symptoms such as wheeze, cough, chest tightness, and shortness of breath. These associations have been observed in adults and children, with particularly robust evidence in indoor environments and workplaces where exposure may be repeated or sustained over time (Lam et al., 2021; La Torre et al., 2023).

Formaldehyde dissolves readily in airway mucus, stimulating nerve endings and provoking inflammation. At higher concentrations, it can damage airway epithelial cells and impair the

lung's barrier function. Repeated low-level exposure sensitises the airways and increases hyperresponsiveness. Such exposure patterns are typical in healthcare settings: for example, short peaks during cleaning, specimen handling or opening jars occur alongside continuous low-level background exposure. Even when measured concentrations remain within regulatory limits, this pattern can lead to chronic airway inflammation. (Lam et al., 2021; La Torre et al., 2023).

A comprehensive systematic review evaluating more than 100 human studies concluded that there is sufficient evidence of toxicity linking formaldehyde exposure with asthma diagnosis and asthma symptom exacerbation in both children and adults. The analysis demonstrated increased odds of asthma diagnosis with incremental increases in airborne formaldehyde concentrations, supporting a clear exposure response relationship (Lam et al., 2021).

Occupational studies provide further support for this association, particularly in healthcare settings. Cross-sectional research among healthcare workers shows elevated rates of work-related asthma symptoms in individuals exposed to mixtures of chemicals that include cleaning agents and products containing formaldehyde. In a study of hospital staff, frequent exposure to cleaning agents, alkali substances, and formaldehyde was associated with a markedly increased risk of work-related asthma symptoms compared with unexposed workers. Workers exposed to this group of substances were more than five times more likely to report asthma symptoms that worsened at work compared with unexposed colleagues, even with adjustment for smoking and individual factors (Al Zoughool and Al Mistneer, 2018). These findings highlight that both medical and non-medical healthcare staff may be affected, reflecting the widespread use of formaldehyde-containing products within hospital environments.

Crucially, respiratory harm is not limited to high-level exposures. Evidence indicates that even lower concentrations are associated with chronic irritation, immune activation, and airway sensitisation. Formaldehyde can function as an allergen sensitiser, promoting inflammatory and immune-mediated responses that increase airway hyperresponsiveness. Repeated exposure may therefore contribute to the development of asthma as well as the exacerbation of existing disease, particularly among workers who may be exposed on a daily basis (Lam et al., 2021).

In healthcare and laboratory settings, these mechanisms are especially relevant. Workers may experience repeated short term exposure peaks during routine tasks such as cleaning, specimen handling, or opening containers, alongside continuous low level background exposure throughout the working day. Over time, this pattern of exposure can drive chronic airway inflammation and persistent respiratory symptoms, even when measured concentrations remain within regulatory limits.

Exposure Control in Occupational Settings

Formaldehyde exposure in healthcare is not confined to the laboratory. Operating theatre nurses handle formalin containers at the point of specimen collection, often without the fume hoods or extraction systems available in laboratory settings. Understanding how exposure is controlled and where current controls fall short is essential context for the whole healthcare team.

Despite clear regulatory standards under the EU Carcinogens, Mutagens and Reprotoxic Substances Directive (CMRD) and the UK COSHH Regulations, practical control of formaldehyde exposure in healthcare settings remains patchy. Specimen collection and storage often rely on open or poorly sealed containers, creating peaks of vapour release at the point of use and during subsequent handling. This exposes staff to unnecessary risk and leaves employers vulnerable to potential legal challenges. Evidence from recent occupational studies shows that compliance with exposure limits alone does not equate to protection; exposure must be eliminated or contained at source.

Environmental monitoring consistently finds that histopathology workers experience significantly higher exposures than administrative staff. A comparative study across four Malaysian hospitals measured time-weighted-average (TWA) airborne concentrations of 0.25 ppm in exposed areas versus 0.08 ppm in non-exposed areas; histopathology laboratory workers were exposed to 140 to 480% higher concentrations than administration workers. Personal sampling identified grossing - the manual slicing and inspection of specimens - as the highest-exposure task, with short-term exposures averaging 0.797 ppm (Zain et al., 2019).

Hospital and job title	Occupational exposure to formaldehyde (ppm)			Mean exposure index (Ei)
	Min	Mean \pm SD	Max	
A				
Pathologist	0.05	0.06 \pm 0.26	0.13	4.32
Lab technician	0.05	0.08 \pm 0.49	0.2	5.45
Housekeeping staff	0.01	0.03 \pm 0.014	0.05	2.90
B				
Pathologist	0.05	0.06 \pm 0.014	0.07	3.60
Lab technician	0.05	0.06 \pm 0.014	0.07	3.60
Housekeeping staff	0.01	0.016 \pm 0.015	0.03	1.17
C				
Pathologist	0.01	0.065 \pm 0.077	0.12	3.94
Lab technician	0.03	0.07 \pm 0.05	0.11	4.33
Housekeeping staff	0.01	0.01 \pm 0	0.01	0.63
D				
Pathologist	0.19	0.19 \pm 0	0.19	11.74
Lab technician	0.02	0.12 \pm 0.14	0.22	7.80
Housekeeping staff	0.02	0.02 \pm 0	0.02	1.25
TLV (NIOSH)		0.016 (ppm)		

Occupational exposure to formaldehyde at studied hospitals (Foroughi et al., 2024)

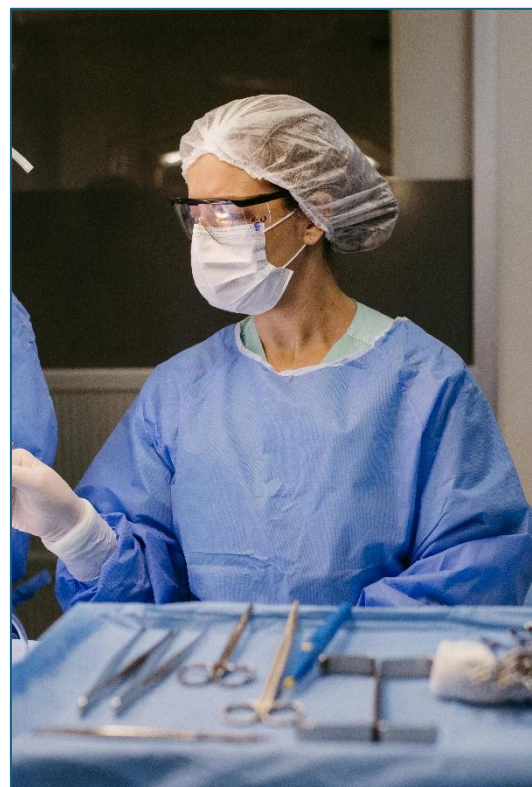
Similar patterns have been documented elsewhere. In North Borneo, monitoring of a histopathology laboratory and a control office showed an eight-hour TWA of 0.113 ppm for laboratory staff versus 0.031 ppm for office workers. Air sampling confirmed higher exposures in the lab (0.108 ± 0.026 ppm) compared with the office (0.028 ± 0.018 ppm). Although these levels were below the OSHA TWA limit (0.75 ppm), 51% of laboratory workers reported symptoms such as irritated eyes, sore throat, cough, runny nose, sneezing, and headache, compared with 35% of the control group (Ramli et al., 2023).

A risk assessment covering five Iranian hospitals found formaldehyde concentrations ranging from 0.019 to 0.326 ppm in pathology departments; laboratory technicians had a weekly exposure index of 0.664 ppm, whereas office workers averaged only 0.025 ppm. Ventilation quality and duration of handling tasks were identified as key determinants of exposure, underscoring that high exposure is a function of work organisation as much as the chemical itself (Foroughi et al., 2024).

Health Effects at Low Dose

It is important to note that this does not mean that low-dose exposure is benign. A cross-sectional study of 414 healthcare workers in Taiwan assessed exposure levels that were all below 10% of the permissible limit. Even at these concentrations, exposed workers reported significantly higher rates of irritation-related symptoms (9.5% vs 0.6% in controls) and skin symptoms (1.7% vs 0%). After adjusting for confounders, formaldehyde exposure was strongly associated with allergic rhinitis (odds ratio 16.78) and allergic dermatitis (odds ratio 18.83); pulmonary function differences were not observed. These data challenge the notion that compliance with a TWA limit is sufficient and highlight the need to minimise exposure to the lowest achievable level (Fan et al., 2025).

Chronic dermal exposure adds another dimension. Formaldehyde is a recognised allergen; sensitisation rates range from 2 to 3% in Europe to 8 to 9% in the United States, and prevalence may be higher among healthcare workers. In patch testing of nurses with suspected occupational skin disease, 20.6% showed a positive reaction to formaldehyde, indicating sensitisation within this symptomatic group. Case reports describe workers developing allergic contact dermatitis despite the use of latex-free gloves, implicating contamination of gloves or other materials. Management of formaldehyde-induced dermatitis depends on avoiding the agent; simply switching glove brands or applying topical treatments does not remove the underlying risk (Duarte et al., 2025).



Healthcare worker wearing PPE

Although rare, long-term exposure can lead to serious diseases like cancer. A case report from Norway described an auxiliary nurse who developed adenoid cystic carcinoma of the maxillary sinus after 11 years of handling biopsies and disinfecting operating theatres without respiratory protection; she poured formaldehyde into sinks, handled tissue containers multiple times per day and sprayed disinfectant containing formaldehyde three to four times daily. Mean formaldehyde concentrations during tissue preparation in histopathology laboratories are approximately 0.5 ppm, while disinfection of operating theatres using formaldehyde-based disinfectants averages 0.8 ppm; levels thought sufficient to induce irritation and possibly cancer. The case underscores the long latency of formaldehyde-related cancers and the need to treat prevention as the only acceptable option (Sandvik et al., 2014).

Limitations of Current Controls



Healthcare worker wearing PPE

Healthcare facilities rely on a combination of engineering controls, administrative measures and personal protective equipment (PPE) to manage exposure. Engineering controls such as ducted backdraft grossing stations, fume hoods and mechanical exhaust ventilation can reduce airborne formaldehyde concentrations, but their effectiveness varies. Studies from Malaysian histopathology laboratories attribute elevated formaldehyde levels to inadequate local exhaust ventilation and improper processing controls (Zain et al., 2019). Even when ventilation systems are present, workers often sit with formalin-soaked specimens close to the breathing zone; personal exposure during grossing can be two to three times higher than ambient levels. Ventilation may reduce concentrations but cannot eliminate peaks at the point of container opening.

Administrative controls such as staff rotation, written procedures, and training programmes provide supplementary protection but do not remove the hazard. Rotating staff through formalin-handling tasks can reduce individual exposure time, but it distributes the risk across a larger number of workers rather than eliminating it. Training must be regular and practical; its effects diminish over time, particularly when high workload or staffing pressures lead to shortcuts. Regular air monitoring is essential to verify that controls are working, yet many facilities lack the real-time monitoring systems needed to detect short-term exposure peaks.

PPE sits at the bottom of the hierarchy of control. Standard surgical masks and nitrile or latex gloves are designed to protect against biological hazards and particulate matter, but they offer little defence against a volatile gas. Studies from Malaysian laboratories found that most workers wore latex gloves, 3-ply masks and plastic coats, none of which are certified for formaldehyde protection (Zain et al., 2019). Effective respiratory protection requires respirators fitted with chemical cartridges designed specifically to adsorb formaldehyde vapour; standard surgical masks do not provide this protection, and chemical-resistant gloves must be selected based on permeation data. Reliance on inappropriate PPE creates a false sense of security and may increase exposure if workers believe they are adequately protected.



Evidence for Closed-System Interventions

The evidence presented in the preceding *Healthcare worker wearing PPE* sections demonstrates that ventilation, administrative measures, and personal protective equipment each have significant limitations when used alone. The most effective strategy is to eliminate vapour release at the source. Closed-system specimen containers achieve this by sealing formalin within the container throughout the specimen pathway, from the operating theatre to the pathology laboratory, preventing the formation of vapour clouds during handling, transport, and storage.

The most detailed published evidence on the effectiveness of closed systems comes from a twenty-year monitoring programme at Careggi University Hospital in Florence. After introducing safe practices in 2019, including pre-loaded containers with a closed-circuit system and vacuum sealing, 94% of airborne measurements fell below $16 \mu\text{g}/\text{m}^3$ (approximately 0.013 ppm), and only 6% of samples ranged between 21 and $75 \mu\text{g}/\text{m}^3$. Implementation of closed-circuit containers and adoption of the Italian standard UNI/TS

11710:2018; which defines acceptance limits and robustness criteria for fume cupboard containment and air-exchange efficiency; were associated with a 93% decrease in both time-weighted and short-term exposures in the gross room, and an 87% decrease at specimen reception and in operating theatres. Further reductions were achieved by combining ergonomic workstations, continuous photoacoustic monitoring and rigorous staff training (Dugheri et al., 2020).

These systems are not complex. Pre-filled containers in which the formalin is sealed within the closure mechanism confine vapours. Under-vacuum storage for larger specimens prevents leaks and agitation during transport. Where multiple closed-system container products were trialled, the hospital found that closed circuits were robust and practical; however, they also noted that containers should be allowed to settle after transport to prevent any residual vapour trapped in the air gap above the liquid from escaping when the container is opened. The Italian experience demonstrates that, when combined with ventilation, training and real-time monitoring, closed systems can reduce occupational exposure to levels far below regulatory limits, while maintaining diagnostic quality and workflow efficiency.

Implications for Compliance

The collective evidence is clear: reliance on open containers, ventilation and basic PPE leaves healthcare workers exposed to formaldehyde vapours that cause irritation, allergic disease and, in rare cases, cancer. Exposure levels remain high in histopathology and operating theatre settings, and symptoms occur even when concentrations are below existing regulatory limits. Engineering and administrative controls reduce exposure but cannot eliminate the peaks associated with specimen handling.

Closed-system specimen containers and vacuum-sealed pathways offer a practical, proven route to eliminating exposure at its source. The CMRD and COSHH frameworks already require employers to use the most effective control measures available; given the demonstrable efficacy of closed systems, continued use of open containers is difficult to justify.

Evaluating Closed-System Solutions

The preceding sections establish that closed-system containers are the most effective engineering control for eliminating formaldehyde exposure at source and during routine operations. However, it should be noted that not all closed system containers are equivalent. Products on the market differ significantly and can vary in their design, regulatory status, and practical suitability for clinical and laboratory workflows. Healthcare institutions evaluating closed-system solutions should consider the following criteria to ensure that the system they adopt delivers genuine protection to their workforce.

Seal Integrity and Leakage Prevention

The primary function of any closed system should be to prevent vapours from escaping during handling, transport, and storage. The robustness of the seal between the lid and the container body is therefore the most critical element. Systems that employ internal threading, where the lid engages within the container wall rather than over it, provide a more reliable and tamper-resistant closure than external-thread or friction-fit designs.

The quality of the plastics used is equally important: containers manufactured from inferior materials may deform under temperature variation or mechanical stress during transport, compromising the seal over time. Institutions should seek evidence that a system has been rigorously tested for leak resistance under realistic day-to-day conditions, including agitation during transit and temperature fluctuations.

Hands-On Complexity and Risk of User Error

In a busy operating theatre, where conditions are often suboptimal, and healthcare workers are operating under pressure, specimen collection is rarely the clinician's primary focus. The system used must therefore be simple enough to operate correctly under time pressure and without specialist training. Systems that require multiple assembly steps (such as separate formalin ampoules that must be broken or inserted, or multi-part containers that must be configured before use) introduce additional handling stages, each of which represents an opportunity for error, spillage, or incomplete closure. Pre-analytical errors account for 60 to 70% of all laboratory errors, with specimen handling identified as a major contributor (Hammerling, 2012). The most effective design should minimise the number of steps between specimen excision and secure containment in formalin.

Single-action mechanisms, in which a press or twist releases pre-loaded formalin into the specimen chamber after the container has been sealed, reduce handling to its minimum and substantially lower the risk of user error. In contrast, systems that require the operator to add formalin separately or to assemble multiple components demand more time, more training, and more attention: resources that are often in short supply in clinical settings.

Regulatory Status

Not all closed-system containers on the market carry the same regulatory credentials. Under the EU In Vitro Diagnostic Regulation (IVDR 2017/746), specimen containers that are intended for use in the collection, transport, or storage of samples for diagnostic examination are classified as in vitro diagnostic medical devices and must meet the applicable conformity requirements (European Parliament, 2017). Healthcare institutions should verify that any system under consideration bears a valid CE marking in accordance with IVDR (EU 2017/746), or holds equivalent regulatory approval in jurisdictions outside of the EU. Use of non-compliant products may expose institutions to regulatory risk and undermine the broader compliance rationale for adopting closed systems in the first place.

Formalin Readiness and the Risks of Prefilled Alternatives

Closed systems broadly divide into two categories: those prefilled with ready-to-use formalin and those prefilled with saline or buffer solution, in which a separate formalin reservoir is released at a later stage. The distinction has practical consequences.

Systems prefilled with saline or buffer require the operator to activate formalin release after the specimen has been placed in the container, typically by pressing, twisting, or breaking an internal reservoir. If this step is overlooked or performed incorrectly, the specimen may remain in saline rather than formalin, delaying or compromising fixation. This is not a trivial concern: delayed formalin fixation has been shown to degrade biomarker integrity, with studies

demonstrating that fixation delay is responsible for a 10 to 20% false-negative rate for oestrogen receptor testing in breast carcinoma, prompting ASCO and CAP to limit recommended cold ischaemic time to 60 minutes (Yildiz-Aktas et al., 2012). In high-throughput clinical environments, the potential for this error is again not trivial. Furthermore, saline-prefilled containers that remain unused for extended periods may be susceptible to microorganism growth within the buffer solution, creating an additional handling concern.

By contrast, systems in which formalin is pre-loaded in a sealed reservoir within the lid and released directly upon activation eliminate the ambiguity. There is no intermediate fluid, no question of whether fixation has commenced, and no risk of bacterial contamination from a standing buffer. For institutions seeking to standardise their specimen pathway and reduce variability, ready-to-use formalin systems offer a more reliable workflow.

Accessibility for Laboratory Processing

The specimen pathway does not end at collection. Once the container reaches the pathology laboratory, technicians must retrieve the specimen for grossing and further processing. Container designs that are difficult to open, that trap specimens in narrow cavities, or that require specialist tools to access the contents create inefficiency and frustration downstream. An effective closed system should be as practical for the laboratory technician who opens it as for the clinician who seals it. Wide-mouth designs, intuitive opening mechanisms, and clear specimen visibility all contribute to a system that supports, rather than hinders, laboratory workflow.

Size Range and Environmental Considerations

The majority of excised tissue specimens fit within containers of 60 mL or less. A system that offers a range of container sizes allows institutions to match the container to the specimen, avoiding the unnecessary use of oversized containers and the associated waste of formalin. Reducing formalin volume per specimen has both environmental and economic benefits, and minimising the quantity of plastic per container contributes to institutional sustainability objectives. Systems that offer only a single container size, or that require disproportionately large volumes of formalin relative to specimen size, represent a less efficient use of resources.

Choosing Wisely

No single evaluation criterion should determine the choice of closed system. Rather, the decision should reflect a balanced assessment of seal integrity, operational simplicity, regulatory compliance, formalin management, laboratory practicality, and environmental efficiency. Systems that perform well across all of these dimensions; such as single-action, press-release designs prefilled with ready-to-use formalin in multiple container sizes; represent the current standard of best practice in closed-system specimen handling.

Conclusion

Formaldehyde remains indispensable to diagnostic pathology. Its unmatched performance as a tissue fixative ensures that formalin will continue to be used in healthcare settings for the foreseeable future. However, routine handling of formalin poses significant and well-documented risks to healthcare workers; risks that current practices fail to adequately address.

The health effects of formaldehyde exposure are not theoretical. Occupational studies consistently show that histopathology workers, theatre nurses, and laboratory staff experience elevated rates of respiratory irritation, allergic rhinitis, contact dermatitis, and other symptoms directly attributable to formalin vapour and dermal contact. These effects occur even when measured exposures fall within regulatory limits, challenging the assumption that compliance with threshold values equates to protection. At higher or prolonged exposures, formaldehyde's classification as a Category 1B carcinogen is borne out by epidemiological evidence linking occupational exposure to cancers of the upper respiratory tract.

The regulatory position is clear. Both the EU Carcinogens, Mutagens and Reprotoxic Substances Directive and the UK Control of Substances Hazardous to Health Regulations require employers to use closed systems for carcinogenic substances wherever technically feasible. Personal protective equipment and ventilation, while useful as supplementary measures, sit at the bottom of the hierarchy of control and cannot substitute for elimination at source.

Closed-system specimen containers represent the practical fulfilment of these regulatory requirements. The evidence from Careggi University Hospital demonstrates that implementation of closed systems can reduce airborne formaldehyde concentrations by over 90%, achieving exposure levels that are effectively negligible from an occupational health perspective. Crucially, these reductions are achieved without compromising diagnostic quality or workflow efficiency.

Closed systems offer healthcare institutions a validated, accessible route to compliance. By encapsulating formalin within the container lid and eliminating vapour release during specimen handling, the system removes the primary source of occupational exposure. It requires no capital expenditure, integrates seamlessly with existing clinical workflows, and has been successfully adopted across hospital and research settings in Europe, the Americas, and Australasia.

The question facing healthcare providers is no longer whether closed-system specimen handling is necessary, but how quickly it can be implemented. Given the demonstrable efficacy of available solutions, continued reliance on open containers, ventilation, and inadequate PPE is increasingly difficult to defend; both as a matter of worker safety and regulatory compliance. Healthcare institutions that delay adoption expose their staff to avoidable harm and themselves to potential legal liability.

The path forward is clear. Closed-system technologies enable healthcare providers to meet their duty of care to staff, satisfy regulatory requirements, and maintain the diagnostic standards on which patient care depends. Adoption is not merely advisable; in the context of current evidence and regulatory expectations, it is the only defensible course of action.

Bibliography

Agency for Toxic Substances and Disease Registry (ATSDR) (1999) *Toxicological profile for formaldehyde*. Addendum published 2010. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Available at: <https://www.atsdr.cdc.gov/toxfaqs/tfacts111.pdf> (Accessed: 17 February 2026).

Akbar Khanzadeh, F., Vaquerano, M.U., Akbar Khanzadeh, M. and Bisesi, M.S. (1994) 'Formaldehyde exposure, acute pulmonary response, and exposure control options in a gross anatomy laboratory', *American Journal of Industrial Medicine*, 26(1), pp. 61 to 75.

Al Zoughool, M. and Al Mistneer, R. (2018) 'Risk of asthma symptoms among workers in health care settings', *International Journal of Environmental Impacts*, 1(2), pp. 172 to 182.

Blair, A., Saracci, R., Stewart, P.A., Hayes, R.B. and Shy, C. (1990) 'Epidemiologic evidence on the relationship between formaldehyde exposure and cancer', *Scandinavian Journal of Work, Environment and Health*, 16(6), pp. 381 to 393.

Duarte, A., Bica Tavares, M., Matos Barbosa, R., Dias, A., Gil Duarte, R., Saldanha, N.A. and Alves de Matos, S. (2025) 'Occupational contact dermatitis to formaldehyde', *International Journal of Clinical Studies and Medical Case Reports*, 49(5).

Danish Broadcasting Corporation (2026) Den Giftige Tvivl [The Toxic Doubt]. Television documentary, February 2026.

Dugheri, S., Massi, D., Mucci, N., Berti, N., Cappelli, G. and Arcangeli, G. (2020) 'How improvements in monitoring and safety practices lowered airborne formaldehyde concentrations at an Italian university hospital: a summary of 20 years of experience', *Arhiv za Higijenu Rada i Toksikologiju*, 71(3), pp. 178 to 189.

European Commission (2014) *Commission Regulation (EU) No 605/2014 of 5 June 2014 amending Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures*. *Official Journal of the European Union*, L 167, pp. 36 to 49. Available at: <https://eur-lex.europa.eu/eli/reg/2014/605/oj/eng> (Accessed: 17 February 2026).

European Commission (2022) *Directive (EU) 2022/431 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens, mutagens and reprotoxic substances*. *Official Journal of the European Union*, L 88/2, 9 March.

European Parliament and Council of the European Union (2017) *Regulation (EU) 2017/746 on in vitro diagnostic medical devices*. *Official Journal of the European Union*, L 117, 5 May.

Fan, H.Y., Lin, J.P., Yang, T.A. and Tsao, Y.C. (2025) 'Health effects of low dose formaldehyde exposure: a cross sectional study in occupational settings', *International Journal of Occupational Medicine and Environmental Health*, 38(3), pp. 236 to 248.

Foroughi, P., Golbabaei, F., Sadeghi Yarandi, M., Yaseri, M., Fooladi, M. and Kalantary, S. (2024) 'Occupational exposure, carcinogenic and non carcinogenic risk assessment of formaldehyde in the pathology labs of hospitals in Iran', *Scientific Reports*, 14, p. 12006.

Glass, V.I. (1961) 'An outbreak of formaldehyde dermatitis', *New Zealand Medical Journal*, 60, pp. 423 to 427.

Hallmark Surgical (2024) 'Timaru Hospital BiopSafe case study'. Available at: <https://www.hallmarksurgical.com/case-studies/timaru-hospital-biopsafe-case-study/> (Accessed: 17 February 2026).

Hammerling, J.A. (2012) 'A review of medical errors in laboratory diagnostics and where we are today', *Laboratory Medicine*, 43(2), pp. 41 to 44.

Health and Safety Executive (HSE) (2002) *Control of Substances Hazardous to Health Regulations 2002 (SI 2002/2677)*. London: The Stationery Office. Available at: <https://www.legislation.gov.uk/ukxi/2002/2677/data.pdf> (Accessed: 17 February 2026).

Health and Safety Executive (HSE) (2020) *EH40/2005 Workplace exposure limits*. Sudbury: HSE Books. Available at: <https://www.hse.gov.uk/pubns/priced/eh40.pdf> (Accessed: 17 February 2026).

Kang, D.S., Kim, H.S., Jung, J.H., Lee, C.M., Ahn, Y.S. and Seo, Y.R. (2021) 'Formaldehyde exposure and leukemia risk: a comprehensive review and network based toxicogenomic approach', *Genes and Environment*, 43, p. 13.

La Torre, G., Vitello, T., Cocchiara, R.A. and Della Rocca, C. (2023) 'Relationship between formaldehyde exposure, respiratory irritant effects and cancers: a review of reviews', *Public Health*, 218, pp. 186 to 196.

Lam, J., Koustas, E., Sutton, P., Padula, A.M., Cabana, M.D., Vesterinen, H., Griffiths, C., Dickie, M., Daniels, N., Whitaker, E. and Woodruff, T.J. (2021) 'Exposure to formaldehyde and asthma outcomes: a systematic review, meta analysis, and economic assessment', *PLoS ONE*, 16(3), e0248258.

Partanen, T., Kauppinen, T. and Nurminen, M. (1993) 'Formaldehyde exposure and respiratory cancer: a meta analysis of epidemiological studies', *Scandinavian Journal of Work, Environment and Health*, 19(1), pp. 8 to 15.

Protano, C., Buomprisco, G., Cammalleri, V., Pocino, R.N., Marotta, D., Simonazzi, S., Cardoni, F., Petyx, M., Iavicoli, S. and Vitali, M. (2022) 'The carcinogenic effects of formaldehyde occupational exposure: a systematic review', *Cancers*, 14(1), p. 165.

Ramli, A., Shamsudin, S.B., Lim, J.F. and Lim, M.C. (2023) 'Occupational formaldehyde exposure and the health symptoms among histopathology laboratory workers in North Borneo', *Pertanika Journal of Science and Technology*, 31(5), pp. 2413 to 2426.

Rostenberg, A. Jr., Bairstow, B. and Luther, T.W. (1952) 'A study of eczematous sensitivity to formaldehyde', *Journal of Investigative Dermatology*, 19, pp. 459 to 462.

Sandvik, A., Klingen, T.A. and Langård, S. (2014) 'Sinonasal adenoid cystic carcinoma following formaldehyde exposure in the operating theatre', *Journal of Occupational Medicine and Toxicology*, 9(1), p. 43.

Scientific Committee on Occupational Exposure Limits (SCOEL) (2016) *Recommendation on occupational exposure limits for formaldehyde*. Opinion SCOEL/REC/125. European Commission. Available at:

https://echa.europa.eu/documents/10162/35144386/095_formaldehyde_oel_en.pdf

(Accessed: 17 February 2026).

United States Department of Labor, Occupational Safety and Health Administration (OSHA) (2011) *Formaldehyde fact sheet*. April 2011. Available at:

<https://www.osha.gov/sites/default/files/publications/formaldehyde-factsheet.pdf> (Accessed:

17 February 2026).

World Health Organization (WHO) (2010) *WHO guidelines for indoor air quality: selected pollutants*. Available at: <https://iris.who.int/server/api/core/bitstreams/202feb0d-06e8-418d-8e38-8927ec2d166b/content> (Accessed: 17 February 2026).

Wang, Q., Liu, H., Gao, H., Jiang, M., Zhu, C. and Wu, X. (2017) 'Association between formaldehyde exposure and miscarriage in Chinese women', *Medicine*, 96(26), e7146.

Yahyaei, E. and Majlesi, B. (2020) 'Occupational exposure and risk assessment of formaldehyde in the pathology departments of hospitals', *Asian Pacific Journal of Cancer Prevention*, 21(5), pp. 1303 to 1309.

Yildiz-Aktas, I.Z., Dabbs, D.J. and Bhargava, R. (2012) 'The effect of cold ischemia time on the immunohistochemical evaluation of estrogen receptor, progesterone receptor, and HER2 expression in invasive breast carcinoma', *Modern Pathology*, 25(8), pp. 1098 to 1105.

Zain, S.M.S.M., Azmi, W.N.F.W., Veloo, Y. and Shaharudin, R. (2019) 'Formaldehyde exposure, health symptoms and risk assessment among hospital workers in Malaysia', *Journal of Environmental Protection*, 10(8), pp. 861 to 879.

This white paper was prepared by the European Biosafety Network with research and editorial support from independent contributors. Its production was supported by industry.

Please contact: josh.cobb@europeanbiosafetynetwork.eu for more information.