Chemical Hazards in Hospitals: Risks, Regulations, and Protective Measures

Zahrah Ali Hussein AL Hamar[1], Talal Hamza Alrashidi[2], Theeb Dashin Alqatani[3], Salamah Jali Alotaibi[4], Saad Mohammed Al Samra[5], Waleed mansour saeed Alqahtani[6], Mohammed saeed Alqahtani[7], Fayez Mathkar Humud Aladhyani[8], Mohammed Hamed Alanazi[9], Motlag Abdullah L Alaotibi [10], Hanan Hassan Jalwai Alanezi[11], Mobark Alqahtani[12]

1. Master of Pharmacology, King Saud bin AbdulAziz University for Health Sciences, King Abdullah International Medical Research Center
2. Diagnostic Radiology Technology , Medina National Guards Hospital
3. EMT TECH, Saudi Arabia
4. Technician-Emergency Medical Services, National Guard
5. Emergency, Technician, King Khalid Military College Health Center
6. Technician-Emergency Medical Services, Saudi Arabia
7. Nursing, Saudi Arabia
8. EMT, Saudi Arabia
9. Technician-Emergency Medical Services, Saudi Arabia
10. Technician-Emergency Medical Services, National Guard, Saudi Arabia
11. Nurse, Public Health to Promote School Health, hhalanezi@moh.gov.sa
12. Health Informatics Specialist, Saudi Arabia

Published: 20 August, 2024

Abstract:

This article examines chemical hazards in hospital settings, focusing on risks from therapeutic, diagnostic, sterilization, and cleaning agents. Healthcare workers face exposure through inhalation, skin contact, or ingestion, with risks compounded by secondary contamination scenarios (e.g., chemically contaminated patients in emergency departments). Key hazards include formaldehyde (pathology), anesthetic gases (operating rooms), and antineoplastic drugs (pharmacies), linked to respiratory, dermatological, and reproductive health effects. The review highlights global regulatory frameworks (e.g., EU REACH, U.S. OSHA) and Saudi Arabia’s adoption of GHS standards. Effective risk management requires environmental/biological monitoring, engineering controls (ventilation, scavenging systems), and staff training. Challenges in Saudi hospitals—extreme climate, multinational workforce, and rapid healthcare expansion—necessitate tailored strategies. The article underscores the need for stringent safety protocols to protect workers and patients.

Chemical Hazards in Hospital Settings: An Overview

Hospitals utilize numerous chemicals for therapeutic, diagnostic, sterilization, cleaning, and research purposes. Healthcare workers may be exposed to these substances through inhalation, skin absorption, ingestion, or mucous membrane contact. Unlike industrial settings where chemical exposures might be more predictable, hospitals present diverse scenarios where multiple chemicals are used simultaneously in different departments (McDiarmid et al., 2006, Vecchio et al., 2003).

The risk profile of hospital chemical hazards is further complicated by secondary contamination scenarios. Stewart-Evans and colleagues (2013) highlighted how primary chemical exposures can lead to secondary hazards, particularly in emergency departments receiving chemically contaminated patients. This creates risks not only for emergency response personnel but potentially for the entire hospital environment if proper decontamination protocols are not followed.

Chemical exposures in hospitals have been associated with various adverse health effects, including respiratory disorders, dermatological conditions, reproductive problems, and increased cancer risks. A systematic review by Leso et al. (2019) found evidence linking occupational chemical exposures, including those found in healthcare settings, to increased breast cancer risk, particularly for hormone receptor-positive tumors.

In Saudi Arabian hospitals, these challenges are amplified by factors such as the rapid expansion of healthcare facilities, the multinational nature of the healthcare workforce, and the extreme climate conditions that may affect chemical storage and ventilation system efficiency. While specific data on chemical exposures in Saudi hospitals remains limited, the general principles of chemical hazard management apply universally, requiring adaptation to local conditions and regulations.

Regulatory Frameworks for Chemical Safety in Healthcare

Global and European Regulatory Framework

The European Union has established comprehensive regulatory frameworks to protect workers from chemical hazards. The European Agency for Safety and Health at Work (EU-OSHA) provides guidance and resources for occupational safety, including specific information for healthcare settings (European Agency for Safety and Health at Work, 2023).

Key European regulations governing chemical safety include REACH (Registration, Evaluation, Authorization and Restriction of Chemicals), implemented through EC Regulation 1907/2006. REACH requires manufacturers and importers to register chemicals and evaluate their hazards. This regulation aims to improve protection of human health and the environment through better identification of chemical properties (European Commission, 2006).

The CLP Regulation (Classification, Labelling and Packaging), established by EC Regulation 1272/2008, ensures that hazards presented by chemicals are clearly communicated to workers and consumers through classification and labeling. This harmonized system includes standardized hazard pictograms, signal words, and hazard statements that facilitate understanding of chemical risks across language barriers (European Commission, 2008).

Similar regulatory frameworks exist in South Korea, with the Act on the Registration and Evaluation of Chemicals (K-REACH) being implemented to align with international standards while incorporating specific national requirements (Ha et al., 2016).

United States Regulatory Framework

In the United States, chemical safety in hospitals is governed by several regulatory bodies and legislation. The Occupational Safety and Health Administration (OSHA), established by the OSH Act of 1970, develops and enforces workplace safety standards, including those for chemical hazards in healthcare settings (Occupational Safety and Health Administration, 1970).

The National Institute for Occupational Safety and Health (NIOSH) conducts research and provides guidance on occupational health matters, including strategies for sampling and monitoring chemical exposures (National Institute for Occupational Safety and Health, 1977).

Saudi Arabian Regulatory Framework

Saudi Arabia has been developing its regulatory framework for occupational health and safety, including chemical safety in healthcare settings. The Saudi Food and Drug Authority (SFDA) regulates medical products and chemicals, while the Ministry of Health oversees hospital standards. The Saudi Occupational Safety and Health standards are largely based on international regulations, particularly those from the United States and Europe.

In recent years, Saudi Arabia has strengthened its regulatory framework for occupational safety and health, including chemical safety. The Saudi Standards, Metrology and Quality Organization (SASO) has adopted the Globally Harmonized System of Classification and Labelling of Chemicals (GHS), aligning with international standards for chemical hazard communication.

The Saudi Ministry of Labor has also implemented workplace safety regulations that apply to healthcare settings, requiring risk assessments, appropriate control measures, and worker training. However, implementation and enforcement can vary between healthcare facilities, with larger, urban, and international-affiliated hospitals typically having more developed chemical safety programs than smaller or rural facilities.

These regulatory frameworks aim to establish standardized approaches to chemical risk assessment, management, and communication. However, implementation and enforcement can vary significantly between countries and even between healthcare institutions within the same jurisdiction. This variability highlights the importance of institutional commitment to safety beyond minimal regulatory compliance.

Monitoring Strategies for Chemical Hazards

Effective management of chemical hazards in hospitals requires comprehensive monitoring strategies. Two primary approaches are environmental (or air) monitoring and biological monitoring, each with distinct advantages and limitations.

Environmental Monitoring

Environmental monitoring involves measuring chemical concentrations in workplace air to assess potential exposure risks. These measurements are then compared to established occupational exposure limits (OELs) to determine compliance with safety standards. As noted by Marć et al. (2015), current air quality analytics have advanced significantly, allowing for more precise detection and quantification of airborne chemicals.

The effectiveness of environmental monitoring depends on several factors. NIOSH's Occupational Exposure Sampling Strategy Manual provides guidance on when, where, and how to collect air samples to ensure representative results (National Institute for Occupational Safety and Health, 1977). The timing and location of sampling must account for variations in work activities and ventilation patterns to capture both typical and worst-case exposure scenarios.

Measured concentrations must be compared against appropriate occupational exposure limits, which may vary between regulatory frameworks. Tynkkynen et al. (2015) noted significant variations between REACH-derived no-effect levels for workers and national occupational exposure limits in Finland, highlighting the challenges of harmonizing exposure standards across different regulatory systems.

In Saudi Arabia, environmental monitoring in hospitals often follows international standards, typically adopting exposure limits from ACGIH or other recognized organizations. The extreme climate conditions in Saudi Arabia, with high temperatures throughout much of the year, can affect chemical volatility and ventilation system efficiency, potentially increasing exposure risks if not properly accounted for in monitoring strategies and control measures.

Biological Monitoring

Biological monitoring assesses chemical exposure by measuring the substance or its metabolites in biological specimens (typically blood, urine, or exhaled air). According to Jakubowski (2012), biological monitoring offers several advantages over air monitoring by integrating all exposure routes. This approach accounts for dermal absorption, ingestion, and inhalation, providing a more comprehensive exposure assessment than air monitoring alone.

Zielhuis (1984) and Manno et al. (2010) emphasized that biological monitoring should complement, not replace, environmental monitoring. The World Health Organization's guidelines on elemental speciation in human health risk assessment provide a framework for incorporating biological monitoring data into risk assessment, recognizing the value of integrating multiple approaches to exposure assessment (World Health Organization, 2006).

For effective biological monitoring, appropriate biomarkers must be selected based on their specificity to the chemical of interest. The ideal biomarker should be uniquely associated with exposure to the chemical being monitored, minimizing confounding from other exposures or endogenous sources. Sensitivity is equally important, as the biomarker should be detectable at relevant exposure levels, particularly at or below those expected to cause adverse health effects.

Mutti et al. (2006) provided comprehensive guidelines for biological monitoring, including sampling strategies and interpretation of results. The American Conference of Governmental Industrial Hygienists (ACGIH) has established Biological Exposure Indices (BEIs) for many workplace chemicals, which serve as reference values for assessing biological monitoring results (American Conference of Governmental Industrial Hygienists, 2001).

In Saudi Arabian hospitals, biological monitoring programs for chemical exposures are not yet widely implemented, representing an area for potential growth in occupational health programs. Cultural considerations and privacy concerns may need to be addressed when implementing such programs, particularly for female healthcare workers who comprise a significant portion of the nursing workforce.

Specific Chemical Hazards in Hospital Departments

Different hospital departments present unique chemical hazard profiles based on their functions. This section examines the specific chemical risks in pathology, surgery, and pharmacy departments, with considerations for the Saudi Arabian context where applicable.

Pathology Departments

Pathology departments present some of the most significant chemical exposures in hospital settings. A study by Dascalaki et al. (2009) found that indoor air quality in pathology laboratories often exceeded recommended limits for volatile organic compounds (VOCs). Similarly, LeBouf et al. (2014) detected numerous VOCs in healthcare settings, with pathology departments showing particularly high concentrations due to the chemicals used in tissue processing and analysis.

Key chemical hazards in pathology include formaldehyde, which is widely used as a tissue fixative and preservative. Cipolla et al. (2017) found that formaldehyde levels in anatomical pathology wards frequently exceeded occupational exposure limits, creating significant health risks for laboratory personnel. Epidemiological studies have shown concerning health outcomes among pathology workers, including elevated mortality from certain cancers potentially linked to chemical exposures, as reported by Hall et al. (1991).

Costa et al. (2011) demonstrated genotoxic effects of formaldehyde exposure through comet assay and micronucleus tests in peripheral lymphocytes of exposed workers. These findings suggest that even exposures below regulatory limits might cause DNA damage with potential long-term health implications. According to Maison and Pasquier (2008), formaldehyde is a potent irritant of the respiratory tract and eyes, with symptoms appearing at concentrations as low as 0.1 ppm, well below the permissible exposure limits in many jurisdictions.

D'Ettorre et al. (2017) emphasized the importance of engineering controls, such as properly designed ventilation systems, to manage formaldehyde exposure in pathology departments. Despite these recommendations, studies by Azari et al. (2012) and Bono et al. (2010) found that formaldehyde levels in many pathology departments exceeded permissible limits, highlighting the challenges of controlling exposures in practice.

Chronic formaldehyde exposure has been associated with chromosomal aberrations, as Costa et al. (2015) found increased levels of chromosomal aberrations in formaldehyde-exposed workers. Sancini et al. (2014) reported alterations in white blood cell differential counts among healthcare workers exposed to formaldehyde, suggesting potential immunological effects. Lin et al. (2013) documented genetic damage in peripheral blood lymphocytes of workers chronically exposed to formaldehyde, adding to the evidence of genotoxicity.

Xylene is another common chemical hazard in pathology, used for tissue processing and as a clearing agent. Kalantari et al. (2016) noted that while alternatives to xylene are being developed, it remains widely used in pathology laboratories worldwide due to its effectiveness and established protocols. McKenzie et al. (2012) highlighted xylene's health effects, including neurological symptoms, respiratory irritation, and reproductive toxicity, emphasizing the importance of proper handling and exposure controls.

A comprehensive review by Niaz et al. (2015) outlined the health concerns associated with xylene exposure, including acute effects such as headache, dizziness, nausea, and irritation of the eyes, nose, and throat. Chronic exposure may affect the central nervous system, liver, kidneys, and skin, potentially leading to persistent neurological symptoms and organ damage.

In Saudi Arabian pathology departments, the challenges of chemical exposure management may be compounded by factors such as building design that may not always prioritize ventilation, particularly in older facilities. The hot climate can affect chemical volatility and air handling system efficiency, potentially increasing exposure risks if systems are not properly designed and maintained. Additionally, in some facilities, language barriers among multinational staff may complicate training and hazard communication, necessitating multilingual approaches to safety information and training.

Operating Rooms

Operating rooms present unique chemical hazards, particularly related to anesthetic gases. Yılmaz and Çalbayram (2016) conducted a systematic review of human biomonitoring studies, finding evidence of genotoxicity among operating room personnel exposed to anesthetic gases. This suggests that despite improvements in ventilation and scavenging systems, significant exposures still occur in many facilities.

Halogenated volatile anesthetics (such as isoflurane, sevoflurane, and desflurane) and nitrous oxide are commonly used in operating rooms. Tankò et al. (2014) reviewed the occupational hazards of halogenated anesthetics, noting that despite improvements in scavenging systems, significant exposures still occur due to leakage from anesthesia equipment, poor scavenging system maintenance, and inadequate ventilation.

Health effects associated with chronic exposure to anesthetic gases include reproductive effects, with historical studies by Guirguis et al. (1990) and Cohen et al. (1971) finding associations between anesthetic gas exposure and increased rates of spontaneous abortion among female operating room personnel. While modern scavenging systems have reduced exposure levels, concerns remain about chronic low-level exposures and their potential reproductive impacts, especially given the predominance of women in many operating room roles.

Wrońska-Nofer et al. (2012) demonstrated oxidative DNA damage and increased oxidative stress biomarkers in subjects occupationally exposed to nitrous oxide. This suggests potential mechanisms for long-term health effects beyond the well-established acute effects of these gases. Chronic exposure to anesthetic gases has also been associated with neurological effects, including headaches, fatigue, irritability, and difficulties with concentration, which may impact both quality of life and work performance.

In Saudi Arabia, operating room design and equipment in major hospitals generally follow international standards, with modern anesthetic gas scavenging systems. However, maintenance practices, staff training on scavenging system use, and monitoring of system performance may vary between facilities. The Saudi Society of Anesthesia has been working to promote awareness of occupational exposures and standardize safety practices across the kingdom's healthcare facilities.

Pharmacy Departments

Hospital pharmacies handle numerous hazardous drugs, particularly antineoplastic agents used in cancer treatment. The manipulation of these drugs during preparation, administration, and disposal creates exposure risks for pharmacy personnel, nurses, and other healthcare workers. These highly potent medications present unique challenges for exposure control due to their inherent toxicity at extremely low concentrations.

Antineoplastic drugs are designed to kill rapidly dividing cells, making them inherently toxic to normal human cells as well as cancer cells. Occupational exposure has been associated with reproductive effects, including increased risks of spontaneous abortion, congenital malformations, and infertility. These effects are particularly concerning for the predominantly female workforce in pharmacy and nursing roles.

Genotoxicity is another significant concern, as chromosomal aberrations and sister chromatid exchanges have been observed in healthcare workers handling these drugs. These genetic changes may serve as early biomarkers of cancer risk, raising concerns about potential carcinogenicity with long-term exposure. Although definitive evidence linking occupational exposure to increased cancer incidence is limited by methodological challenges and long latency periods, the genotoxic properties of these drugs warrant a precautionary approach to exposure control.

In Saudi Arabia, pharmacy practices in major hospitals increasingly follow international standards for handling hazardous drugs, including the use of biological safety cabinets, closed-system transfer devices, and personal protective equipment. The Saudi Pharmaceutical Society and the Ministry of Health have developed guidelines for handling hazardous drugs based on international best practices. However, implementation may vary across facilities, with tertiary care centers typically having more advanced safety systems than smaller hospitals.

The Saudi Center for Disease Prevention and Control has also begun addressing occupational exposures in healthcare settings, including chemical hazards, as part of its broader public health mission. These efforts represent growing recognition of the importance of occupational health in the Saudi healthcare system.

Risk Assessment and Management Strategies

Effective management of chemical hazards in hospitals requires a systematic approach to risk assessment and implementation of control measures. The hierarchy of controls provides a framework for prioritizing interventions based on their effectiveness and sustainability.

The most effective approach is to eliminate hazardous chemicals or replace them with safer alternatives. Examples include replacing formaldehyde with lower-concentration formulations or alternative fixatives, adopting formaldehyde-free tissue processing methods, using water-based alternatives to xylene in histology, and implementing closed-system drug transfer devices for handling antineoplastic drugs (D'Ettorre et al., 2017). Substitution not only reduces exposure risk but may also simplify waste management and regulatory compliance.

When hazardous chemicals cannot be eliminated, engineering controls should be implemented to minimize exposure. These include local exhaust ventilation systems for formaldehyde workstations, properly designed and maintained laboratory fume hoods, biological safety cabinets for handling hazardous drugs, anesthetic gas scavenging systems in operating rooms, and automated systems for chemical processing to minimize direct handling (LeBouf et al., 2014). Engineering controls are particularly effective because they reduce exposure at the source without relying on worker behavior.

Administrative controls include policies, procedures, and work practices designed to reduce exposure. Standard operating procedures for chemical handling provide consistent guidance on safe practices. Rotation of personnel to limit individual exposure time may be appropriate for certain high-risk activities, though care must be taken not to simply distribute risk among more workers. Restricted access to areas with high chemical exposure risk helps minimize unnecessary exposures. Training programs on chemical hazards and safe handling ensure that workers understand risks and protective measures (McDiarmid, 2006). Regular maintenance schedules for ventilation systems are essential for sustained effectiveness, and proper waste management protocols help prevent secondary exposures during disposal.

Personal protective equipment should be considered the last line of defense, used in conjunction with other control measures. Gloves appropriate for the specific chemicals being handled provide barrier protection against dermal absorption. Respiratory protection may be necessary when engineering controls are insufficient to reduce airborne concentrations to acceptable levels. Eye protection against chemical splashes is essential in many laboratory and pharmacy activities. Protective clothing helps prevent skin contact and contamination of personal clothing that could lead to extended exposure or take-home contamination (Vecchio et al., 2003).

In Saudi Arabia, implementing this hierarchy of controls must consider local factors such as climate, building design, workforce diversity, and healthcare system structure. The extreme heat can affect chemical volatility and ventilation system efficiency, requiring more robust engineering controls. The multinational nature of the healthcare workforce necessitates multilingual and culturally sensitive approaches to training and hazard communication. The rapid expansion of healthcare facilities presents both challenges in ensuring consistent safety standards and opportunities to incorporate state-of-the-art safety features in new construction.

Special Considerations for Saudi Arabian Hospitals

Several factors unique to Saudi Arabia influence chemical safety management in hospitals. The kingdom's extreme climate, with temperatures frequently exceeding 40°C (104°F) in summer months, affects chemical volatility, storage requirements, and ventilation system design. Air conditioning systems are essential not only for comfort but also for controlling chemical exposures, making power reliability and system maintenance critical safety considerations.

The multinational nature of the Saudi healthcare workforce presents both challenges and opportunities for chemical safety management. Staff from diverse educational and cultural backgrounds may have different understandings of chemical hazards and safety practices. This diversity necessitates multilingual training materials, clear visual hazard communication, and culturally sensitive approaches to safety promotion. Conversely, this diversity can bring together international best practices when effectively managed through knowledge sharing and standardized protocols.

The Saudi healthcare system is undergoing rapid expansion and modernization, with numerous new facilities being constructed. This presents an opportunity to incorporate state-of-the-art safety features into facility design, including advanced ventilation systems, purpose-built chemical storage areas, and modern laboratory facilities with integrated safety features. New construction should prioritize chemical safety through thoughtful design of spaces where hazardous chemicals are used and stored.

Saudi Arabia's Vision 2030 includes healthcare sector transformation, with increased focus on quality and safety. This national priority creates momentum for improving occupational health practices, including chemical safety in hospitals. The Saudi Patient Safety Center, established in 2017, has begun addressing worker safety as an integral component of overall healthcare quality, recognizing that worker well-being directly impacts patient care.

Religious and cultural factors also influence occupational health practices in Saudi Arabia. Prayer times and fasting during Ramadan may affect work schedules and chemical handling practices. Gender segregation in some workplaces may influence facility design and staff training approaches. Respect for these cultural factors while maintaining high safety standards requires thoughtful adaptation of international best practices to the local context.

Training and Education

Comprehensive training programs are essential for ensuring that hospital workers understand chemical hazards and implement appropriate protective measures. Effective training should include hazard identification, teaching workers how to recognize potentially hazardous chemicals and situations based on labeling, physical properties, and workplace location. Understanding exposure routes helps workers appreciate how chemicals enter the body and cause harm, influencing protective behaviors.

Training on control measures should cover proper use of engineering controls, work practices, and PPE. Workers need to understand not just what protective measures to use but why they are important and how to verify they are functioning correctly. Emergency procedures training prepares workers to take appropriate actions in case of spills, leaks, or exposures, potentially preventing minor incidents from becoming major emergencies (Stewart-Evans et al., 2013).

In Saudi Arabia, training programs must address several unique challenges. Language diversity among healthcare workers necessitates multilingual training materials and approaches. Cultural factors may influence risk perception and safety behaviors, requiring culturally sensitive training approaches. The hierarchical nature of many Saudi healthcare organizations may affect communication patterns and incident reporting, necessitating specific attention to creating psychological safety for raising safety concerns.

Saudi professional organizations, including the Saudi Society for Clinical Chemistry, the Saudi Pharmaceutical Society, and the Saudi Society of Anesthesia, increasingly offer specialized training in chemical safety relevant to their respective fields. These efforts complement broader occupational health training and help build capacity for chemical safety management across the kingdom's healthcare system.

Conclusion

This review underscores the critical need for comprehensive chemical hazard management in hospitals, where exposure to therapeutic, diagnostic, and cleaning agents poses significant risks to healthcare workers and patients. Key hazardous substances—including formaldehyde, anesthetic gases, and antineoplastic drugs—are linked to respiratory, dermatological, and reproductive health effects, necessitating stringent controls such as engineering solutions (e.g., ventilation, closed-system drug transfer), regular environmental and biological monitoring, and targeted staff training. While global frameworks like EU REACH and OSHA provide guidelines, implementation gaps persist, particularly in rapidly expanding healthcare systems like Saudi Arabia, where extreme climate and workforce diversity demand tailored strategies. To mitigate risks, hospitals must prioritize substituting hazardous chemicals, enforcing international standards locally, and investing in research on long-term health impacts. Proactive, context-specific safety programs are essential to protect workers, ensure patient safety, and maintain high-quality care in evolving healthcare environments.

References:

1. McDiarmid MA. Chemical hazards in health care: high hazard, high risk, but low protection. Ann N Y Acad Sci 2006;1076:601-6. [DOI] [PubMed] [Google Scholar]

2. Vecchio D, Sasco AJ, Cann CI. Occupational risk in health care and research. Am J Ind Med 2003;43:369-97. [DOI] [PubMed] [Google Scholar]

3. Stewart-Evans JL, Sharman A, Isaac J. A narrative review of secondary hazards in hospitals from cases of chemical selfpoisoning and chemical exposure. Eur J Emerg Med 2013;20:304-9. [DOI] [PubMed] [Google Scholar]

4. Leso V, Ercolano ML, Cioffi DL, Iavicoli I. Occupational exposure and breast cancer risk according to hormone receptor status: a systematic review. Cancers (Basel) 2019;11:1882. [DOI] [PMC free article] [PubMed] [Google Scholar]

5. European Agency for Safety and Health at work. Available from: https://osha.europa.eu/en/about-eu-osha [Google Scholar]

6. European Commission. EC regulation N 1907/2006 (2006) of the European Parliament and of the Council concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), establishing a European Chemicals Agency. [Google Scholar]

7. Ha S, Seidle T, Lim KM. Act on the Registration and Evaluation of Chemicals (K-REACH) and replacement, reduction or refinement best practices. Environ Health Toxicol 2016;31:e2016026. [DOI] [PMC free article] [PubMed] [Google Scholar]

8. European Commission Health and Consumers Directorate-General. Guidelines for Good Manufacturing Practice (GMP). Public Health and Risk Assessment Medicinal Product – quality, safety and efficacy. 2013. [Google Scholar]

9. European Commission. EC directive 2004/10/EC (2004). Council Directive 2004/10/EC on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances. [Google Scholar]

10. European Commission. EC regulation N° 605/2014 (2014) of the European Parliament and of the Council amending, for the purposes of introducing hazard and precautionary statements in the Croatian language and its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures. [Google Scholar]

11. Italian Government. Legislative Decree 1994 n.626, G.U. n265 (November 12,1994). [Google Scholar]

12. European Commission. EC directive 89/391/EEC (1989). Council Directive 89/391/EEC on the introduction of measures to encourage improvements in the safety and health of workers at work. (89/391/EEC). [Google Scholar]

13. European Commission. EC regulation N° 1272/2008 (2008) of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures. [Google Scholar]

14. Occupational Safety and Health Administration. OSH Act of 1970. Available from: https://www.osha.gov/lawsregs/oshact/toc [Google Scholar]

15. National Institute for Occupational Safety and Health (NIOSH). Occupational Exposure Sampling Strategy Manual. Cincinnati: NIOSH. 1977. [Google Scholar]

16. Environmental Protection Agency (EPA). Regulatory Reform - Laws & Regulations. 2017. Available from: https://www.epa.gov/laws-regulations/regulatory-reform [Google Scholar]

17. Environmental Protection Agency. Summary of the toxic substances control act. TSCA; 1976. [Google Scholar]

18. Jakubowski M. Biological monitoring versus air monitoring strategies in assessing environmental-occupational exposure. J Environ Monit 2012;14:348-52. [DOI] [PubMed] [Google Scholar]

19. Marć M, Tobiszewski M, Zabiegała B, et al. Current air quality analytics and monitoring: a review. Anal Chim Acta 2015;853:116-26. [DOI] [PubMed] [Google Scholar]

20. Roberts SM, Rohr AC, Mikheev VB, et al. Influence of airborne particulates on respiratory tract deposition of inhaled toluene and naphthalene in the rat. Inhal Toxicol 2018;30:19-28. [DOI] [PubMed] [Google Scholar]

21. Tynkkynen S, Santonen T, Stockmann-Juvala H. A comparison of REACH-derived no-effect levels for workers with EU indicative occupational exposure limit values and national limit values in Finland. Ann Occup Hyg 2015;59:401-15. [DOI] [PubMed] [Google Scholar]

22. Zielhuis RL. Recent and potential advances applicable to the protection of workers' health - Biological Monitoring. II. Assessment of toxic agents at the workplace - Roles of ambient and biological monitoring. Boston: Martinus Nijhoff Publishers; 1984. p. 84-94. [Google Scholar]

23. Manno M. Viau C in collaboration with Cocker J et al. Biomonitoring for occupational health risk assessment (BOHRA). Toxicol Lett 2010;192:3-16. [DOI] [PubMed] [Google Scholar]

24. World Health Organization. Technical guides. Elemental speciation in human health risk assessment / authors: Postoli P., et al. Geneva: World Health Organization; 2006. [Google Scholar]

25. Mutti A, De Palma G, Manini P, et al. Linee guida per il monitoraggio biologico. Pavia: PIME; 2006. [Google Scholar]

26. American Conference of Governmental Industrial Hygienists (ACGIH). Documentation of the threshold limit values and biological exposure indices, 7th Ed. Cincinnati: ACGIH Signature Publications; 2001. [Google Scholar]

27. Dascalaki E, Gaglia AG, Balaras C, Lagoudi A. Indoor environmental quality in Hellenic hospital operating rooms. Energ Build 2009;41:51-60. [Google Scholar]

28. LeBouf RF, Virji MA, Saito R, et al. Exposure to volatile organic compounds in healthcare settings. Occup Environ Med 2014;71:642-50. [DOI] [PMC free article] [PubMed] [Google Scholar]

29. Cipolla M, Izzotti A, Ansaldi F, et al. Volatile organic compounds in anatomical pathology wards: Comparative and qualitative assessment of indoor airborne pollution. Int J Environ Res Public Health 2017;14:609. [DOI] [PMC free article] [PubMed] [Google Scholar]

30. Fritzsche FR, Ramach C, Soldini D, et al. Occupational health risks of pathologists--results from a nationwide online questionnaire in Switzerland. BMC Public Health 2012;12:1054. [DOI] [PMC free article] [PubMed] [Google Scholar]

31. Hall A, Harrington JM, Aw TC. Mortality study of British pathologists. Am J Ind Med 1991;20:83-9. [DOI] [PubMed] [Google Scholar]

32. Costa S, Pina C, Coelho P, et al. Occupational exposure to formaldehyde: Genotoxic risk evaluation by comet assay and micronucleus test using human peripheral lymphocytes. J Toxicol Environ Health A 2011;74:1040-51. [DOI] [PubMed] [Google Scholar]

33. Maison A, Pasquier E. [Institut National de Recherche et de Sécurité – Technical guides. Le point des connaissances sur le formaldehyde].[in French]. ED 5032. 1-4. 3ème Edition. Paris: Institut National de Recherche et de Sécurité; 2008. [Google Scholar]

34. D'Ettorre G, Criscuolo M, Mazzotta M. Managing formaldehyde indoor pollution in anatomy pathology departments. Work 2017;56:397-402. [DOI] [PubMed] [Google Scholar]

35. Azari MR, Asadi P, Jafari MJ, et al. Occupational exposure of a medical school staff to formaldehyde in Tehran. Tanaffos 2012;11:36-41. [PMC free article] [PubMed] [Google Scholar]

36. Bono R, Romanazzi V, Munnia A, et al. Malondialdehydedeoxyguanosine adduct formation in workers of pathology wards: the role of air formaldehyde exposure. Chem Res Toxicol 2010;23:1342-8. [DOI] [PMC free article] [PubMed] [Google Scholar]

37. Costa S, Carvalho S, Costa C, et al. Increased levels of chromosomal aberrations and DNA damage in a group of workers exposed to formaldehyde. Mutagenesis 2015;30:463-73. [DOI] [PubMed] [Google Scholar]

38. Sancini A, Rosati MV, De Sio S, et al. Exposure to formaldehyde in health care: an evaluation of the white blood count differential. G Ital Med Lav Ergon 2014;36:153-9. [PubMed] [Google Scholar]

39. Lin D, Guo Y, Yi J, et al. Occupational exposure to formaldehyde and genetic damage in the peripheral blood lymphocytes of plywood workers. J Occup Health 2013;55:284-91. [DOI] [PubMed] [Google Scholar]

40. Peteffi GP, Antunes MV, Carrer C, et al. Environmental and biological monitoring of occupational formaldehyde exposure resulting from the use of products for hair straightening. Environ Sci Pollut Res Int 2016;23:908-17. [DOI] [PubMed] [Google Scholar]

41. Nielsen GD, Larsen ST, Wolkoff P. Recent trend in risk assessment of formaldehyde exposures from indoor air. Arch Toxicol 2013;87:73-98. [DOI] [PMC free article] [PubMed] [Google Scholar]

42. Kalantari N, Bayani M, Ghaffari T. Deparaffinization of formalin- fixed paraffin-embedded tissue blocks using hot water instead of xylene. Anal Biochem 2016;15:507:71-3. [DOI] [PubMed] [Google Scholar]

43. McKenzie LM, Witter RZ, Newman LS, Adgate JL. Human health risk assessment of air emissions from development of unconventional natural gas resources. Sci Total Environ 2012;424:79-87. [DOI] [PubMed] [Google Scholar]

44. Niaz K, Bahadar H, Maqbool F, Abdollahi M. A review of environmental and occupational exposure to xylene and its health concerns. EXCLI J 2015;14:1167-86. [DOI] [PMC free article] [PubMed] [Google Scholar]

45. Inoue O, Seiji K, Kawai T, et al. Excretion of methylhippuric acids in urine of workers exposed to a xylene mixture: comparison among three xylene isomers and toluene. Int Arch Occup Environ Health 1993;64:533-9. [DOI] [PubMed] [Google Scholar]

46. Yılmaz S, Çalbayram NÇ. Exposure to anesthetic gases among operating room personnel and risk of genotoxicity: A systematic review of the human biomonitoring studies. J Clin Anesth 2016;35:326-31. [DOI] [PubMed] [Google Scholar]

47. Tankò B, Molnàe L, Fülesdi B, Molnàr C. Occupational hazards of halogenated volatile anesthetics and their prevention: review of the literature. J Anesth Clin Res 2014;5:1-7. [Google Scholar]

48. Guirguis SS, Pelmear PL, Roy ML, Wong L. Health effects associated with exposure to anaesthetic gases in Ontario hospital personnel. Br J Ind Med 1990;47:490-7. [DOI] [PMC free article] [PubMed] [Google Scholar]

49. Cohen EN, Bellville JW, Brown BW. Anesthesia, pregnancy and miscarriage. A study of operating room nurses and anesthetists. Anesthesiology 1971;35:343-7. [DOI] [PubMed] [Google Scholar]

50. Wrońska-Nofer T, Nofer JR, Jajte J, et al. Oxidative DNA damage and oxidative stress in subjects occupationally exposed to nitrous oxide (N(2)O). Mutat Res 2012;731:58-63. [DOI] [PubMed] [Google Scholar]