Guidance for the safe management of hazardous medicinal products at work[1]

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[1]European Commission. 2023 *Guidance for the safe management of hazardous medicinal products at work*. Accessed on January 15, 2024, at https://osha.europa.eu/sites/default/files/documents/guidance%20for%20the%20safe%20management%20of%20hazardous%20medicinal-KE0723274ENN.pdf

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EXPOSURE CONTROL
monitoring and consultancy

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1980 - 1988	Chemistry
1988 - 1993	PhD study / Thesis “Monitoring of occupational exposure to antineoplastic agents”
1995	Exposure Control (NL-SE) Consultancy for monitoring of occupational exposure to antibiotics and antineoplastic drugs (sampling – analysis – advise)
1996	PhD Medical Sciences

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Section 1 - Introduction

- **Why is it important to manage exposure to Hazardous Medicinal Products (HMPs)?**
  - HMPs can cause unintended effects in workers
  - HMPs can cause Carcinogenic, Mutagenic or Reprotoxic (CMR) and other adverse effects
- **What is the purpose of the guide?**
  - Increase awareness of the risks handling HMPs
  - Increase the uptake of good practice
  - Improve the flow of information
  - Reduce inequalities between Member States
  - Be a flexible and up to date tool
  - To be used by employees, employers, occupational health and safety experts, and public authorities
- **Nature, scope and structure of the guide**
  - Non-binding
  - Providing an overview of good practices available
  - Advice provided without prejudice to national provisions
  - 15 Sections and 7 Annexes covering whole life cycle of HMPs from manufacturing in industry till waste management

Section 2 – Identification of Hazardous Medicinal Products

- **Working definition of HMPs**
  - Medicinal products that contain one or more substances that meet the criteria for classification as carcinogenic (category 1A or 1B), mutagenic (category 1A or 1B) or toxic for reproduction (category 1A or 1B)
  - Medicinal products for both human and veterinary use
  - HMPs fall within the scope of the CMR Directive

- **Examples of HMPs**
  - Antineoplastics, antivirals, hormones and hormonal antagonists, immunosuppressants and some antibiotics
  - Treatment areas: mainly oncology, transplantation, HIV and Hepatitis B & C treatment and rheumatology

- **Methods of determining whether a medicinal product is an HMP (list published by European Commission April 2025)**
  - Existing national lists and databases
    - NIOSH list (USA)
    - EU: ETUI list published in 2022 as starting point available online free of charge
      https://www.etui.org/publications/etuis-list-hazardous-medicinal-products-hmps
  - Safety Data Sheets, Summaries of Product Characteristics

Section 4 – Risk assessment

- The risk assessment enables decisions about appropriate risk management measures, training, exposure assessment and health surveillance as may be required by legislation
- Responsibility for the risk assessment and for developing and implementing a risk management plan based on the risk assessment lies with the employer
- Risk assessments are performed by Occupational Safety and Health (OSH) experts. Not by pharmacists!
- Risk assessments must be undertaken for all activities where workers are likely to be exposed to HMPs
- First step in a risk assessment is to identify the hazard: is the product an HMP? (Section 2)
- Second step is to assess whether the hazard is a risk (locations and activities where HMPs are used, which workers exposed to HMPs, workers at greater risk, measuring exposure levels, etc.)
- The risk assessment should evaluate the likelihood of adverse health effects at the assessed exposure levels
- The risk assessment process should be recorded
- The risk management plan must be in line with the hierarchy of controls in Directive 2004/37/EC
- Risk assessment and associated risk management plan must be reviewed regularly
- Authorities can request for data on risk and exposure assessment

Section 5 – Exposure assessment (1/2)

Introduction

- Workers' exposure to HMPs **MUST** be measured regularly or when procedures, processes or HMPs used are changed
- Workers' exposure can be measured by workplace monitoring and/or biomonitoring
- Should cover all areas where HMP are handled from receiving, storage, preparation, administration, etc.
- Protocols must be implemented, type of exposure and degree and duration should be determined to assess the risk

Exposure routes

- In hospitals and pharmacies, dermal uptake is the key route of exposure. Therefore, workplace monitoring of HMPs is mostly performed by surface wipe sampling
- Inhalation might happen in specific situations (handling powders and accidents with spills)

Section 5 – Exposure assessment (2/2)

Surface wipe sampling

- Practically, it is not possible to measure all HMPs. Focus on the most frequently used HMPs as markers for all HMPs
- Start with an initial measurement and establish the sampling frequency (monthly, quarterly or half yearly) based on the frequency and volume of HMPs handled. Measure **BEFORE** cleaning. Review frequency based on the results
- There are no official limit values for surface contamination with HMPs. Compare with previous measurements or other studies. Some studies present a guidance value or safe reference value of **0.1 ng/cm^2** or alert and action levels

Air monitoring

- Air monitoring can be applied during specific processes when particles and aerosols are expected in the air such as weighing and dissolving HMPs, production of capsules, and crushing tablets
- Measurements can be compared with official published Occupational Exposure Limits (OELs) or OELs provided by the manufacturer/supplier as Safety Data Sheets or otherwise
- Currently, there are no European OELs for HMPs. However, some member states have OELs

Biomonitoring

- Biomonitoring can be used to measure exposure of the workers to HMPs. Biomonitoring integrates HMP exposure from different sources and by different routes of uptake. It is available for some HMPs

Section 10 – Preparation (1/3)

Management and organisation

- Centralisation: preparation should be centralised within pharmacies in dedicated confined areas
- Preparation in administration areas should only occur when there is no possible alternative and after a risk assessment has been carried out
- For administration of parenteral HMPs in non-surgical settings, spiking should be performed at the pharmacy
- Activities related to HMP preparation should be developed, organised and supervised by a competent, designated person
- Relevant activities should only be carried out by trained workers
- Report instances where instructions are not/cannot be followed to the management

Section 10 – Preparation (2/3)

Technical measures

Technical measures should be used for the preparation of all forms of HMPs (vials, ampoules, tablets, bottles) and can include:

- External ventilation of preparation rooms to the outside of the building
- Cabinets, isolators, robotic systems in accordance with national/international standards exhausting 100% out of the building
- Needle-free systems: Luer-lock syringes, systems with a physical barrier, syringe-to-syringe connectors
- The use of single-use absorbent mats in case of contamination or spill
- Spiked bags and primed tubing before the addition of HMPs

The use of Closed System Transfer Devices (CSTDs) is the decision of management/staff in accordance with the risk assessment and relevant national legislation

CSTD definition EU guidance: A medicine transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of the HMP or vapour concentrations outside the system

CSTD definition NIOSH: A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of the hazardous drug or vapour concentrations outside the system

Section 10 – Preparation (3/3)

Organisational measures

- A list of HMPs should be developed
- Document Standard Operating Procedures (SOPs)
- High risk activities should be avoided: dose fractionation, weighing, crushing and mixing tablets (use BSC)

Personal Protective Equipment (minimum!)

- Protective gloves type B
- Protective face shield/goggles
- Protective gown/coverall
- Respiratory protection

Section 11 – HMP administration (1/3)

- **Different settings**
  - Hospitals, hospital satellite clinics, mobile administration units, local oncology centres
  - Healthcare facilities other than hospitals, nursing homes
  - Care homes, hospices, home care

- **Management and organisation**
  - Centralise administration to the maximum degree possible
  - Preparation activities should typically take place in a pharmacy
  - Administration only by trained and competent workers
  - Supervision by competent/trained dedicated person
  - Syringes with needles should be avoided
  - If possible, patient should self-administer

Section 11 – HMP administration (2/3)

- **Risk assessment for HMP administration**
  - The main exposure route for HMP in administration is dermal uptake
  - If good practice is used in infusion procedures, aerosols are only released by pressure build-up in the infusion line to the patient
  - Withdrawing the needle from the container/bag or patient can result in release of aerosols. Use instead needle-free or Luer-lock connections

- **Technical measures**
  - Choice of technical measures based on the HMP, dosage, volume and frequency of the HMP administered
  - Consultation of staff involved in preparation and administration on the choice of technical measures
  - Techniques and procedures must be used to reduce exposure risks
  - The use of CSTDs is the decision of the management/staff in accordance with the risk assessment and relevant national legislation
  - Procedures should be validated and periodically re-evaluated with appropriate measuring and monitoring techniques

Section 11 – HMP administration (3/3)

- **Organisational measures**
  - Work should be organised in advance
  - Facility layout should allow for effective cleaning
  - Standard Operating Procedures (SOPs) should be in place for patient care, handling excreta, waste, cleaning, laundry

- **Personal Protective Equipment for IV infusions (minimum!)**
  - **Infusion bag with a physical barrier**
  - Protective gloves type B

  - **Infusion bag without physical barrier or if dripping is expected during disconnection**
  - Protective gloves type B
  - Protective gown
  - Protective face shield/goggles if indicated by the risk assessment

  - Protective gloves should be used for removing other PPE

  - Differentiation in PPE depending on the type of administration

Thank you for your attention !