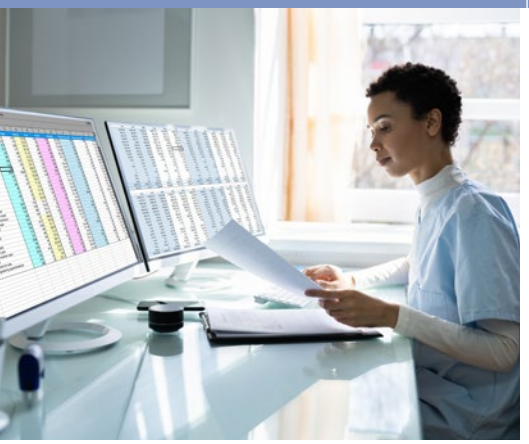
European Commission

7.2 - Dispositivi medici: stato dell'arte per un maggiore riconoscimento del ruolo dei farmacisti ospedalieri

Guidance for the safe management of hazardous medicinal products at work

SECOND EDITION






Employment, Social Affairs and Inclusion

10

Preparation (pharmacies and healthcare establishments)

Cover image: Preparation at the Masaryk Memorial Cancer Institute, Czech Republic

10.1 Introduction

This section of the guide focusses on occupational exposure of workers from hazardous medicinal products (HMPs) preparation activities at pharmacies both inside and outside of hospitals. Additionally, preparation at the ward is also covered in this section. Specifically, the following aspects are covered:

- Management and overall organisation (including preparation at the administration area)
- Technical measures
- Organisational measures (procedures)
- Personal protective equipment (PPE)
- Hygiene measures

This guide is for both hospital and community pharmacies. However, it is understood that there may be differences between hospital and community pharmacies in some European Union (EU) Member States and the guidance provided in this document should be tailored to the specificities of the relevant Member State.

It is also important that relevant EU resolutions are followed during preparation activities.[212, 213]

10.1.1 Sterile and non-sterile preparation

Preparation of HMPs can involve both sterile preparation and non-sterile preparation. There are some differences between sterile preparation and non-sterile preparation. Sterile preparation involves protecting the HMP from microbial contamination. The sterile area should meet the requirements of a clean room as set out in ISO 14644-1[214] and also in Annex 1 of Volume 4 of the Good Manufacturing Practice (GMP) guidelines.[215]

This section covers both sterile and non-sterile preparation, and, where there are differences, these are highlighted in the guide.

10.1.2 Compounding centres

There is an increasing trend towards outsourcing preparation from pharmacies to external preparation at compounding centres, especially where standard doses are required in large quantities. There is a potential for increased use of automated robotic systems at such facilities. It should be recognised that not all preparation can be outsourced to such facilities. The extent of further expansion of this trend and the potential for the involvement of the pharmaceutical industry is unknown. This section may not be fully applicable to some compounding centres where activities are more akin to an HMP production environment.

212 Resolution CM/Res (2016)1 on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients https://statements.eahp.eu/resources/legislation/resolution-cmres20161-quality-and-safety-assurance-requirements-medicinal

213 Resolution CM/Res (2016)2 on good reconstitution practices in health care establishments for medicinal products for parenteral use https://www.edqm.eu/en/d/162941

214 ISO 14644-1, (2015), Cleanrooms and associated controlled environments- Part 1: Classification of air cleanliness by particle concentration

215 Annex 1 of Volume 4 of the Good Manufacturing Practice (GMP) guidelines, https://health.ec.europa.eu/system/files/2022-08/20220825_gmp-an1_en_0.pdf

10.2 Management and organisation

10.2.1 Centralisation

The preparation of HMPs should be centralised within the pharmacies (or, alternatively, compounding centres). This helps reduce the number of workers potentially exposed to HMPs and allows HMP preparation to be performed only by trained staff. However, there may be situations in which centralisation is not possible, such as for the reconstitution of extemporaneous oral suspensions and the adjustment of doses. In these cases, a risk assessment must be performed to ensure the required measures are undertaken for worker safety, see section 4.[216]

The design of the centralised preparation area should take into account the prevention and minimisation of exposure to HMPs (for example, the surfaces should be easy to clean, and separate areas should be used for HMPs and non-HMPs).

10.2.2 Use of dedicated areas

A confined and exclusive area should be used for preparing HMPs, with a warning and hazard sign outside, to alert other workers that HMPs are being prepared in this area. Access to this room should only be available for trained, competent personnel involved in preparation activities and a prohibited entry sign used when activities are being undertaken.[217]

Figure 10-1: Warning signs demarcating a pharmacy area where HMPs are prepared

Sources: Meander Medical Centre, The Netherlands and Sahlgrenska University Hospital, Sweden

[216] Directive 2004/37/EC, Article 3(2)
[217] Directive 2004/37/EC, Articles 5(5)(b) and 9

10.2.3 Workers and organisation

Any activities that are related to the preparation of HMPs should be developed, organised and supervised by a competent/trained, designated person. Workers involved in preparation should be trained and competent for preparing HMPs and their competence should be tested.[218] Clear, written instructions should be prepared and followed.[219] It is useful to report instances where instructions are not/cannot be followed to the management.

The following detailed (non-exhaustive) list of HMP training could be given to workers preparing HMPs, in addition to the core and basic training in handling HMPs, see section 6:

- Basic pharmacology of HMPs
- Routes of exposure to HMPs
- Correct use of PPE, see Annex 4
- Correct use of preparation devices
- Theory of aseptic technique
- Operational standards for aseptic HMP preparation and HMP clean room standards
- Safe handling approaches for HMPs received from the manufacturer such as wiping the outside of vials
- Safe handling aseptic techniques and protective routines
- Safe handling of oral, topical, and pre-packaged hazardous drug dosage forms
- Theory of containment devices and barriers
- Operational standards for containment secondary engineering controls (C-SEC) including airflow, pressures, and safe operating parameters
- Use of a relevant containment primary engineering control (C-PEC): suitable biological safety cabinet (BSC); compounding aseptic containment isolator (CACI); or cytotoxic drug safety cabinets (CDSC), including the parameters for safe operation
- Use of institution-specific specialised equipment
- Use of supplementary engineering controls
- Theory of hierarchy of controls
- Verification of HMP prescriptions and pharmacy medication checks (clinical, computer order entry, and final product release)
- Processes using HMPs (HMP selection, prescription verification, preparation (or purchasing), dispensing, administration, and drug use evaluation)
- Documentation requirements for pharmacy medication checks, HMP clean room standards, and cleaning
- Reducing contamination on the outside of the packaging of the prepared HMPs before transport for administration
- Documentation requirements for pharmacy medication checks and hazardous drug clean room standards

10.2.4 Preparation of HMPs in the administration area

As noted above, preparation activities should be centralised in a pharmacy department (or, alternatively in a compounding centre). However, there are occasions where the preparation of HMPs at the administration area cannot be avoided. This should only occur when there is no possible alternative. For the administration of parenteral HMPs in non-surgical settings, spiking should be performed at the pharmacy. Where an organisation permits preparation outside a pharmacy (or compounding centre), it may be useful to restrict this practice to specific HMPs or HMP groups – this should be determined based on the outcome of the risk assessment. An example of such approach is set out in Box 10-1, based on SESCAM (2022).[220]

[218] See also Directive 2004/37/EC, Article 11; and Directive 89/391/EEC, Article 6(3) (b) and (d)
[219] See also Directive 89/391/EEC, Article 6(2)(i)
[220] SESCAM - Servicio de Salud de Castilla-La Mancha (2022), Guidelines for action on the risk of exposure to hazardous drugs for health service workers in Castile-la Mancha, Rev. 2022

Box 10-1: Example of a group-based approach to permitting HMP preparation in an administration area

Group 1 HMPs and Group 2 parenteral HMPs should always be prepared at the pharmacy.

Non-parenteral Group 2 HMPs, parenteral Group 2 HMPs (in exceptional circumstances) and Group 3 HMPs where preparation at the pharmacy cannot be performed, should be performed under strict working conditions and with the use of PPE.

Note: The HMP groups are from the classifications by the National Institute for Occupational Safety and Health (NIOSH)[221]: (1) Antineoplastic medicinal products; (2) Non-antineoplastic hazardous medicinal products; and (3) Medicinal products with reproductive effects.

Source: SESCAM, 2022[222]

Where preparation needs to be carried out in the administration area, a risk assessment must first be performed to assess the risks and determine the measures to be taken[223], see section 4. At a minimum, the PPE used should include the PPE listed for use during preparation at the pharmacy, see section 10.5. Staff involved in the preparation of HMPs at wards should be trained and competent for this specific activity.[224] Clear, written instructions should be provided to workers, and followed during preparation.[225]

10.3 Technical measures

Engineering and technical measures should be used for the preparation of HMPs to reduce the potential exposure to workers during preparation activities.

Technical measures (whose feasibility should be considered during the risk assessment) should be used and can include the following for the preparation of all forms of HMPs (such as vials, ampoules, tablets, bottles):

- External ventilation of preparation room(s) (C-SEC) to the outside of the building
- A BSC Class II Type 2B[226] in accordance with national/international standards, for example DIN 12980.[227] A BSC Class II Type 2B is particularly important where there is a possibility of activities that may generate airborne particles.
- A laminar air flow cabinet with an upstream main filter stage which is immediately beneath the working surface
- An isolator[228] (preferably negative pressure to protect the worker), certified in accordance with ISO 14644[229]). An isolator is particularly important

[221] NIOSH, (2016), NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, https://www.cdc.gov/niosh/docs/2016-161/default.html
[222] SESCAM, (2022), Guidelines for action on the risk of exposure to hazardous drugs for health service workers in Castile-la Mancha, Rev. 2022
[223] Directive 2004/37/EC, Article 3
[224] See also Directive 2004/37/EC, Article 11; Directive 89/391/EEC, Article 6(3)(b) and (d)
[225] See also Directive 89/391/EEC, Article 6(2)(i)
[226] To maintain the efficiency of the BSC, it should be kept free of all but essential preparation equipment.
[227] DIN 12980. Laboratory installations - Safety cabinets and glove boxes for cytotoxic substances and other CMR drugs. Deutsches Institut Fur Normung E.V. 2017
[228] This should be in accordance with national/international standards. To maintain the efficiency of the isolator, it should be kept free of all but essential preparation equipment.
[229] ISO 14644 (2015). Cleanrooms and associated controlled environments

Figure 10-2: HMP preparation in isolators (externally vented) at the Masaryk Memorial Cancer Institute, Czech Republic

where there is a possibility of activities that may generate airborne particles and also if ampoules are used.

- A CDSC in accordance with national/international standards, for example DIN 12980[230]. A CDSC is particularly important where there is a possibility that activities may generate airborne particles.
- A robotic system for the preparation of HMPs
- A fume hood (when fume hoods are used, they should be used in accordance with EN14175[231])

The technical measures listed above should exhaust 100% out of the building.

In addition, the following measures should be used:

- Needle-free systems should be used, where possible. For example, using syringes with Luer-locks, using needle-free systems with a physical barrier and using syringe-to-syringe connectors for transferring solutions.
- A sterile, impermeable, single-use, waterproof and non-slip absorbent mat with the absorbent side up, should be used. This should be replaced daily, following contamination, or after a spill.
- Fluid bags should be spiked, and tubing should be primed with a compatible fluid before the addition of HMPs.

There is differing information in the literature on the effectiveness of use of closed system transfer devices (CSTDs) for reducing the risks in the preparation of HMPs. It is the decision of the management/staff on whether CSTDs are to be used in accordance with the risk assessment performed and relevant legislation. The technical measures that are used should also be validated with appropriate monitoring techniques.

Examples of technical measures, which can be used for sterile preparation, are shown in Box 10-2.

[230] DIN 12980, Laboratory installations - Safety cabinets and glove boxes for cytotoxic substances and other CMR drugs, Deutsches Institut Fur Normung E.V. 2017

[231] EN 14175, Fume cupboards https://www.en-standard.eu/search/?q=14175

Figure 10-3: Preparation of infusion bags with HMPs in an automated robotic system at the Amsterdam UMC, The Netherlands. Operators are wearing PPE.

Box 10-2 : Measures for reducing exposure during sterile preparation

- Use needle free systems if possible. If this is not possible, take appropriate measures i.e. syringes with Luer-lock connections
- Use wide-bore needles
- Use air-venting devices to equalise pressure and to minimise powder and liquid passage, and use an additional carbon filter along with the hydrophobic filter in the air-venting device to minimise aerosol passage
- Use a biological safety cabinet for preparation
- Purge preparations with dissolvent
- Use a sterile, impermeable, single-use, waterproof and non-slip absorbent mat with the absorbent side up

An antechamber/anteroom should be used for pre-package and storage. This room should also be used to allow access to the clean room and should be at pressure (preferably negative pressure). If it is not feasible to use the anteroom due to the need to doff the PPE in the anterooms, then consider using personal locks.

Note: The use of CSTDs is the decision of the management/staff in accordance with the risk assessment and relevant legislation.

Figure 10-4: A Luer-lock: a commonly used needle-free connection system used for ensuring a firm connection to minimise the possibility of slippage of the needle or tube and leakage

Figure 10-5:
Aerosols escaping during HMP preparation when a vial is spiked by needle

10.4 Organisational measures

10.4.1 Safe working practices

Safe working practices should be used in the preparation of HMPs and it is useful for them to be documented. Workers should also be competent in preparation activities. It is useful to develop standard operating procedures (SOPs) manuals and review and update them as required. At each pharmacy, a list should be developed for the HMPs prepared. This could also include an alert and advice for workers on the prescription system.

Dose fractionation should be avoided where possible and single-dose mixtures used where possible. Where dose fractionation is needed to be performed, then a risk assessment, see section 4, should be carried out to determine the measures required to protect the worker. A spill kit should be available, see section 13.3.

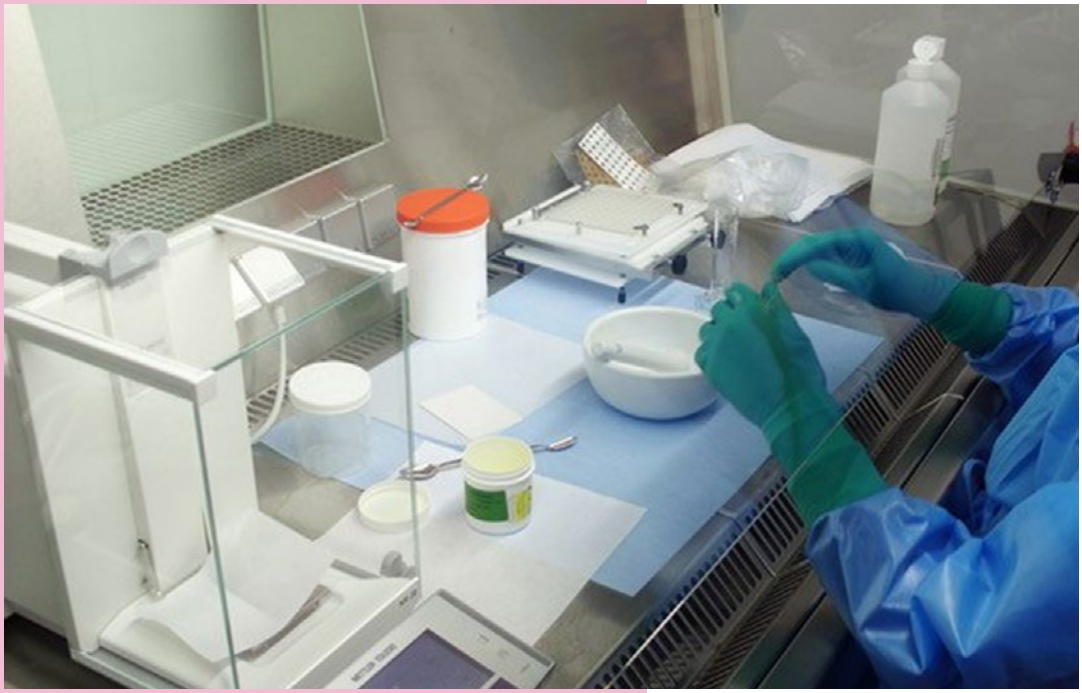
10.4.2 Particle generation

A number of activities should be avoided where possible because of the potential of airborne particle generation, this includes weighing, crushing and/or mixing tablets. If unavoidable, these activities should be performed in a BSC, see section 10.3. Measures should also be taken to minimise the possibility of the high-efficiency particulate air (HEPA) filter becoming clogged, such as using a mortar and pestle inside a plastic bag whilst crushing tablets (not shown in Figure 10-6).

10.4.3 Packaging of HMPs

Prepared HMPs should be sealed in a leakproof plastic bag and labelled. Those that are not used immediately should be stored in appropriate conditions.

Figure 10-6: Capsule production in a BSC at Pharma Assist BV, The Netherlands. Using HMP powders is a high-risk activity that has the potential to generate airborne particles.



10.4.4 Organisational measures by presentation

10.4.4.1 Oral forms (tablets, capsules, powders and liquids)

Oral forms such as tablets and capsules should be packed as individual doses where possible. Unit dose packaging is preferred if possible. Oral forms should be handled in a manner that avoids contact with the skin and protective gloves should be worn.

Figure 10-7: The use of break ampoules should be avoided

Tablets and capsules should not be crushed. For patients who have swallowing difficulties or feeding tubes and for paediatric patients, other forms (such as solutions and suspensions) or dosages should be considered. These should be prepared using special precautions.

A counting machine should not be used for HMP capsules and tablets. Dedicated equipment for HMPs should be used for dispensing HMP oral forms, and this equipment should be correctly labelled and also cleaned after use. To dispose of containers with damaged contents, see section 15.

There may be cases where fractionation or pulverisation is needed. In these cases, alternatives should be considered such as using liquid doses or changing the medication.

10.4.4.2 Ampoules

Where feasible, the use of glass ampoules should be avoided to reduce the risk of contamination and sharps injury. If this is not possible, break ampoules should be avoided.

10.4.4.3 Topical forms preparation (suspensions / solutions / creams / ointments)

Referenced protocols should also be followed for extemporaneous solutions which can be compounds using ampoules and/or vials. If leftover solutions are kept for later use, they should be kept in a dedicated area and should be marked for later use. These solutions should also be kept in a sealed leakproof plastic bag.

10.5 Personal protective equipment (PPE)

To select the PPE, see Annex 4. The PPE used should be determined by the risk assessment, see section 4 and Annex 4.

At a minimum, the following PPE should be used during preparation activities:

- Protective gloves type B, see Annex 4
- Protective face shield/goggles (when using a BSC/isolator this may not be required and should be determined during the risk assessment, see section 4)
- Protective gown/coveralls
- Respiratory protection, see Annex 4

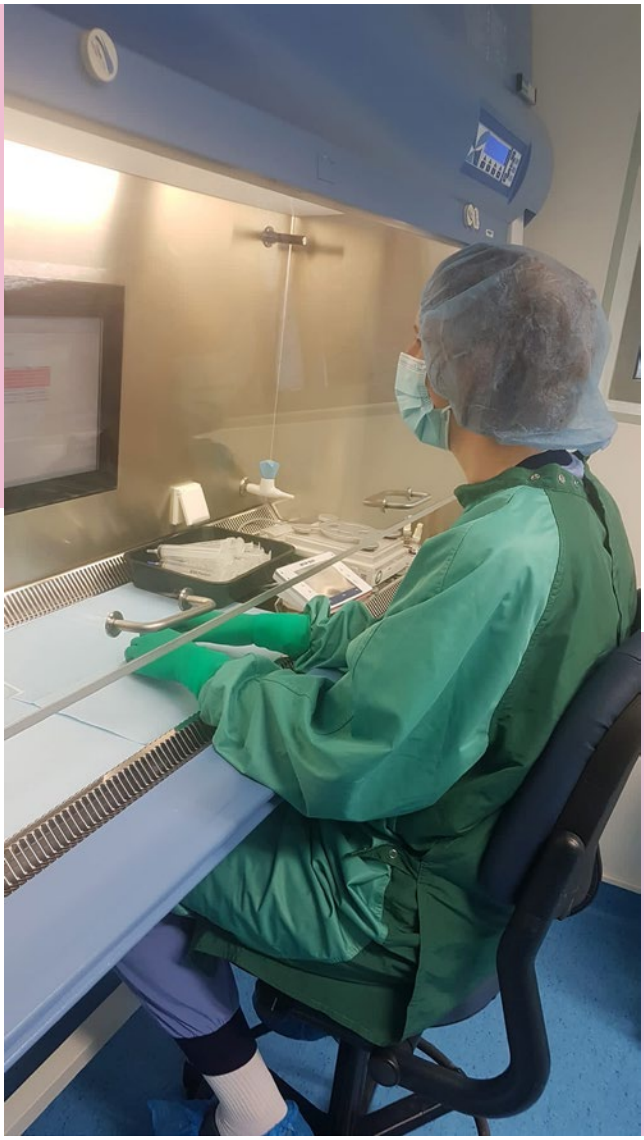


Figure 10-8:
A pharmacist applying the correct protection measures whilst working in BSC Class II
Source: Meander Medical Centre, The Netherlands

Figure 10-9:
A visual reminder of PPE to be worn on the door leading to a restricted area where HMPs are prepared
Source: Meander Medical Centre, The Netherlands

10.6 Hygiene measures

During preparation activities, at least the following hygiene procedures should be followed:

- No hand and wrist jewellery, long necklaces or large earrings
- Keep nails short and clean, do not wear make-up, nail varnish, artificial nails or perfume
- No food, drink, cigarettes/vaporisers, medication for personal use, or chewing gum in the preparation area
- No mobile phones, personal devices and headphones in the preparation area
- Tie back long hair
- Wash hands before putting on and after removing protective gloves

Box 10-3: Ensuring proper hygiene

The employer shall take adequate measures to ensure proper hygiene (minimising the risk of contamination with HMPs). Provisions and conditions must be free of charge for the workers, and will include:

- The prohibition of eating/drinking/smoking/vaping in contamination risk areas
- Provision of appropriate protective clothing
- Provision of separate storage places for working/protective clothing and for street clothes
- Access to appropriate and adequate washing and toilet facilities
- Availability of cleaned, checked and maintained protective equipment, stored in a well-defined place
- Repair and replacement of defective equipment

Source: Article 10(1) of Directive 2004/37/EC[232]

10.7 Secondary packaging and labelling

To protect against potential damage, primary packaging and HMPs should be protected with secondary packaging. It is useful to use single-use containers (such as sealed plastic bags) where possible. Mixtures should be individually packaged in a labelled, sealed, leak-proof container, with outer bags heat-sealed where possible. The potential for leakage and breakages during transport should be considered as part of the risk assessment, see section 4, when deciding on secondary packaging.

All secondary packaging should be labelled in accordance with the approaches set out in section 2.

[232] Directive 2004/37/EC of the European Parliament and of the Council of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens, mutagens or reprotoxic substances at work https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02004L0037-20220405

10.8 Waste

Single-use PPE as well as used materials that have been in contact with HMPs should be disposed of as hazardous waste in a closable hazardous waste container. Non-disposable equipment and PPE should be cleaned immediately after use.

10.9 Cleaning and laundry

Surfaces, clothing, etc. that have been in contact with HMPs should be considered as contaminated with HMP. These surfaces should be cleaned according to cleaning protocols, see section 14.1.

Non-disposable laundry should be treated as HMP-contaminated laundry, see section 14.2.

10.10 Summary of advice in section 10

Management and organisation

- Centralisation: preparation of hazardous medicinal products (HMPs) should be centralised within pharmacies in dedicated, confined areas designed to take into account the exposure prevention and minimisation principle, resulting in fewer exposed workers, a controlled environment, and work carried out by trained workers only.
- Preparation in administration areas should only occur when there is no possible alternative and after a risk assessment has been carried out. For the administration of parenteral HMPs in non-surgical settings, spiking should be performed at the pharmacy.
- Where an organisation permits preparation outside a pharmacy (or compounding centre), it may be useful to restrict this practice to specific HMPs or HMP groups.
- At a minimum, the same personal protective equipment (PPE) as at a pharmacy should be used for preparation in administration areas. Again, requirements such as trained staff only, clear written instruction, etc. apply.
- Activities that are related to the preparation of HMPs should be developed, organised and supervised by a competent/trained, designated person.
- The relevant activities should only be carried out by trained workers.
- Report instances where instructions are not/cannot be followed to the management.

Technical measures

- Technical measures that could be used to prepare of all forms of HMPs such as vials, ampoules, tablets and bottles, include:
  - Preparation room(s) should be externally vented to the outside of the building.
  - Examples of suitable equipment are listed in section 10.3.
  - Closed system transfer devices (CSTDs) are the decision of the country / organisation / management / staff in accordance with the risk assessment and relevant legislation.

Organisational measures

- A list of HMPs should be developed. This can include creating an alert in the prescription system.
- It is useful to document standard operational procedures (SOPs).
- High risk activities that should be avoided include: dose fractionation; activities that can generate airborne particles (weighing, crushing and mixing tablets). If unavoidable, these activities should be performed in a biological safety cabinet (BSC)
- The advice for oral forms includes:
  - Unit dose packaging preferred
  - Use protective gloves
  - Avoid crushing or using counting machines
  - Alternatives to fractionation or pulverisation
  - Ampoules: avoid glass ampoules, if possible. If not possible, break ampoules should be avoided

PPE

- At a minimum, the following PPE should be used during preparation activities:
  - Protective gloves type B
  - Protective face shield/goggles
  - Protective gown/coveralls
  - Respiratory protection

Hygiene measures

- Hygiene measures include no eating, drinking, mobile phones, or jewellery.

Secondary packaging and labelling

- To protect against potential damage, primary packaging and HMPs should be protected with secondary packaging.

Waste

- All materials that have been in contact with HMPs should be disposed of as hazardous waste. Non-disposable equipment and PPE should be cleaned immediately after use.

11

Administration

This section focuses on administration of hazardous medicinal products (HMPs) to patients and other activities related to patient care in the following settings:

Hospitals, hospital satellite clinics (such as outreach centres run by hospitals), **mobile administration units** (such as chemotherapy buses), and **local oncology centres**. The scope of this section includes both inpatient and outpatient administration at hospitals but excludes HMP preparation at hospital pharmacies, see section 10.

Healthcare facilities other than hospitals. The relevant facilities (non-hospital healthcare facilities) may include general practitioners' (GP) practices, local health centres and nursing homes. A pharmacy is generally not physically attached to such patient care facilities. The practices and equipment in place at these facilities may differ from hospitals and, consequently, separate advice is provided for some situations.

Home care, care homes and hospices. This includes administration of HMPs to patients and/or the physical care of these patients after receiving HMPs. The administration of HMPs and patient care in hospices, care homes and home care have similar characteristics which differ from healthcare establishments such as hospitals. A care home is defined as a house or institution providing accommodation and care for people who are unable to look after themselves. A hospice is a medical care facility that gives special care to people who are near the end of life and have stopped treatment to cure or control their disease.

This section has four major subsections:

- General remarks and comments are in section 11.1
- Specific remarks for administration and patient care in hospitals are in sections 11.2 - 11.8
- Focus areas for administration and patient care in other healthcare facilities are mentioned in section 11.9
- Focus areas for administration and patient care in care homes, hospices and homes are in section 11.10

The following administration procedures are considered in this section:

- Oral (tablets, capsules, powders, and liquids)
- Intravenous (IV) infusion
- Injections
- Intravesical (bladder) instillation and transarterial chemoembolisation (TACE) (liver, etc.)
- Inhalation
- Topical
- Surgical procedures

Other relevant activities in which occupational exposure to HMPs may occur in healthcare and care establishments (such as transport, intermediate storage, and cleaning) are covered in separate sections - this section should be read in conjunction with the remainder of this guide.

11.1 Management and organisation

11.1.1 Centralisation

The administration of HMPs should be centralised in a dedicated area to the maximum degree possible to prevent unnecessary contamination and to ensure that HMPs are handled by properly trained workers who have been informed about the relevant risks and protective measures. Centralisation is also helpful in ensuring that facilities for administration are designed to enable safe handling of HMPs and effective and efficient cleaning. If centralisation is not possible, workers should have the necessary tools, equipment and furniture to reduce exposure and workplace contamination to a minimum.

Preparation activities should typically take place in a pharmacy (see section 10).

11.1.2 Risk assessment

A risk assessment must be performed to identify the risks for each particular situation and location[233], see section 4.

The main exposure route for HMPs in administration is dermal. Exposure by ingestion will be negligible as drinking and eating must be forbidden[234] during the handling of HMPs. However, hand-to-mouth contact may still result in exposure by ingestion after touching contaminated surfaces. Unprotected contact (no protective gloves) with contaminated surfaces, tools or equipment should be avoided. Unprotected contact should also be avoided with droplets released from connecting or disconnecting syringes or lines to the infusion container / bag or the patient. Spiking of containers / bags should be done in a pharmacy.

If good practice is used in infusion procedures, aerosols are only released from the infusion system by pressure build-up in the infusion line to the patient. If the infusion procedure is based on gravity, the infusion stops automatically. Modern infusion pumps detect the pressure build-up, stop pumping and give an alarm. An infusion pump is shown in Figure 11-1.

Figure 11-1:
An infusion pump with automatic stop function

Inhalation exposure of HMPs is possible when patients are administered inhalable HMPs. Aerosols may also be released when HMPs are injected into the infusion container / bag or into the patient. Withdrawing the needle from the container / bag or patient can result in a release of aerosols due to a pressure drop or incident when the needle disconnects from the syringe during the procedure. Use of needle-free connections or Luer-lock helps to avoid the pressure change.

The choice of PPE in administration should be based on the risk assessment and the presence of technical and/or organisational measures.[235] In Annex 4, the minimum PPE required to protect the worker during different activities is listed.

[233] Directive 2004/37/EC, Article 3(2)
[234] Directive 2004/37/EC, Article 10(1)(a)
[235] See also Directive 89/656/EEC, Articles 3, 4 and 5

11.1.3 Workers and organisation

Developing and adhering to procedures for e.g. administration, patient care, handling excreta and / or blood, cleaning, waste handling, laundry and incident management is the responsibility of the employer. Only procedures that provide safe administration of the HMPs for workers, patients, and carers should be used.

It is helpful[236] for activities related to HMP administration to be supervised by a dedicated person, such as the head or manager of the centralised administration unit or ward.

Only trained and competent workers should be involved in the administration of HMPs.[237]

The following detailed (non-exhaustive) list of HMP training could be given to workers administering HMPs, in addition to the core and basic training in handling HMPs, see section 6:

- Basic pharmacology of HMPs
- Routes of exposure to HMPs
- Safe administration practices; correct hygiene procedures
- Receipt, unpacking, transport, and storage of HMPs
- Correct use of PPE
- Use of institution-specific specialised equipment for example administration pumps/safe systems for administration
- Theory of hierarchy of controls
- Health and safety legislation
- Waste management legislation
- Risk assessment process and HMP risk management plan, see section 4
- Disposal of HMP waste and patient excreta
- Handling of HMP laundry
- Management of incidents including contamination and spillage
- Health surveillance
- Workplace monitoring
- Pregnancy, breastfeeding, and planned parenthood

11.1.4 Communicate risks associated with patients

Ensuring that patients that have undergone treatment with HMPs are easily identifiable and are identified as such to relevant workers in other wards or departments for therapy or diagnostics over the entire period during which HMPs could be present in excreta (urine, faeces, vomit and sweat) and blood can be very helpful for the protection of the safety and health of such workers. However, any such identification needs to be in conformity with applicable data protection rules.[238]

In case of outpatient treatment, it is important to share information about the entire period during which HMPs could be present in excreta with any employer responsible for care of the patient (for instance nursing homes, care homes or organisations providing home care).[239] Sharing the same information with the patient is good practice that facilitates the awareness of other relevant employers, such as agencies supplying carers or domestic cleaners. Although every patient (and their treatment) is different, and the organisations to which the patients are going vary significantly, a set of information or brochures could be prepared for at least two situations:

- Instructions for the patient
- Instructions for the caring organisation

11.1.5 Technical measures

The choice of products and devices used has an impact on administration practices and should be based on the (type of) HMP, dosage, volume and frequency of administration.

[236] However, supervision of the work with dangerous substances may be mandatory under national legislation – readers are advised to check their national requirements.
[237] See also Directive 2004/37/EC, Article 11; Directive 89/391/EEC, Article 6(2)(i), 6(3)(b) and (d)
[238] Taking also into account that personal data concerning health are a special category of data (sensitive data) – see Regulation (EU) 2016/679
[239] Whilst ensuring that rules on personal data protection are respected – see previous footnote and Regulation (EU) 2016/679

To avoid exposure and for reasons of practicability and ease of use, representatives of all professional groups involved in HMP preparation and administration should be consulted in the process to select the devices used within the hospital.

Techniques and procedures must be used to reduce occupational risks from exposure to HMPs.[240] The use of syringes with needles should be avoided as much as possible in parenteral administration of HMPs.

The use of closed system transfer devices (CSTDs) is the decision of the management/staff in accordance with the risk assessment and relevant national legislation.

All procedures (including personnel, products and devices) used for administration and patient care should be validated with the appropriate measuring and monitoring techniques.

More specific advice is provided in sections 11.2 to 11.8 for each of the administration methods.

11.1.6 Organisational measures

The location where HMPs are administered, or where care for patients whose excreta and/or blood can be contaminated with HMPs is taking place, should have an adequate layout for effective cleaning. It is good practice to have separate toilet facilities for patients.

Protocols for administration, patient care, handling excreta and/or blood, cleaning, waste handling and incident management should be in place and all workers should receive training to ensure that they are familiar with these protocols prior to commencing the relevant activities, see section 6. Activities related to HMP administration should be supervised by a dedicated, trained, person.

11.1.7 Operational procedures and hygiene measures

Care should be taken to avoid the generation of airborne particles (solid or liquid), liquid or powder spills or splashes, and sharps injuries, such as from needles or broken glass.

The general principles for administration of HMPs include, for example:

- Organise work before starting the administration, for example, place all equipment (materials, PPE and waste container) within easy reach
- Put on PPE before starting to handle HMPs or getting in contact with contaminated excreta and blood, see Annex 4
- Wash hands before putting on and after taking off protective gloves. Instruction should be given on how to wash hands properly and how to take off protective gloves correctly
- Use protective gloves to remove protective gown and protective face shield/goggles
- No food, drink, cigarettes/vaporisers, medication for personal use, or chewing gum in the administration area

More information on the provisions for hygiene procedures in the carcinogens, mutagens and reprotoxic substances directive (CMRD)[241] is provided in Box 10-3 in section 10.6.

11.1.8 Excreta and blood

Excreta (urine, faeces, vomit and sweat) and blood should be treated as contaminated with HMPs during the time HMPs are being taken by the patient and generally up to 7-14 days after administration. As noted in section 8.6, it would be useful to have information about the presence of HMPs in excreta and blood supplied by the pharmaceutical manufacturer (for instance in a safety data sheet (SDS) and/or the summary of product characteristics (SmPC/SPC)) to enable the pharmacist to inform the workers involved in patient care about the time excreta and blood should

[240] Directive 2004/37/EC, Article 5

[241] Directive 2004/37/EC of the European Parliament and of the Council of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens, mutagens or reprotoxic substances at work https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02004L0037-20220405

Figure 11-2:
A closed bedpan washer at Sahlgrenska University Hospital, Sweden

be considered as contaminated. An overview can also be found in pharmaceutical guidelines[242].

Decanting urine manually should only be performed for 24-hour urine collection. Patients should be asked to go to the toilet themselves. Excreta (faeces, vomit and urine) should be handled with care. If possible, excreta should be transported in closed containers (urinals and bedpans). Decanting and washing should preferably be performed automatically inside a closed bedpan washer.

In specific surgical procedures, procedures where cavities / organs are locally treated and topical procedures with HMPs, the systemic uptake of HMPs in the patient is lower than in oral and parenteral procedures. This means that the presence of HMP in excreta differs and that the risk period may be shorter. In the absence of specific information, it should be assumed that the risk period is the same as for the same HMP in other administration forms.

11.1.9 Cleaning and laundry

High concentrations of HMPs can be present in the fluids used in the procedures or body fluids directly after treatment. Any single-use cloths or PPE that have been in contact with excreta from the patient (urine, faeces, vomit and sweat) or blood should be considered as contaminated with HMPs and should be disposed of as hazardous waste.

Any clothing, non-disposable bed linen and other laundry or bed linen that have been in contact with excreta from the patient or blood should be treated as HMP-contaminated laundry, see section 14.2.

Any floors, surfaces and administration areas, such as patient rooms, sanitary facilities, operating rooms, radiology rooms, mattresses, and urinals or bedpans, should be cleaned according to cleaning protocols in section 14.

[242] A regularly updated overview of the recommended duration of protective measures is provided, for example, in the full version of Quapos 6 (Quality Standard for the Oncology Pharmacy Service) Commentary Version. See https://esop.li/

11.2 Administration – oral

11.2.1 Management and organisation

Oral formulations of HMPs should not be crushed, dissolved or otherwise altered on the administration ward without the advice of the pharmacy. Tablets and capsules should be packed in individual packages.

If possible, patients should self-administer. When a patient cannot self-administer, another type of administration should be considered, in consultation with the pharmacist.

11.2.2 Technical measures

Dedicated spout cups should be used for administration of liquids whilst keeping a distance during administration, if possible.

11.2.3 Organisational measures

Workers involved in patient care should take into account the potential for exposure during the period that HMPs are present in excreta (urine, faeces, vomit and sweat) and blood. In case of continuous oral administration of HMP, the HMP will be always present in the excreta and blood of the patient.

Administration should be performed by trained workers and supervised.

11.2.4 Personal protective equipment (PPE)

A risk assessment, see section 4, should be performed to determine the PPE required for oral administration of HMPs and patient care (for minimal requirements and procedures for PPE, see Annex 4).

The following minimum PPE should be used for the administration of tablets and capsules (coated and uncoated):

- Type B protective gloves

The following minimum PPE should be used for the oral administration of HMP containing liquids, handling patient excreta or patient care:

- Type B protective gloves
- Protective gown

Figure 11-3:
Giving oral HMPs to patients for self-administration at the Sahlgrenska University Hospital, Sweden

- Protective face shield/goggles (to provide protection from splashes)

PPE should be worn during administration of HMPs and disposed of or cleaned immediately afterwards to avoid transfer of potential contamination.

11.2.5 Operational procedures and hygiene measures

General operational and hygiene principles for oral administration of HMPs should include:

- Workers should wash their hands before putting on and after taking off protective gloves
- The patient should use a drink container to self-administer tablets and capsules, and a spout cup for liquids

11.2.5.1 Tablets and capsules

- Touching the tablets / capsules should be reduced to a minimum
- Place all equipment (small single-use drink container and tablet pot) within easy reach
- Wash hands and put on protective gloves
- Place a single-use pad over the surface to protect it from contamination in case of a spill
- Let the patient open the primary package with the tablets/capsules or open the package for the patient and add the tablets to the tablet pot
- Use the tablet pot for administration of the HMP and let the patient drink
- Consider used single-use material as hazardous waste
- Remove protective gloves
- Wash hands

11.2.5.2 Liquids

- Place all equipment (small single-use drink container, or a spout cup) within easy reach
- Wash hands and put on protective gloves, gown and face shield/goggles
- Place a single-use pad over the surface that can be contaminated in case of a spill
- Open the container with the HMP liquid and pour it into the drink container
- Use the drink container for administration
- Dispose of the (drink) container as hazardous waste or clean immediately if re-used
- Remove protective gown and face shield/goggles
- Remove protective gloves
- Dispose of disposable PPE as hazardous waste
- Wash hands

11.2.6 Waste

Single-use PPE as well as packaging and drink containers (single-use containers used for the application of a liquid medicine) that have been in contact with HMPs should be disposed of as hazardous waste in a closable hazardous waste container, see section 15.

Non-disposable equipment and PPE should be cleaned immediately after use.

11.2.7 Excreta and blood

Excreta (urine, faeces, vomit and sweat) and blood should be treated as contaminated with HMPs during the time HMPs are being taken by the patient and generally up to 7-14 days after administration (see section 11.1.9).

11.2.8 Cleaning and laundry

Surfaces, bed linen, and clothing that have been in contact with HMP containing solution or excreta (urine, faeces, vomit and sweat) or blood should be considered as contaminated with HMP. These surfaces should be cleaned according to cleaning protocols, see section 14.1.

Non-disposable bed linen and other laundry that is used during the procedure should be treated as HMP-contaminated laundry, see section 14.2.

11.3 Administration – IV infusion

This section deals with administration by means of an infusion system (with or without the use of an infusion pump).

11.3.1 Management and organisation

Infusion systems should be filled in the pharmacy with an HMP-free solution before the HMP is added to the infusion bag/bottle or connected to the HMP container.

Figure 11-4:
A nurse wearing protective gloves and a gown administering an IV infusion (with a pump) to a patient at the Sahlgrenska University Hospital, Sweden

Figure 11-5:
Do's and don'ts of HMP administration

LEFT: Do: Administration using gloves, bag is spiked in the pharmacy with side line with clamp (only neutral fluid in side line below the clamp) and using Luer-locks

RIGHT: Don't: No gloves worn AND bag is directly spiked in the administration area

Source: Photos provided by Amsterdam UMC, The Netherlands

11.3.2 Technical measures

Luer-slip connections and needles should not be used.

Preferably, infusion systems with a functional physical barrier between the HMP-containing infusion bag/bottle/container and the connection point for the infusion-port at the patient, should be prepared in the pharmacy. Systems with a physical barrier could be, for example:

- Infusion lines filled with an HMP-free solution
- Systems with a physical barrier for injecting HMP-containing solution into the infusion bag on the ward

Another solution could be to use a system based on filtering the outgoing air.

The effectiveness of all systems used should be validated before being introduced and periodically re-validated when in use.

Figure 11-6: A nurse wearing PPE at Sahlgrenska University Hospital, Sweden

11.3.3 Organisational measures

The connection and disconnection of infusion systems with administration bags should be kept to a minimum and avoided when possible. The risk of HMP-containing liquid dripping can be reduced by not disconnecting the infusion system from the guard infusion after administration.

Disconnection of the infusion system from a patient should be performed after the system has been flushed with at least 100 ml of HMP-free solution.

Administration should be performed by trained workers and supervised.

11.3.4 Personal protective equipment (PPE)

A risk assessment, see section 4, should be performed to determine the PPE required for infusion of HMPs and patient care (for minimal requirements and procedures for PPE, see Annex 4). PPE should be worn during administration of HMPs and disposed of or cleaned immediately afterwards to avoid transfer of potential contamination.

The following PPE should be used as a minimum for handling infusion bags with a physical barrier:

- Type B protective gloves

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

- Type B protective gloves
- Protective gown
- If indicated by a risk assessment: protective face shield/goggles, see section 4

11.3.5 Operational procedures and hygiene measures

General operational and hygiene principles for IV infusion of HMPs are described below for procedures with and without a physical barrier.

11.3.5.1 Procedure for infusion bags with a physical barrier

- Connect guard infusion with neutral IV fluid to the patient
- Place all equipment within easy reach
- Wash hands and put on protective gloves
- Place a single-use pad on the working surface to protect it from contamination
- Connect the infusion line from infusion bag with HMP to the guard infusion
- Close clips and/or clamps from guard infusion
- Open clips and/or clamps for HMP administration
- Remove protective gloves
- Wash hands
- Infusion takes place
- Wash hands and put on new protective gloves
- Close clips and/or clamps and flush with at least 100 ml of neutral IV fluid
- Disconnect the total infusion set from the patient
- Dispose of the materials; consider used single-use material as hazardous waste
- Remove protective gloves and dispose of as hazardous waste
- Wash hands

11.3.5.2 Procedure for infusion bags without a physical barrier

- Connect guard infusion with neutral IV fluid to the patient
- Place all equipment within easy reach
- Wash hands and put on protective gloves, gown and face shield/goggles
- Place a single-use pad on the working surface to protect it from contamination
- Connect the infusion line to the infusion bag with HMP
- Fill the line (partially) with the HMP infusion liquid; prevent dripping using a hydrophobic stop filter
- Check if the drip chamber in the guard infusion is sufficiently filled to accommodate the air in the infusion line from the infusion bag with HMP
- Connect the infusion line from the infusion bag with HMP to the guard infusion
- Close clips and/or clamps from the guard infusion
- Open clips and/or clamps for HMP administration
- Remove protective gown and face shield/goggles, then gloves
- Wash hands
- Infusion takes place
- Wash hands and put on new protective gloves, gown, and face shield/goggles
- Close clips and/or clamps and flush with at least 100 ml of neutral IV fluid
- Disconnect the total infusion set from the patient
- Remove protective gown and face shield/goggles
- Remove protective gloves
- Dispose of the materials and PPE; consider single-use material and PPE as hazardous waste
- Wash hands

11.3.6 Waste

Administration lines should only be disconnected after they have been flushed with at least 100 ml of a compatible non-HMP solution. Administration sets should not be removed from an IV bag and the

complete set that has been in contact with HMPs should be disposed of as hazardous waste, in a closable hazardous waste container.

Single-use PPE used during infusion should be disposed of as hazardous waste. Non-disposable PPE should be cleaned immediately after use.

For more information on waste disposal, see section 15.

11.3.7 Excreta and blood

Excreta (urine, faeces, vomit and sweat) and blood should be treated as contaminated with HMPs during the time HMPs are being taken by the patient and generally up to 7-14 days after administration (see section 11.1.9).

11.3.8 Cleaning and laundry

Surfaces, bed linen, and clothing that have been in contact with HMP containing solution or excreta (urine, faeces, vomit and sweat) or blood should be considered as contaminated with HMP. These surfaces should be cleaned according to cleaning protocols, see section 14.1.

Non-disposable bed linen and other laundry that is used during the procedure should be treated as HMP-contaminated laundry, see section 14.2.

11.4 Administration – injections

11.4.1 Management and organisation

Intrathecal administration should be performed in designated areas.

Figure 11-7:
DO vs DON'T: use Luer-lock (left), not Luer-slip (right) connections

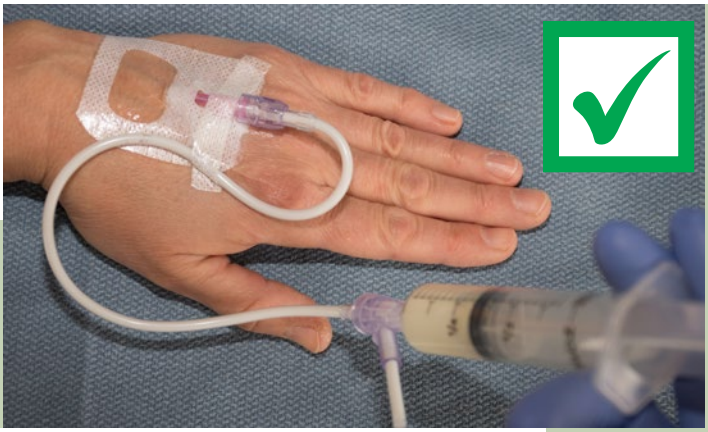


Figure 11-8: Bolus injection administration using a system with a Luer-lock, worker wearing PPE (only protective gloves visible in the picture)

Figure 11-9: Avoid using Luer-slip connections if possible: this photo shows administration by injection using a Luer-slip connection

11.4.2 Technical measures

Needles with a Luer-lock should be used to minimise the possibility of slippage of the needle and leakage. Luer-slip connections and needles should not be used.

For a bolus injection, a peripherical access system for administration should be applied before connecting the syringe.

11.4.3 Organisational measures

Bolus, intramuscular, subcutaneous and intrathecal injections should be performed by trained workers and supervised.

11.4.4 Personal protective equipment (PPE)

A risk assessment, see section 4, should be performed to determine the PPE required for injection of HMPs and patient care (for minimal requirements and procedures for PPE, see Annex 4).

PPE should be worn during administration of HMPs and disposed of or cleaned immediately afterwards to avoid transfer of potential contamination.

The following PPE should be worn as a minimum for the injection of HMPs:

- Type B protective gloves
- Protective gown
- If indicated by a risk assessment, a protective face shield/goggles (to provide protection in the event of splashing during injection of HMPs with needles without Luer-lock), see section 4

11.4.5 Operational procedures and hygiene measures

General operational and hygiene principles for administration of HMPs by injection are described for respectively bolus injection, subcutaneous injection, and intrathecal injection.

11.4.5.1 Procedure for bolus injection

- Place all equipment within easy reach
- Wash hands and put on protective gloves, gown and face shield/goggles
- A peripherical access system for administration should be placed before connecting the syringe (Luer-lock)
- Connect the syringe or CSTD
- After administration, flush with neutral fluid
- Disconnect the total injection set from the patient
- Dispose of the materials; consider used single-use material as hazardous waste
- Remove protective gown and face shield/goggles
- Remove protective gloves
- Dispose of PPE; consider used single-use PPE as hazardous waste
- Wash hands

11.4.5.2 Procedure for intramuscular and subcutaneous injection

- Place all equipment within easy reach
- Wash hands and put on protective gloves, gown and face shield/goggles
- Place a single-use pad under the parts of the body to be treated
- Perform the injections in accordance with the medical protocol
- After removing the needle, swab the site and apply a dressing when needed to avoid drop spilling
- Dispose of the materials; consider used single-use material as hazardous waste
- Remove protective gown and face shield/goggles
- Remove protective gloves
- Dispose of PPE; consider used single-use PPE as hazardous waste
- Wash hands

11.4.5.3 Procedure for intrathecal injection

- Place all equipment within easy reach
- Wash hands and put on protective gloves, gown and face shield/goggles
- Lay the patient on the side and place a single-use pad under the parts of the body to be treated
- Localize and disinfect the insertion point
- Put on sterile protective gloves
- Perform lumbar puncture
- Connect the T-connector and allow it to fill with cerebrospinal fluid (CSF), collect CSF
- Connect the locked/secured syringe containing the HMP with a Y-system to the T-connector
- Open the three-way valve to the Y-system and open the clamp on the locked/secured syringe containing the cytostatic
- After administering the cytostatic, close the clamp (of the cytostatic syringe) and open the clamp of the 10 ml locked/secured syringe with neutral liquid and flush with several millilitres
- Close the three-way valve
- Disconnect the Y-system from the T-connector; hold a gauze pad under it to catch any drops and place gauze under T-connector on pad. Place syringes with Y-system on the pad
- Remove lumbar needle with the T-connector and dispose of in a needle container
- After removing the needle, swab the injection site and apply a dressing when needed to avoid drop spilling
- Dispose of the pad with Y-system (syringes) and gauze as hazardous waste
- Dispose of the materials and the outer protective gloves; consider used single-use material as hazardous waste
- Remove protective gown and face shield/goggles
- Remove protective gloves
- Dispose of PPE; consider used single-use PPE as hazardous waste
- Wash hands

11.4.6 Waste

Syringes, containers with used needles, peripherical access system and single-use pads should be disposed of as hazardous waste, in a closable hazardous waste container.

Single-use PPE used during infusion administration should be disposed of as hazardous waste. Non-disposable PPE should be cleaned immediately after use.

For more information on waste disposal, see section 15.

11.4.7 Excreta and blood

Excreta (urine, faeces, vomit and sweat) and blood should be treated as contaminated with HMPs during the time HMPs are being taken by the patient and generally up to 7-14 days after administration (see section 11.1.9).

11.4.8 Cleaning and laundry

Surfaces, bed linen, and clothing that have been in contact with HMP containing solution or excreta (urine, faeces, vomit and sweat) or blood should be considered as contaminated with HMP. These surfaces should be cleaned according to cleaning protocols, see section 14.1.

Non-disposable bed linen and other laundry that is used during the procedure should be treated as HMP-contaminated laundry, see section 14.2.

11.5 Administration – intravesical instillation & transarterial chemoembolisation

Intravesical instillations and transarterial chemoembolisation (TACE) are special administration techniques that should only be performed in specialised hospital departments.

11.5.1 Management and organisation

Intravesical (bladder) instillation should be performed in designated units.

TACE microspheres should be prepared in the pharmacy and the procedure should be performed at the radiology department.

11.5.2 Technical measures

Luer-slip connections and needles should not be used.

A peripherical access system for administration with Luer-lock connections should be applied before connecting the syringe.

11.5.3 Organisational measures

Intravesical instillations and TACE administrations should be performed by trained workers and supervised.

11.5.4 Personal protective equipment (PPE)

A risk assessment, see section 4, should be performed to determine the PPE required for intravesical instillation, TACE and patient care (for minimal requirements and procedures for PPE, see Annex 4).

PPE should be worn during administration of HMPs and disposed of or cleaned immediately afterwards to avoid transfer of potential contamination.

The following PPE should be used as a minimum for intravesical instillation and TACE of HMPs:

- Type B protective gloves
- Protective gown
- If indicated by a risk assessment, see section 4, protective face shield/goggles (to provide protection in the event of splashing during intravesical instillation of HMPs)

11.5.5 Operational procedures and hygiene measures

General operational and hygiene principles for administration of HMPs by intravesical instillations and TACE should include:

- Place all equipment within easy reach
- Wash hands and put on protective gloves, gown and face shield/goggles
- Place a single-use pad over body parts that can be contaminated in case of spill and underneath the parts of the body to be treated
- Apply the HMP according to medical protocol
- Dispose of the materials; consider used single-use material as hazardous waste
- Remove protective gown and face shield/goggles
- Remove protective gloves
- Dispose of PPE; consider used single-use PPE as hazardous waste
- Wash hands

11.5.6 Waste

Catheters or sondes, access systems and single-use pads should be disposed of as hazardous waste, in a closable hazardous waste container.

Single-use PPE used during infusion administration should be disposed of as hazardous waste. Non-disposable PPE should be cleaned immediately after use.

For more information on waste disposal, see section 15.

11.5.7 Excreta and blood

In specific procedures where cavities/organs are locally treated with HMPs, the systemic uptake of HMPs in patients is lower than from oral and other parenteral procedures. This means that the presence of HMP in excreta (urine, faeces, vomit and sweat) and blood differs and that the risk period may be shorter. In the absence of the appropriate information, the times are applied that are common for the HMP in other administration forms.

11.5.8 Cleaning and laundry

Surfaces, bed linen, and clothing that have been in contact with HMP containing solution or excreta (urine, faeces, vomit and sweat) or blood should be considered as contaminated with HMP. These surfaces should be cleaned according to cleaning protocols, see section 14.1.

Non-disposable bed linen and other laundry that is used during the procedure should be treated as HMP-contaminated laundry, see section 14.2.

11.6 Administration – inhaled medications

Inhaled medication is administered through an inhaler, which the patient usually keeps throughout their treatment for use in hospital and/or at home. In a hospital setting, the inhaler may be supplied and disposed of after each treatment.

Metered-dose inhalers (MDIs), dry powder inhalers, nebulisers and soft mist inhalers are currently available for administration of different medicines. If the device produces mist (dry or aerosols) into the working environment, workers may be exposed to HMPs.

11.6.1 Management and organisation

Inhalation therapy of HMPs for lung treatment should be performed in designated areas.

Patients should self-administer as much as possible.

11.6.2 Technical measures

The release of direct or patient-exhaled mist or aerosols in the room where the administration is performed should be avoided. Devices that produce no mist or aerosols in the room should be preferred. If devices need to be used that produce aerosols, or if during administration the exhaled breath of the patients into the room may contain aerosols, a local exhaust tent should be used around the head of the patient to prevent spreading of the HMP in the room.

11.6.3 Organisational measures

Workers should avoid being present during the treatment. If no local exhaust ventilation is used, the room should be ventilated for at least half an hour for the concentration of HMPs to be reduced before entering without respiratory protection.

Administration should be performed by trained workers and supervised.

11.6.4 Personal protective equipment (PPE)

A risk assessment, see section 4 and Annex 4, should be performed to determine the PPE required for inhalation administration.

PPE should be worn during administration of HMPs and disposed of or cleaned immediately afterwards to avoid transfer of potential contamination.

The following PPE should be used as a minimum for inhalation treatment with mist/aerosols containing HMPs:

- Type B protective gloves
- Protective gown
- If indicated by a risk assessment, a FFP3 single-use face mask, see section 4

11.6.5 Operational procedures and hygiene measures

General operational and hygiene principles for administration of HMPs by inhaled medications should include:

- Place all equipment within easy reach
- Wash hands and put on protective gloves, gown and face mask
- Apply the HMP according to medical protocol
- Consider used single-use material as hazardous waste and dispose of accordingly
- Remove protective gown and face mask/goggles
- Remove protective gloves
- Dispose of PPE; consider used single-use PPE as hazardous waste
- Wash hands

11.6.6 Waste

Single-use equipment for inhalation treatment and single-use PPE should be disposed of as hazardous waste, in a closable hazardous waste container. Non-disposable equipment and PPE should be cleaned immediately after use.

For more information on waste disposal, see section 15.

11.6.7 Excreta and blood

In inhalation, the systemic uptake of HMPs in the patient is lower than from oral and other parenteral procedures. This means that the presence of HMP in excreta (urine, faeces, vomit and sweat) and blood differs and that the risk period may be shorter. In the absence of the appropriate information, the times are applied that are common for the HMP in other administration forms.

11.6.8 Cleaning and laundry

Surfaces, bed linen and clothing that have been in contact with aerosols or dust during the administration should be considered as contaminated with HMP. Surfaces and administration areas, such as patient rooms, sanitary facilities, and mattresses should be cleaned according to cleaning protocols, see section 14.1, or treated as HMP-contaminated laundry, see section 14.2.

11.7 Administration – topical

11.7.1 Management and organisation

Patients should self-administer HMPs as much as possible.

11.7.2 Technical measures

Single-use spatulas should be used, if possible.

11.7.3 Organisational measures

Administration should be performed by trained workers and supervised.

11.7.4 Personal protective equipment (PPE)

A risk assessment, see section 4 and Annex 4, should be performed to determine the PPE required for topical administration.

PPE should be worn during administration of HMPs and disposed of or cleaned immediately afterwards to avoid transfer of potential contamination.

The following PPE should be used as a minimum for topical treatment of HMPs:

- Type B protective gloves
- Protective gown

11.7.5 Operational procedures and hygiene measures

General operational and hygiene principles for topical administration of HMPs should include:

- Place all equipment within easy reach
- Wash hands and put on protective gloves and gown
- Put the patient in a suitable position and ask the patient to bare the skin to be treated
- Place a single-use pad under the parts of the body to be treated
- Apply the ointment thinly using a single-use spatula
- Cover the affected parts of the client's skin with a bandage
- Consider used single-use material as hazardous waste and dispose of accordingly
- Remove protective gown
- Remove protective gloves
- Dispose of PPE; consider single-use PPE as hazardous waste
- Wash hands

11.7.6 Waste

Packaging, spatula and PPE should be disposed of as hazardous waste, in a closable hazardous waste container.

For more information on waste disposal, see section 15.

11.7.7 Excreta and blood

In topical procedures with HMPs, the systemic uptake of HMPs in the patient is lower than from the oral and infusion and injection procedures. This means that the presence of HMP in excreta (urine, faeces, vomit and sweat) and blood differs and that the risk period may be shorter. In the absence of specific information, it should be assumed that the risk period is the same as for the same HMP in other administration forms.

11.7.8 Cleaning and laundry

Any surfaces, bed linen or clothing that have been in contact with HMP creams or lotions should be considered as contaminated with HMPs.

These surfaces should be cleaned according to cleaning protocols, see section 14.1. Non-disposable bed linen and other laundry should be treated as HMP-contaminated laundry, see section 14.2.

11.8 Administration – surgical procedures

This section applies to the following surgical procedures that involve HMPs:

- Intra-peritoneal administration (HIPEC (Hyperthermic IntraPEritoneal Chemotherapy) and PIPAC (Pressurized Intra-Peritoneal Aerosol Chemotherapy))
- Intra-pleural administration
- Regional perfusions

11.8.1 Management and organisation

A sign should be placed outside the operating room indicating that HMPs are used. In case of HIPEC or PIPAC, the sign should be placed before the start of the administration of the HMPs until the operating room is cleaned.

11.8.2 Technical measures

The following technical measures should be used:

- Floor protective sheets
- Buffalo filter system

- Patient's body covered with a sheet (for example for open HIPEC), similar to those used for a Caesarean section
- For PIPAC: A laminar airflow, controlled aerosol waste and protection curtain. A three way stopcock connected to the syringe and cap applied to balloon of the trocars. A protective sheet placed under the injector and next to the patient (Solaß, W. 2013, Willaert, W. 2017)[243].

11.8.3 Organisational measures

The number of workers in the surgery team should be as limited as possible. It is important to consider whether male or female workers who are trying to conceive or female workers that are pregnant or breastfeeding should participate in the operating procedure. This is particularly relevant to surgical procedures where there may be personnel present in the operating room that does not handle HMPs but can be exposed to them.

In the case of the PIPAC procedure, the patient is guarded from the outside of the operating room during the actual administration (no staff present during the administration procedure). When the surgeon has ended the administration and the pressure in the abdomen is deflated, the surgical team can enter the operating room to finish the procedure.

Administration should be performed by trained workers and supervised.

11.8.4 Personal protective equipment (PPE)

A risk assessment, see section 4 and Annex 4, should be performed to determine the PPE required for surgical procedures that involve HMPs.

The following PPE should be used as a minimum for surgical procedures that involve HMPs:

- Double long-sleeve surgical gloves
- Protective surgical masks with face shield/goggles
- Reinforced gowns/plastic gowns
- Shoe covers

11.8.5 Operational procedures and hygiene measures

The normal routine for surgical procedures should be followed but special attention should be given to prevent spillage and splashing of HMP containing fluid.

11.8.6 Waste

An HMP-waste bin should be present in the operating room. The HMP-containing perfusion liquids that are used in the procedure should be disposed of as hazardous liquid waste. Single-use sheets, covering material, PPE and surgical material should be disposed of as hazardous waste, in a closable hazardous waste container.

Non-disposable equipment and PPE should be cleaned immediately after use.

Surgical equipment should be cleaned according to protocol or disposed of as hazardous waste, in a closable hazardous waste container.

For more information on waste disposal, see section 15.

[243] Solaß, W, et al, (2013), Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC): Occupational Health and Safety Aspects, Annals of surgical Oncology 20, 3504-3511. Willaert, W. et al, (2017), Occupational safety of pressurized intraperitoneal aerosol chemothearpy (PIPAC), Pleura and Peritoneum (2017) 1-7.

11.8.7 Excreta and blood

In surgical procedures, the systemic uptake of HMPs in the patient is lower than from oral and injection administration. This means that the presence of HMP in excreta (urine, faeces, vomit and sweat) and blood lower and that the risk period may be shorter. In the absence of specific information, it should be assumed that the risk period is the same as for the same HMP in other administration forms. A high concentration of HMPs can be present in the fluids used in the procedures or in body fluids that have been in contact with the treatment fluid.

11.8.8 Cleaning and laundry

Surfaces, bed linen, and clothing that have been in contact with HMP containing solution or excreta (urine, faeces, vomit and sweat) or blood should be considered as contaminated with HMP. These surfaces should be cleaned according to cleaning protocols, see section 14.1.

Non-disposable bed linen and other laundry that is used during the procedure should be treated as HMP-contaminated laundry, see section 14.2. A separate washing protocol for surgical laundry may apply based on the specific needs for this type of laundry.

11.9 Administration at other healthcare facilities

This section focuses on administration of HMPs at healthcare and care facilities other than hospitals. A pharmacy is generally not physically attached to such patient care facilities.

Examples of the relevant facilities (non-hospital healthcare facilities) include:

- GP practices or local health centres
- Nursing homes

The practices and equipment at these facilities may differ to those at hospitals and, consequently, separate advice is provided for these facilities in this section of the guide.

11.9.1 Management and organisation

Developing and adhering to procedures for patient care, handling excreta, waste, cleaning, and laundry is the responsibility of the employer.

A risk assessment should be performed[244], see section 4. For further guidance on risk and exposure assessment for HMP administration, see section 11.1.2.

In healthcare and care settings outside of a hospital, effective coordination and cooperation between the different employers involved in HMP preparation, transport, administration, and patient care should be established. One organisation should be nominated as being responsible for overall coordination, for example the organisation responsible for the treatment of the patient.

For example, a pharmacy could be responsible for preparing, packaging, delivering (transport) of HMPs and the provision of information about the HMPs to the employer/department involved in the administration. This could include information about the risk period during which the HMP remains present in the excreta (urine, faeces, vomit and sweat) and blood (ideally obtained from the manufacturer), how to use the provided equipment in administration procedures, and how to handle patient-related incidents with HMPs (for instance extravasation).

Administration of HMPs and the associated patient care should only be performed by trained workers. The training is determined by the risk assessment, see section 4.

11.9.1.1 Centralisation

The administration of HMPs should be centralised in a dedicated area to the maximum degree possible to prevent unnecessary contamination and ensure that HMPs are handled by properly trained workers

[244] Directive 2004/37/EC, Article 3(2)

that have been informed about the relevant risks and protective measures. The facilities for administration should also be designed to enable safe handling of HMPs and effective and efficient cleaning. If centralisation is not possible, workers should have the necessary tools, equipment and furniture to ensure that the risk from occupational exposure to HMPs is eliminated or reduced to a minimum in a decentralised environment.

11.9.2 Organisational measures

Activities related to HMP administration should be supervised by a dedicated, trained, person, such as the head or manager of the non-hospital facility.

Only trained and competent workers should be involved in the administration of HMPs. Pharmacists' instructions should be followed, see section 10.

11.9.2.1 Communicate risks associated with patients

In case of outpatient treatment, it is important to share information about the entire period during which HMPs could be present in excreta with any employer responsible for care of the patient.[245] Sharing the same information with the patient can facilitate the awareness of other relevant employers, such as agencies supplying carers or domestic cleaners.

11.9.3 Excreta and blood

Excreta (urine, faeces, vomit and sweat) and blood should be treated as contaminated with HMPs during the time HMPs are being taken by the patient and generally up to 7-14 days after administration. As noted in section 8.6, it would be useful if information about the presence of HMPs in excreta and blood is supplied by the pharmaceutical company in the safety data sheet. An overview can also be found in peer-reviewed and published pharmaceutical guidelines[246].

For handling excreta with care, see section 11.1.8.

11.9.4 Personal protective equipment (PPE)

A risk assessment, see section 4, should be performed to determine the PPE required in the administration areas of HMPs and sanitary facilities. See also Annex 4 for advice on the appropriate PPE.

Surfaces and administration areas (bedroom), sanitary facilities, and mattresses should be cleaned using at least:

- Type B protective gloves
- Protective gown
- Protective face shield/goggles (in case of splashing)

11.9.5 Waste

Packages, drink containers (single-use containers used for the application of liquid HMPs), administration spatula/bags/syringes/infusion systems, single-use PPE and protective sheets that have been used during administration of HMPs or HMP contaminated excreta (urine, faeces, vomit and sweat) should be disposed of as hazardous waste, in a closable hazardous waste container.

For more information on waste disposal, see other parts of section 15.

11.9.6 Cleaning and laundry

Surfaces, bed linen and clothing that has been in contact with excreta (urine, faeces, vomit and sweat) and blood from the patient should be treated by workers as HMP contaminated. HMP laundry should be washed twice separately from other laundry; first cold pre-wash programme followed by normal warm programme, see section 14.2. Surfaces and equipment should be cleaned directly after administration using regular cleaning detergents. It is useful for cleaning to be recorded (for example, in an activity control log).

Cleaning agents should be selected based on compatibility, effectiveness and possible residues. Water and

[245] Whilst ensuring that rules on personal data protection are respected – see footnote 238 and Regulation (EU) 2016/679

[246] A regularly updated overview of the recommended duration of protective measures is provided, for example, in the full version of Quapos 6 (Quality Standard for the Oncology Pharmacy Service) Commentary Version. See https://esop.li/

cleaning agent should be used in combination with dedicated cloths.

For example, the following items may need regular cleaning in administration areas:

- Equipment, floor and surfaces
- Chair / bed / bedside table
- Carpet
- Door handles
- Phones, TV remote and keyboards
- Toilet / shower
- Equipment for handling excreta

11.10 Administration and care in care homes, hospices, and in homes

This section focuses on administration in two types of location:

- Care homes or hospices
- In patient's home

Patients who were receiving treatment in hospital or other medical facility prior to moving to a care home or hospice or returning to their home, may need to continue such treatment in the new care setting. HMPs could still be present in the excreta (urine, faeces, vomit and sweat) and blood and may need attention during patient care.

The responsibility for preparation, transport, administration of HMPs and patient care can be divided across several employers.

For administration, the same preventive measures should be taken as for healthcare facilities other than hospitals, see section 11.9.

11.10.1 Management and organisation

See section 11.9.1.

11.10.2 Communicate risks associated with patients

In case of outpatient treatment, it is important to share information about the entire period during which HMPs could be present in excreta (urine, faeces, vomit and sweat) and blood with any employer responsible for care of the patient.[247] Sharing the same information with the patient can facilitate the awareness of other relevant employers, such as agencies supplying carers or domestic cleaners.

11.10.3 Organisational measures

Developing and adhering to procedures for patient care, handling excreta, waste, cleaning, and laundry is the responsibility of the employer. Only procedures that provide safe administration of the HMPs for workers, patients, and carers should be used. A risk assessment, see section 4, should be performed to determine the PPE required. For guidance to perform a risk assessment and exposure assessment, see section 11.1.2.

The choice of products and devices used has an impact on reconstitution and administration practices. All professional groups involved in HMP preparation and familiar with home care administration should be consulted in the selection of devices used within the home care situation.

Preparation activities should typically take place in a pharmacy, except for HMPs that need to be prepared in the home of the patient. In such a case, it is useful that the pharmacy provides specific instructions for preparation, administration, and handling of waste.

Only trained workers should be involved in the preparation, administration, and waste handling of

[247] Whilst ensuring that rules on personal data protection are respected – see footnote 238 and Regulation (EU) 2016/679

HMPs, see section 6. Pharmacists' instructions should be followed, see section 10.

Workers should have sufficient and adequate training, necessary tools, PPE, and equipment.

Special attention should be paid to the transport and intermediate storage of HMPs. Where possible, HMPs should be stored in a designated, sealable cabinet at the patients' home, care home or hospice. It is important for workers, patients, and carers to be informed / instructed about the risks the HMPs might pose to workers.

11.10.4 Procedures and technical measures

The same preventive measures apply as those taken at healthcare facilities other than hospitals, see section 11.9.

Protect surfaces, carpets and furniture with protective sheets when required by the risk assessment, see section 4.

11.10.5 Personal protective equipment (PPE)

A risk assessment, see section 4, should be performed to determine the PPE required in the administration areas of HMPs and sanitary facilities. See also Annex 4 for advice on the appropriate PPE to use for cleaning.

Surfaces and administration areas (bedroom), sanitary facilities, and mattresses should be cleaned using at least:

- Type B protective gloves
- Protective gown
- Protective face shield/goggles (in case of splashing)

11.10.6 Waste

Packages, drink containers (single-use containers used for the application of liquid HMPs), administration spatula/bags/syringes/infusion systems, single-use PPE and protective sheets that have been used during administration of HMPs or HMP contaminated excreta (urine, faeces, vomit and sweat) should be disposed of as hazardous waste, in a closable hazardous waste container.

For administration at home, waste take-back schemes should be established to ensure a safe disposal of HMP-contaminated waste, see section 15.4.4. For more information on waste disposal, see other parts of section 15.

11.10.7 Cleaning and laundry

Surfaces, bed linen and clothing that have been in contact with excreta (urine, faeces, vomit and sweat) and blood from the patient should be treated by (home)care workers as HMP contaminated. HMP laundry should be washed twice separately from other laundry; first cold pre-wash programme followed by normal warm programme, see section 14.2. Cleaning protocols should be available for all care workers that enter the home, see section 14.1, for example, nurses, rehabilitation workers, cleaners. Surfaces and equipment should be cleaned directly after administration using regular cleaning detergents. It is useful for cleaning to be recorded (for example, in an activity control log).

Cleaning agents should be selected based on compatibility, effectiveness and possible residues. Water and cleaning agent should be used in combination with dedicated cloths.

For example, the following items may need regular cleaning in administration areas:

- Equipment, floor and surfaces
- Chair / bed / bedside table
- Carpet
- Door handles
- Phones, TV remote and keyboards
- Toilet / shower
- Equipment for handling excreta

11.11 Summary of advice in section 11

Management and organisation

- Administration should be centralised in a dedicated area to the maximum degree possible.
- Preparation activities should typically take place in a pharmacy.
- Only trained and competent workers should be involved in the administration of hazardous medicinal products (HMPs).
- The relevant activities should be supervised by a competent/trained dedicated person, such as the head or manager of the centralised administration unit or ward.
- The use of syringes with needles should be avoided as much as possible.
- If possible, patients should self-administer (oral, topical or inhalation).

Risk assessment for HMP administration

- The main exposure route for HMP in administration is dermal exposure.
- If good practice is used in infusion procedures, aerosols are only released by pressure build-up in the infusion line to the patient. If the infusion procedure is based on gravity, the infusion stops automatically.
- Withdrawing the needle from the container/bag or patient can result in a release of aerosols due to a pressure drop or incident when the needle disconnects from the syringe during the procedure. The use of needle-free connections or Luer-lock helps avoid the pressure change.
- The previous bullet points focus on the infusion procedure, which is a common method of HMP administration. For information on other administration procedures (oral, topical, etc.) please refer to 11.2 and 11.4 to 11.8.

Technical measures

- Choice of technical measures should be based on the HMP, dosage, volume and frequency of the HMP administered.
- The use of closed system transfer devices (CSTDs) is the decision of the management/staff in accordance with the risk assessment and the relevant national legislation.
- The use of all technical measures should be validated and periodically re-evaluated.

Organisational measures

- Work should be organised in advance.
- Facility layout should allow for effective cleaning.
- Standard Operating Procedures (SOPs) should be in place for e.g. for patient care, handling excreta, waste, cleaning, and laundry.

Personal protective equipment (PPE)

- PPE should be used for administration based on risk assessment and in line with the advice in sections 11.2 to 11.10.
- Protective gloves should be used for removing other personal protective equipment (PPE).

Hygiene measures

- Examples of hygiene measures include no food, drink, cigarettes/vaporisers, jewellery, medication for personal use, or chewing gum in the administration area.

Excreta and blood

- Due to risk of HMPs being present in excreta and blood, ensuring that patients that have undergone treatment with HMPs are easily identifiable can be very helpful. However, any such identification needs to be in conformity with applicable data protection rules. Excreta and blood is contaminated generally up to 7-14 days after administration.
- In case of outpatient treatment, information about the entire period during which HMPs could be present in excreta and blood should be shared with any employer responsible for care of the patient, whilst ensuring that rules on personal data protection are respected.

Waste

- All materials that have been in contact with HMPs should be disposed of as hazardous waste. Non-disposable equipment and PPE should be cleaned immediately after use.

For an example of a summary of advice on controlling exposure to HMPs for oral and intravenous (IV) administration of HMPs, see Annex 7.