Occupational safety

Occupational safety for antineoplastic preparation in Europe is built on a hierarchy of controls to minimize worker exposure to these hazardous drugs, which pose risks of cancer, reproductive issues, and other toxic effects. The core principles are based on European Union (EU) directives and guidance from bodies like the European Commission

The EU Commission uses the following working definition of Hazardous medicinal products (HMPs) in its Guidance for the safe management of hazardous medicinal products at work: HMPs are defined as *medicinal products that contain one or more substances that meet the criteria for classification as:*
- Carcinogenic
- Mutagenic
- Toxic for reproduction

Hazardous medicinal products (HMPs) are pharmaceutical substances that pose potential risks to individuals handling them.

Several organizations have provided definitions and classifications for hazardous drugs or hazardous medicinal products. Some examples are:

- The American Society of Health System Pharmacists (ASHP) gave the first definition of hazardous drugs: *Drugs that meet one or more of the following criteria: genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems); carcinogenicity in animal models, in the patient population, or both, as reported by the International Agency for Research on Cancer (IARC); teratogenicity or fertility impairment in animal studies or in treated patients; and evidence of serious organ or other toxicity at low doses in animal models or treated patients.*
- The National Institute for Occupational Safety and Health (NIOSH) defines hazardous drugs as: *Drugs that meet one or more of the following criteria: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity, organ toxicity at low doses, genotoxicity, structure and toxicity profiles of new drugs that mimic existing hazardous drugs in scope of the hazard, and drugs that meet the criteria for hazardous waste.*

Occupational Risks and Hazards

Workers exposed to HMPs

Workers who are exposed to HMPs can be classified into several categories based on their roles in the different life cycle stages of HMPs and the level of contact they have with HMPs or patients using HMPs.

- Manufacturing:

    - Workers involved in pharmaceutical production handle for instance the synthesis, formulation, and packaging of HMPs, which may involve exposure for example during the unpacking and shelving of these products.
    - Laboratory staff conduct research, testing, and quality control of HMPs, potentially encountering hazardous materials during experimentation.
- Transport and storage:
    - Workers in stores and warehouses handle the storage and retrieval of HMPs, which may involve exposure for instance during the unpacking and shelving of these products.
    - Delivery drivers transport HMPs between facilities and may be exposed to hazardous substances in the event of accidental spills or leaks during transit.
- Preparation:
    - Pharmacists and pharmacy support staff prepare, compound, and dispense HMPs, requiring direct contact with these substances and increasing the risk of exposure.
- Administration:
    - Medical personnel such as nurses and doctors, administer HMPs to patients, potentially encountering hazardous substances during the preparation or handling of drug delivery devices.
    - Healthcare assistants, auxiliary nurses, care home workers, ambulance workers, paramedics and emergency response workers may assist in administering HMPs or come into contact with patients using HMPs, resulting in potential exposure.
- Veterinary practices:
    - Veterinary surgeons, nurses, and students, as well as animal attendants, may be exposed to HMPs when treating animals or handling medications in a veterinary setting.
- Cleaning, laundry, maintenance and incident management:
    - Cleaners, laundry workers and maintenance workers may be exposed to HMP residues when cleaning surfaces, equipment, or textiles, or during the maintenance of facilities or devices where HMPs are handled.
    - Mortuary workers may be exposed to HMPs when handling deceased patients who were treated with these substances.
- Waste (water) management:
    - Waste handlers and waste transporters are responsible for the collection, transport, and disposal of HMP-contaminated waste, which may involve exposure to hazardous substances during these processes.

Individuals such as workers of contractors, temporary workers, trainees, apprentices, students, and volunteers, carrying out some of the tasks above, for example cleaning or waste collection, may require special attention due to:

1. Lack of familiarity with the specific workplace environment, protocols, and procedures for handling HMPs could increase their risk of exposure and potential harm.
2. Inadequate training: these categories of workers often don't receive comprehensive training regarding the safe handling of HMPs or the use and disposal of personal protective equipment (PPE). Without proper training, they may be more likely to make errors or engage in unsafe practices.
3. Limited experience: Individuals new to the field or working in a temporary capacity, such as students or trainees, may have limited experience in dealing with HMPs. This lack of experience makes them more prone to mistakes and accidents, increasing their risk of exposure.

4. Inconsistent supervision: Temporary or relief workers may not receive the same level of supervision as regular employees, potentially resulting in a lack of guidance or oversight. This can lead to an increased likelihood of unsafe practices or non-compliance with safety protocols.
5. Communication challenges: Workers from different backgrounds or those with language barriers may face communication challenges, which can hinder their understanding of safety procedures and increase the risk of exposure to HMPs.
6. Lower priority for protection: Employers might unintentionally prioritise the safety of their permanent staff over temporary or volunteer workers. This could result in inadequate provision of PPE or training for these individuals, increasing their risk of exposure to HMPs.

Other groups of workers may be more vulnerable or have special circumstances that put them at greater risk. Some of these groups include:

1. Pregnant or breastfeeding women: Exposure to HMPs may pose risks to the developing foetus or be transmitted through breast milk.
2. Workers planning to conceive: Some HMPs can have adverse effects on fertility or cause damage to genetic material, potentially impacting future pregnancies.
3. Immunocompromised workers: Individuals with weakened immune systems due to medical conditions or treatments may be more susceptible to the harmful effects of HMPs.
4. Workers with pre-existing medical conditions: Employees with certain pre-existing medical conditions, such as respiratory or skin disorders, may be at higher risk of experiencing adverse reactions or complications from exposure to HMPs.
5. Young workers: Individuals in the early stages of their careers, particularly those in vocational training programs such as nursing, may be at heightened risk due to their relative lack of experience and knowledge about handling HMPs. Additionally, as their bodies are still developing, they may be more susceptible to the harmful effects of these substances.
6. Older workers: Age-related physiological changes can affect the body’s ability to metabolize and eliminate hazardous substances.
7. Workers with a history of allergies or hypersensitivity[23]: Employees with a history of allergies or hypersensitivity to certain substances may be more likely to experience adverse reactions when exposed to HMPs.

Negative health effects

Exposure of workers to HMPs can result in various negative health effects, which can be categorised based on the specific hazards associated with these substances.

Carcinogenic effects: HMPs that are classified as carcinogens can increase the risk of developing cancer in exposed workers. The International Agency for Research on Cancer (IARC) has identified a number of these substances as having a potential carcinogenic effect. Studies have estimated that occupational exposure to HMPs in EU hospitals and clinics could result in up to 54 cases of breast cancer and 13-19 cases of hematopoietic cancer per year[3]. However, these estimates come with a degree of uncertainty.

Mutagenic effects: Some HMPs are mutagenic, meaning they can cause changes in genetic material, leading to genetic mutations that may result in cancer or other health issues. Workers exposed to mutagenic HMPs may experience chromosome abnormalities, increasing their risk of developing health problems.

Reprotoxic effects: Exposure to reprotoxic HMPs can negatively impact fertility and reproductive health, leading to foetal loss, malformations in offspring, infertility, and low birth weight. Studies have estimated that occupational exposure to HMPs in EU hospitals and clinics could result in 1,300-2,200 miscarriages per year, although these numbers also carry a degree of uncertainty.

Other negative health effects that may arise from exposure to HMPs include contact dermatitis, abdominal pain, hair loss, nasal sores, nausea and vomiting, cough, dizziness, headaches, or hypersensitivity to HMPs. In some cases, HMP exposure may also lead to alterations in normal blood cell count and platelet function, chromosome abnormalities and damage to organs such as the nervous system, liver, heart, or lungs.

Tobacco consumption combined with exposure to HMPs may further increase the risk of adverse health effects. Smoking can exacerbate the negative impact of HMP exposure, leading to a higher incidence of health issues. For example, carcinogenic substances found in both tobacco smoke and certain HMPs could potentially have a synergistic effect, increasing the risk of cancer. Similarly, both tobacco smoke and some HMPs contain mutagenic substances, which can damage DNA and increase the risk of genetic mutations. Furthermore, tobacco smoking and exposure to certain reprotoxic HMPs may jointly impact fertility or reproductive health, leading to an increased likelihood of reproductive disorders or complications. While more research is needed to fully understand these interactions, it's pivotal to underline that the primary protective measure for workers should be the stringent control of exposure to HMPs in occupational settings, rather than personal lifestyle adaptations.

Risk Assessment and Management

General principles

Risk assessment and management play crucial roles in ensuring worker safety when working with HMPs. According to the OSH Framework Directive 89/391/EEC, and more specifically, the CMR Directive 2004/37/EC, employers have a responsibility to undertake workplace risk assessments and develop HMP risk management plans that encompass appropriate risk management measures, training, exposure assessment, and health surveillance.

The following general principles should be followed for risk assessment and management when working with HMPs:

1. Purpose: The primary goal of risk assessment is to make informed decisions about risk management measures, training, exposure assessment, and health surveillance for workers exposed to HMPs.
2. Scope: Risk assessments must be performed for all activities and scenarios where workers might be exposed to HMPs, ensuring a safeguard for everyone from direct to inadvertent exposure. This includes not only medical staff who administer HMPs but also encompasses a wide array of professionals and non-professionals, such as temporary, casual and agency workers, contractors, students, and volunteers in various roles. Attention should also be given to individuals who may not directly handle HMPs but could be exposed through secondary contact. For instance, personnel managing materials contaminated by HMPs – such as bed linens, waste handlers dealing with discarded HMPs, cleaners tasked with maintaining spaces where HMPs are used, and those transporting HMPs within healthcare, pharmaceutical production, or veterinary establishments – all should be meticulously assessed for risk. Furthermore, assessments should vigilantly extend to workers in locations where HMPs are utilised, involved in activities around HMP usage, and those providing care to patients being treated with HMPs. Additional consideration should be given to workers who might be incidentally at risk, such as those in proximity to contaminated waste or those in veterinary settings where HMPs might be utilised. These risk assessments are imperative to identify and mitigate potential exposures across the varied contexts of HMP utilisation and handling.
3. Hazard identification: The first step in conducting a risk assessment is identifying the hazards or HMPs potentially present in the workplace.
4. Risk assessment: Assess whether the identified hazard poses a risk to workers by considering factors such as the locations and activities where HMPs are used, and workers who may be exposed to HMPs, for instance because they are cleaning areas where HMPs are being used or where patients are treated. Particular attention should be given to workers at greater risk, including pregnant workers, workers who have recently given birth, and workers who are breastfeeding, young workers, and the environment of patients being treated with HMPs.
5. Risk management plan: Based on the risk assessment, develop a risk management plan in line with the hierarchy of controls outlined in the CMRD (Directive 2004/37/EC).
6. Documentation and review: Record the risk assessment process and ensure that the risk assessment and associated risk management plan are reviewed regularly, with an agreed-upon frequency, such as every year or every two years. Additionally, a review should take place whenever any change occurs that may affect workers' exposure to HMPs or in case of an incident.

By adhering to these general principles for risk assessment and management, employers can better protect workers from the potential hazards associated with HMPs and maintain a safe working environment.

Shared Responsibilities and Roles

The responsibility of ensuring worker safety when working with HMPs falls on various entities within an organisation, each with a unique role in risk assessment and management. This includes not only healthcare providers and manufacturing facilities but also waste management entities, veterinary practices, cleaning services, and other workplaces where exposure to HMPs might occur. It's essential to clarify and assign these responsibilities effectively to ensure a safe work environment. Here are the roles typically involved:

1. Employers: As per Directive 89/391/EEC, and CMR Directive 2004/37/EC, employers hold the prime responsibility for risk assessment and development of HMP risk management plans. This includes arranging suitable training, exposure assessment, and health surveillance. Employers must consult workers or their representativeness in the process of risk assessment and the setting of preventive measures.
2. Occupational Safety and Health (OSH) Team: A well-trained OSH team, often within larger organisations, helps implement, monitor, and improve health and safety measures. Their responsibilities typically include regular risk assessments, development and implementation of safety protocols, and staff training.
3. Employees and their representatives: Employees or their representatives voice the concerns, suggestions, and experiences of the workforce in safety discussions, helping to ensure that all workers' perspectives are considered in the development and implementation of risk management plans. Employee representatives often serve on safety committees, where they contribute to decision-making processes related to workplace safety and health.
4. Temporary, Casual, and Agency Workers: These individuals should also be aware of the risks and trained to handle HMPs safely. They should adhere to the safety protocols set by the organisation.
5. Occupational Health Services and Occupational Physicians: These professionals play a vital role in complex or resource-limited organisations. They conduct health surveillance, provide advice on risk management, offer guidance if exposure occurs, and provide training on handling HMPs.
6. Shared Premises: If different employers share a premise, they should collaborate to ensure safety measures are consistently implemented across all activities involving HMPs. Clear communication and cooperation are crucial for effective risk management in such cases.

By understanding and effectively executing their roles and responsibilities, all involved parties can contribute to ensuring a safe and healthy work environment when dealing with HMPs.

Identify hazards

The identification of hazards is a critical step in the risk assessment and management process when dealing with HMPs. Employers should use a combination of methods to ensure accurate hazard identification. This should consider the employer's role within the overall lifecycle of the HMPs, as hazards can vary depending on whether the employer is involved in the manufacturing, distribution, application, or disposal of the HMPs. Additionally, if the hazards of certain HMPs have been previously identified by other entities higher in the supply chain, this information should be utilised in the risk assessment process.

1. Medicinal Product Inspection: Examining the medicinal products produced, used, stored, transported, or disposed of in the workplace to determine if they are HMPs.
2. Manufacturer's Input: Manufacturers can assist in hazard identification by labelling HMPs with a validated symbol and providing relevant information through a Safety Data Sheet

(SDS) or a Summary of Product Characteristics [1].
Based on the REACH Regulation 2006/1907/EC manufacturers are obliged to provide safety data sheets for hazardous chemicals they place on the market. However, medicinal products for human and veterinary use in the finished state, intended for the final user, are exempted from this requirement. These products fall under the scope of Directive 2001/83/EC relating to medicinal products for human use or the Regulation 2019/6/EU on veterinary medicinal products and include the obligation for manufacturers to provide a Summary of Product characteristics.

3. Review Safety Data Sheets and Summaries of Product Characteristics: Employers should thoroughly review the Safety Data Sheets (SDS) and Summaries of Product Characteristics (SPCs) to gather information about potential hazards associated with the medicinal products in use.
4. Utilise Existing Lists and Databases: Employers can refer to existing lists and databases, such as those from regulatory agencies or professional organisations, to identify HMPs (see also above *Examples of HMPs*).
5. Inspect Packaging Labels: Another method of hazard identification is inspecting labels on product packaging for any information about the hazardous nature of the medicinal product.
6. Maintain a List of HMPs: Employers should keep an up-to-date list of all HMPs that workers may be exposed to.

By employing a combination of these methods, employers can accurately identify HMPs which is key for proper risk assessment.

Identify locations and activities where HMPs are used

To assess risks associated with HMPs, it is important to identify where, when, and how workers could potentially be exposed to them. The following may be relevant when conducting a risk assessment for a particular workplace:

- Consider workplace activities involving HMPs in the relevant life cycle stage(s) for workers, such as manufacturing, preparation, transportation and storage, administration, cleaning, laundry, and equipment maintenance, as well as waste and sewage disposal.
- Analyse any past incidents, such as accidents or near-misses (e.g. spills and accidental exposure), to understand their causes and prevent similar occurrences in the future.
- Identify and evaluate tasks where there is potential for incidents to occur, assessing the associated risks and implementing preventative measures.
- Identify pathways for exposure within the facility. This includes understanding the various ways HMPs might be encountered in the workplace. Exposure can occur through several routes including inhalation, skin contact, ingestion, or accidental injection. For each task involving HMPs, identify which of these exposure routes are relevant. For instance, a worker handling HMP-contaminated linens might be at risk of inhalation or skin contact, while a healthcare provider administering injections could be at risk of accidental self-injection or spills. Identifying these exposure routes can guide risk reduction efforts, such as using appropriate personal protective equipment or improving ventilation.
- Review building plans to identify locations where HMPs are used, such as the administration ward, pharmacy, storage area, and waste disposal area.
- Determine which locations are likely to be "contaminated" or "clean" zones, and ensure they are strictly separated.

- Assess requirements for changing clothes and Personal Protective Equipment (PPE): Evaluate the specific areas or processes where workers might be exposed to HMPs and determine the need for changing clothes or using PPE. The level of protection required can vary depending on the type of HMP, the exposure route, and the duration and frequency of exposure. For example, if a task involves potential aerosol generation of HMPs, respiratory protection might be necessary, and changing clothes before leaving the work area could prevent the spread of contamination. This evaluation should guide the development and implementation of policies and procedures regarding clothing and PPE use in the facility.
- Understand the methods used to administer and prepare HMPs.
- Identify risks associated with different types of HMPs.

In situations where multiple undertakings share a workplace, cooperation and coordination between employers are crucial in implementing HMP-OSH measures and protecting all staff potentially exposed to HMPs.

Gather information to assess whether a hazard is a risk

Gathering relevant information is crucial for determining whether a hazard poses a risk to workers. This involves several interconnected activities that help in assessing potential risks associated with hazardous medicinal products (HMPs) and implementing appropriate measures to minimise or eliminate those risks.

1. Identify locations and activities: Determine the locations and activities within the workplace where HMPs are used, stored, or handled (see above).
2. Identify exposed workers: Identify the workers who are exposed to HMPs during their regular job tasks or due to their proximity to the work areas where HMPs are used.
3. Identify workers at higher risk: Identify workers who are at a higher risk of negative health effects from HMP exposure, such as pregnant workers, workers who have recently given birth, and workers who are breastfeeding, and young workers.
4. Identify patients undergoing treatment: Take note of patients receiving treatment with HMPs, as they may expose workers in direct or indirect contact with them, for example through urine, sweat or blood.
5. Determine exposure characteristics: Understand the type, intensity, and duration of workers' exposure to HMPs. This helps assess any health or safety risk and guides the development of risk management strategies. Professional exposure assessments may be utilised where necessary and feasible. Exposure measurement may be applied in some contexts and involve monitoring air samples, surface contamination, or biomonitoring of workers.
6. Assess potential risks: Based on the information gathered from the previous steps, evaluate the potential risks associated with HMP exposure.

By thoroughly examining these factors, a more accurate risk assessment can be made, leading to the implementation of suitable risk management measures to protect workers from the hazards associated with HMPs.

According to the European Medicines Agency, a document describing the properties and the officially approved conditions of use of a medicine. Summaries of product characteristics form the basis of information for healthcare professionals on how to use the medicine safely and effectively. Abbreviated as SmPC.

Prevention and Control Measures

When dealing with HMPs, implementing effective prevention and control measures is vital for ensuring worker safety and minimising the risk of adverse health effects. These measures should follow the hierarchy of controls, which is an established framework for managing occupational risks. The hierarchy prioritises measures based on their effectiveness in reducing risk, starting with elimination of the hazard or otherwise substitution and favours collective over individual protection.

Elimination or substitution of HMPs is usually not possible because these substances are specifically designed for their potent biological effects, which often result in their hazardous properties. Since the primary goal of these medications is to improve patient outcomes and save lives, the benefits they provide often outweigh the risks associated with their hazardous nature. Consequently, elimination or substitution of HMPs is typically not a viable option, making it essential to focus on other control measures to protect workers who handle, store, prepare, administer, or dispose of these substances. For instance, an automated closed system could replace manual handling during manufacturing, preparation, and administration of HMPs.

As an introduction to more in-depth discussion, it is important to understand that each level of the hierarchy should be considered and implemented in the order presented, with the goal of achieving the highest level of protection possible. By adhering to this hierarchy, employers can systematically address the risks associated with HMPs and create a safer work environment for all employees involved in the handling, storage, preparation, administration, and disposal of these hazardous substances.

The non-binding guidelines issued by the EU Commission on the safe management of hazardous medicinal products at work[7] provide advice on reducing workers' exposure to hazardous medicinal products covering each stage of the life cycle of HMPs and good practice examples. The following paragraphs cite some examples from this guide for the manufacturing of HMPs.

Technical measures

The choice of technical measures, also known as engineering controls, to manage exposure to HMPs varies based on several factors. These factors include the type of HMP involved and the amount and frequency of exposure. While these controls are universal, they may differ depending on the context, such as manufacturing, preparation, or storage.

For instance, in the context of manufacturing[7], various measures can be employed to mitigate risks. These include:

- Use of closed systems or physical barriers in manufacturing processes: These systems can be seen in automated drug compounding systems or in glove boxes that provide a protective barrier between the operator and the product.
- Local exhaust ventilation (LEV) systems: Specific examples include fume hoods in laboratories where HMPs are prepared or analysed, or dust extraction systems at tablet crushing stations.
- Airlocks, changing rooms, pass-through hatches, and decontamination showers: These can be particularly essential in areas handling highly potent or toxic HMPs.
- Suitably designed facilities and environmental control systems: Such as dedicated HVAC systems for areas handling HMPs, with appropriate air filtration and negative pressure systems to prevent escape of HMPs into other areas.
- Separate preparation areas for each HMP: For example, dedicated production lines or isolated rooms for handling specific HMPs to prevent cross-contamination.
- Detailed operational plans for the manufacturing site and specific design of manufacturing equipment: For instance, equipment with smooth, non-porous surfaces for easy cleaning, or automatic clean-in-place (CIP) systems for equipment decontamination.

It's important to note that while many of these measures are specific to manufacturing, similar yet distinct measures may be applied in other contexts such as preparation or storage of HMPs.

Organisational measures

Organisational measures play a key role in ensuring effective worker protection against occupational exposure to HMPs. Monitoring adherence to operating controls is essential, and facilities could be graded to encourage and reward adherence[7]. Organisational measures can be grouped into several key areas:

- Access Control and Area Labelling:
    - Restricting access to production facilities or other high-risk areas to authorised personnel only.
    - Labelling of areas with clear signs indicating potential exposure risks, and using a colour-coding system, such as black/white areas, to distinguish between areas of different exposure risk.
- Process Organisation:
    - Establishing standard operating procedures (SOPs) to be followed at all times, including procedures for cleaning and decontamination, waste management, handling of HMPs, and response to exposure incidents.
    - Regular review and updating of these SOPs to ensure they remain effective and reflect the most current knowledge and best practices.
    - Implementing a clear organisational structure for health and safety oversight, including a well-trained Health, Safety & Environment (HSE) team with defined roles and responsibilities.
- Hygiene and Maintenance Measures:

- Ensuring cleaning and maintenance practices comply with good manufacturing and industry good practice.
  - Validating the efficacy and reproducibility of cleaning and decontamination procedures through documented experimentation and challenge studies.
- Industrial Hygiene:
  - Industrial hygiene monitoring of staff exposure levels and appropriate response to any potential exposure incidents.

Each of these elements is a piece of a comprehensive organisational approach to controlling exposure risks.

In addition to the above measures, the general principles in for example administering HMPs include organising work before starting the administration, such as preparing materials, providing appropriate PPE and instructions on how to use them, and providing waste containers. For example, personnel should put on PPE before handling HMPs or providing patient care and wash hands before putting on and after taking off gloves. Proper instruction should be given on how to wash hands properly and take off gloves correctly. It is essential to use gloves to remove protective gowns and protective face shields/goggles, and personnel should refrain from eating, drinking, and chewing gum while working with HMPs.

The EU Guidance for the safe management of hazardous medicinal products at work goes into further detail for every type of activity.

Personal protective equipment (PPE)

According to Article 3 of Directive 89/656/EEC on the use of personal protective equipment[30] and the CMRD[8], PPE must be employed when risks cannot be avoided or sufficiently limited by technical means of collective protection or by organisational means. This requirement applies to all stages of the HMP life-cycle, including manufacturing, handling, administration, cleaning, patient care, laundry, and waste management.

A task-based risk assessment should be carried out to determine the appropriate protective measures for each specific task. This risk assessment should consider the type and magnitude of exposure risk, and the effectiveness of existing control measures.

When it comes to personal protective equipment (PPE), careful consideration should be given to the risk assessment to determine the appropriate PPE.

For example, in manufacturing facilities, PPE may include:

- Protective "space" suits, where the air pressure inside the suit is greater than the facility's environment.
- Breathing air supplied to protective suits should be filtered through a high-efficiency particulate air (HEPA) filter.

- Breathing air supply systems should have a 100% back-up system in case of failure of the main system, such as a gas bottle providing at least 5 minutes of air supply.
- If space suits are not necessary, then glasses, masks, gowns, gloves, boots, shoe covers, and glove ports or glove bags may be used.

For the administration of HMPs and patient care, the appropriate PPE should be worn and correctly disposed of immediately afterwards to prevent potential contamination. The PPE needed varies depending on the mode of administration – infusion, aerosol, injection, or topical surgical - and potential exposure risks. For example, the following PPE should be used as a minimum for handling infusion bags with a physical barrier:

- Type B protective gloves (type B based on EN ISO 374-1:2016[31])

When handling infusion bags without a physical barrier or after administration if dripping cannot be avoided in disconnecting the infusion set, the following PPE should be used as a minimum:

- Type B protective gloves
- Protective gown
- Protective face shield or protective goggles, if indicated by the risk assessment.

The specific types and applications of PPE in various exposure scenarios are detailed in the table on page 194 of the non-binding guidelines issued by the EU Commission on the safe management of hazardous medicinal products at work[7], which provides a more comprehensive resource on this topic. PPE should always be used as part of a comprehensive strategy to protect workers from HMP exposure, and not as a replacement for technical and organisational control measures.

Health surveillance

The primary purpose of health surveillance is to monitor and counsel individuals who may be exposed to workplace chemicals and detect any changes in their health status that may be attributed to such exposure. This process aims to identify early and reversible signs of work-related diseases, promoting a comfortable and healthy work environment.

Employers must recognise the risks associated with their workplace and, where appropriate, implement appropriate and specific health surveillance programs tailored to the type of exposure to HMPs. These programs should include regular medical examinations, assessment of exposure levels through biomonitoring, and monitoring for early signs of adverse health effects associated with HMP exposure.

As part of a health surveillance program, organisations may use biomonitoring (biomarkers of exposure and effect) to collect data on worker exposure and effects. Biomonitoring should follow best practices and be:

- Reproducible under the same conditions

- Sensitive
- Specific
- Fast
- Cost-effective/inexpensive
- Preferably non-invasive and cause no distress or anxiety for those being tested
- Provide quantitative measurements

Some examples of biomonitoring methods for detecting exposure to HMPs or monitoring early signs of adverse health effects are[32][33]:

1. Biological monitoring of exposure:
    1. Urine samples: For certain HMPs, such as antineoplastic agents, measuring drug metabolites or parent compounds in workers' urine samples can help determine the extent of exposure.
    2. Blood samples: Blood tests can be used to measure specific HMP metabolites, parent compounds, or biomarkers of exposure, depending on the substance in question.
2. Biological monitoring of effect:
    1. Haematological tests: Changes in blood cell counts (e.g. leukocytes, erythrocytes, or platelets) can be indicative of early signs of adverse health effects due to exposure to certain HMPs.
    2. Liver function tests: Monitoring liver enzyme levels in blood samples can help detect early signs of liver damage caused by some HMPs.
    3. Kidney function tests: Assessing kidney function through blood and urine tests can help identify early signs of kidney damage resulting from exposure to certain HMPs.
    4. Cytogenetic tests: Chromosome aberrations, micronuclei, or other genetic changes in peripheral blood lymphocytes can be used as biomarkers of genotoxic effects due to exposure to mutagenic or carcinogenic HMPs.

It is essential to select the most appropriate biomonitoring methods based on the specific HMPs and the associated health risks. Consultation with occupational health professionals and toxicologists is crucial for developing a suitable biomonitoring program tailored to the workplace and the workers exposed to HMPs. Additionally, biomonitoring should be performed in compliance with ethical and legal requirements, ensuring confidentiality and informed consent from workers.

In the context of HMP exposure, health surveillance should also involve training workers to recognise and report any signs or symptoms related to potential exposure. This will allow for timely intervention and the implementation of appropriate control measures to mitigate risks and protect workers' health.

Training and Education

Training scope

All workers who may come into contact with HMPs should receive sufficient information and training to carry out their duties safely. This includes not only regular staff but also cleaners, transport workers, those handling waste and laundry, and any temporary, subcontracted, occasional or young workers. Employers need to set up a training programme and HMP training should encompass [7] [26] :

- Preventing workers' exposure to HMPs and related risks during regular tasks, transport, waste handling, and spill incidents.
- Tailoring training to workers' activities and potential HMP exposure levels as identified in the workplace risk assessment and outlined in the risk management plan.
- Ensuring only trained workers handle HMPs, with staff competency assessed initially and regularly.

Requirements

HMP training should be based on a comprehensive assessment of workers' roles and activities, and tailored to their tasks considering:

- Risk levels associated with HMPs
- Specific workplace activities
- Workers' roles, responsibilities, education, and language skills
- Effectiveness of prior training
- Appropriate training delivery methods

A structured training program should be developed to address all relevant roles, activities, and HMP-related workplaces. Specific training may vary depending on the worker's role. It is important to:

- Encourage continuous learning through courses, workshops, seminars, and conferences, and provide training in an accessible format.
- Offer training for newcomers, after extended absences, role changes, or when new HMPs or processes are introduced.
- Evaluate and revise training annually, assessing worker competency and determining if the program requires updates.
- Keep records of training courses, worker completion, and education providers in accordance with legislation or guidance, maintaining a record in each worker's HR file.

Annual refresher courses and competency checks are recommended.

Core training topics

Core training, depending on the workers' tasks, should cover (non-exhaustive list):

- HMP identification
- Labelling and packaging of HMPs
- HMP-related health risks
- Workers' rights and risk assessment
- HMP risk awareness
- PPE use, disposal, and personal hygiene
- Access to first aid, safety stations, and SOPs for exposure management
- Incident management, including emergency procedures and spill kits

- Handling and disposal of contaminated patient excreta
- Hazardous waste management.

Training should be regularly evaluated and updated as knowledge evolves.

Additional training

Additional HMP training may include:

- Compliance with health, safety, and waste management legislation
- International agreements and Member State legislation
- Standard operating procedures and risk management plans
- Workers' responsibilities and workplace hazard identification for exposure to HMPs and related waste
- Handling, transportation, and storage of HMPs and waste
- PPE selection, use, cleaning, and disposal
- Equipment use and maintenance
- HMP receiving, unpacking, and storage
- Cleaning and laundry procedures
- Health surveillance and workplace monitoring
- Pregnancy, breastfeeding, and planned parenthood considerations.

European Guidance and Directives

The EU strategic framework on health and safety at work (2021-2027) addresses the risks associated with hazardous medicinal products, including antineoplastics. The European Commission published new guidance for their safe management in 2023. Further information can be found through resources from the European Agency for Safety & Health at Work (EU-OSHA)

Conclusion

In conclusion, workers who are exposed to HMPs may experience unintended effects, including carcinogenic, mutagenic or reprotoxic and other adverse effects. It is the responsibility of the employers to ensure the safety and health of their workers. This includes assessing and preventing occupational risks, providing information and training, and implementing appropriate control measures. The European Commission is currently working on a list of HMP to complement the CMRD, which will further facilitate employers' efforts to identify and manage these hazards.

However, it is often not possible to replace HMPs with less dangerous medicines due to their essential properties for patient treatment. In situations where multiple undertakings share a workplace, cooperation and coordination between employers are crucial in implementing HMP-OSH measures and protecting all staff potentially exposed to HMPs. Employers must also ensure that workers and their representatives are informed about the risks associated with HMPs, tasks involving HMPs, and measures in place to reduce exposure.

Creating a high level of safety culture that proactively anticipates problems is important for effective management of HMPs in the workplace.

References

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