GUIDELINES FOR ACTION ON THE RISK OF EXPOSURE TO HAZARDOUS DRUGS FOR HEALTH SERVICE WORKERS IN CASTILE-LA MANCHA (SESCAM).

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Castilla-La Mancha

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CONTENTS

Guidelines for action on the risk of exposure to hazardous drugs for health service workers in castile-la mancha (sescam).

1. FOREWORD

This Guidance is based on current scientific knowledge and, due to the important advances in this field, this Guidance will be a living document subject to regular updating.

1.1. RATIONALE AND BACKGROUND

HAZARDOUS DRUGS (hereinafter HD) are those that present one or more of the following six characteristics in humans or animals:

1. Carcinogenicity.
2. Teratogenicity or other developmental toxicity.
3. Reproductive toxicity.
4. Evidence of severe organ toxicity or other low-dose toxicity in animal specimens or in treated patients.
5. Genotoxicity.
6. Structure and toxicity profiles of new drugs that have been determined to be dangerous according to the above criteria.

NIOSH (National Institute for Occupational Safety and Health) classifies HD into:

• **Group 1:** antineoplastic drugs.

• **Group 2:** non-antineoplastic drugs that meet at least one of the above criteria.

• **Group 3:** drugs which present a risk to the reproductive process and which may affect men and women who are actively trying to conceive, and women who are pregnant or breastfeeding, but which do not pose a risk to other staff. The most likely avenues of exposure are inhalation and contact/absorption through the skin, although accidental ingestion by hand-to-mouth contact and accidental injection through needle pricks or sharps injuries are also possible.

Occupational exposures to HD can cause:

1) Acute effects such as skin rashes.

2) Chronic effects such as adverse reproductive events and

3) Abnormalities in chromosomes 5 and 7 and possibly cancer.

Against this backdrop, the main scientific societies involved prepared a Consensus Document in January 2015, in which the situation was analysed and a series of recommendations were proposed, such as the need to review and analyse the critical points for the prevention of exposure to HD among healthcare professionals in the preparation, transport and administration phases. In September 2016, the National Institute for Occupational Health and Safety (INSHT) published the Technical Document: Hazardous drugs. Prevention Measures for their preparation and administration. At SESCAM, we, as an organisation, must protect the health of workers by reducing their exposure to HD to the lowest level that is reasonably possible.

1.2. APPLICABLE LEGISLATION

Prevention of Occupational Risks:

• European Directive 2004/37/EC of the European Parliament and of the Council.

• Law 31/1995, dated 8 November, on Prevention of Occupational Risks.

• Royal Decree 39/1997, dated 17 January, approving the Regulations on prevention services.

• Royal Decree 485/1997, dated 14 April, regarding minimum provisions on health and safety signs in the workplace.

• Royal Decree 486/1997, dated 14 April, establishing the minimum health and safety requirements in the workplace.

• Royal Decree 665/1997, dated 12 May, regarding the protection of workers against risks related to carcinogenic agents at work.

• Royal Decree 773/1997, dated 30 May, regarding the minimum health and safety requirements relating to the use by workers of personal protective equipment.

• Royal Decree 1215/1997, dated 18 July, establishing the minimum health and safety requirements for the use of work equipment by workers.

• Royal Decree 374/2001, dated 6 April, regarding the protection of the health and safety of workers against risks related to chemical agents at work. Modified by RD 598/2015 dated 3 July.

• Order ESS/1451/2013, dated 29 July, establishing provisions for the prevention of injuries caused by sharp instruments in the health sector.

• CE marking in accordance with Royal Decree 1407/1992. Replaced by Regulation (EU) 2016/425 of the European Parliament and of the Council, dated 9 March 2016, regarding personal protective equipment and replacing Council Directive 89/686/EEC (OJEU No L 81 dated 31/03/2016). Applicable as from 21 April 2018.

Drugs and Health Products:

• Commission Directive 2003/94/EC, dated 8 October. This establishes principles and guidelines for good manufacturing practice for medicinal products for human use and research medicinal products for human use.

• Directives 2004/27/EC of the European Parliament and of the Council, dated 31 March 2004, amending Directive 2001/83/EC, laying down a Community code for medicinal products for human use.

• Royal Decree 175/2001, dated 23 February, approving the standards for the correct preparation and quality control of master formulas and official preparations.

• Royal Legislative Decree 1/2015, dated 24 July, approving the revised text of the Law on Guarantees and Rational Use of Medicines and Health Products.

• Royal Decree 618/2007, dated 11 May, regulating the procedure for the establishment, by visa, of exceptional reserves for the conditions for prescribing and dispensing medicines.

• Royal Decree 1345/2007, dated 11 October, regulating the procedure for the authorisation, recording and dispensing conditions of industrially manufactured medicines for human use.

• Royal Decree 1591/2009, dated 16 October, regulating health products.

• Royal Decree 577/2013, dated 26 July, regulating the pharmacovigilance of drugs for human use.

Environment:

• Royal Decree 833/1988, dated 20 July, approving the Regulations for the implementation of Law 20/1986, on basic toxic and hazardous waste.

• Royal Decree 363/1995, dated 10 March, approving the Regulation on the classification, packaging and labelling of hazardous substances.

• Regulation (EC) No 1907/2006 of the European Parliament and of the Council (REACH Regulation).

• Regulation (EC) No 1272/2008 of the European Parliament and of the Council, dated 16 December 2008, on the classification, labelling and packaging of substances and mixtures, amending and replacing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

• Law 11/1997, dated 24 April, on packaging and packaging waste.

• Order MAM/304/2002, dated 8 February, publishing waste recovery and disposal operations and the European waste list.

• Royal Decree 255/2003, dated 28 February, approving the Regulation on the classification, packaging and labelling of hazardous preparations.

• Law 22/2011, dated 28 July, on contaminated soil and waste.

Installations:

• Royal Decree 842/2002, dated 2 August, approving the Low Voltage Electro-technical Regulations and Supplementary Technical Instructions ITC BT 01 to ITC BT 51.

• Royal Decree 865/2003, dated 4 July, establishing the hygiene-sanitary criteria for the prevention and control of legionellosis.

• Royal Decree 314/2006, dated 17 March, approving the Technical Building Code.

• Royal Decree 1027/2007, dated 20 July, approving the Regulation on Thermal Installations in Buildings.

• Royal Decree 2060/2008, dated 12 December, approving the Pressure Equipment Regulation and its supplementary technical instructions.

• UNE 100713. Air conditioning installations in hospitals.

• UNE 171340. Validation and qualification of atmosphere controlled rooms in hospitals.

2. DEFINITIONS, OBJECTIVE AND SCOPE

2.1. DEFINITIONS

Accident at work (Article 156, Royal Legislative Decree 8/2015, dated 30 October, approving the revised text of the General Law on Social Security): any bodily injury suffered by the worker due to or as a consequence of work as an employee.

Accidents at work shall be deemed to be:

a) Those suffered by the worker when going to or returning from the workplace.

b) Those suffered by the worker due to or as a consequence of holding elective positions of a trade union nature, as well as those occurring on leaving or returning from the place where the duties associated with these positions are exercised.

c) Those that occur due to or as a consequence of the tasks that, although different from those of their professional group, the worker performs in compliance with the orders of the employer or spontaneously in the interest of the efficient running of the company.

d) Those occurring in salvage operations and others of a similar nature, when they are connected to work.
e) Illnesses contracted by workers in connection with the performance of their work, provided that it is proven that the illness was exclusively caused by the performance of the same.

f) Illnesses or abnormalities previously suffered by the worker which are aggravated as a consequence of the injury that constituted the accident.

g) Consequences of the accident that are altered in nature, duration, severity or termination, by intercurrent diseases, that constitute complications derived from the pathological process determined by the accident itself or have their origin in diseases acquired in the new environment in which the patient has been placed for healing.

Chemical Agent (Royal Decree 374/2001, regarding the protection of the health and safety of workers against risks related to chemical agents at work): any chemical element or compound, on its own or mixed, as it occurs in its natural state or is produced, used or dumped, including dumping as waste, in a work activity, whether or not it has been produced intentionally and whether or not it has been marketed.

Hazardous chemical agent: chemical agent which may represent a risk to the health and safety of workers because of its physico-chemical, chemical or toxicological properties and the way in which it is used or present in the workplace. Included in this definition, in particular are:

a) Chemical agents meeting the criteria for classification as hazardous substances or preparations laid down respectively in the regulations on notification of new substances and classification, packaging and labelling of hazardous substances and in the regulations on classification, packaging and labelling of hazardous preparations, whether or not the agent is classified under those regulations, with the exception of agents which only meet the requirements for classification as hazardous to the environment.

b) Chemical agents that have an Environmental Limit Value among those indicated in section 4 of article 3 of Royal Decree 374/2001, on the protection of the health and safety of workers against risks related to chemical agents during work.

Administration of emergency doses: administration of a dose that cannot be delayed due to a risk to the patient's health, with this definition being based on the need for an immediate effect and taking into account the stability of the drug.

Work suitability: issuing a medical judgement of the suitability of a person's health conditions with regard to the characteristics of a given job. This judgement must be based on the non-existence of psychophysical deficiencies that prevent the normal performance of the work and on the identification of individual characteristics that pose a risk to the individual or to third parties. These values must be taken into account when determining whether the post has adequate working conditions.

Carcinogens: substances and preparations that may cause cancer or increase its incidence.

Cytostatic: pharmaceuticals that inhibit cell multiplication or development. Any substance capable of inhibiting or impeding the evolution of neoplasia, restricting the maturation and proliferation of malignant cells, acting on specific

phases of the cell cycle and therefore active on cells that are in the process of division. This mechanism makes them, in turn, carcinogenic, mutagenic and/or teratogenic.

Cytotoxic: the property that a chemical possesses that produces a toxic effect on the cell.

ONB device: the American FDA (Food and Drugs Administration) established the classification of ONB devices, assigned to those devices it considers closed systems for administering medication. This ONB classification can be obtained for the preparation or administration of medication. Hence, a device can be considered closed for preparing medication but not for its administration and vice versa. The studies requested by the FDA to classify a device as ONB vary from case to case, but all of them seek to demonstrate that the device meets 3 characteristics: does not allow the exit or entry of vapours, does not allow the exit or entry of sprays and prevents the possibility of dripping or leakage of drugs. If these 3 characteristics are met, the NIOSH definition of a closed drug transfer system is met.

Occupational disease: that which is contracted as a result of work performed as an employee in the activities specified in the table approved by the provisions implementing and applying the General Law on Social Security, and which is caused by the action of the elements or substances indicated in that table for each occupational disease. These provisions shall determine the procedure to be followed for the inclusion in the table of new occupational diseases which it is considered should be incorporated into the table. This procedure shall include, in all cases, as a mandatory formality, the Health, Social Services and Equality Report. (Article 157, Royal Legislative Decree 8/2015, dated 30 October, approving the revised text of the General Law on Social Security).

Pack or unit dose: is that which contains a dosage in a way in which the following requirements are met:

1. Identification of the content: trade name, active substance and dose, mandatory notifiable excipients, pharmaceutical form, lot and expiry date.

2. Isolation from possible sources of deterioration and degradation.

3. Fast, easy and safe use through the dispensing units.

Personal protective equipment: any equipment intended to be carried or held by the worker to protect him or her from one or more risks likely to threaten his or her safety or health, and any attachment or accessory intended for that purpose. Personal protective equipment includes: gloves, gowns, protective breathing equipment, eye protection equipment, etc. (RD 773/1997 on minimum health and safety requirements for the use of personal protective equipment by workers).

Exposure to a chemical agent: the presence of a chemical agent in the workplace that involves contact between the chemical agent and the worker, usually by inhalation or through the skin (RD 374/2001, on the protection of the health and safety of workers against risks related to chemical agents at work). It is defined as the presence of a chemical agent in the air within the worker's breathing zone. It is quantified in terms of the concentration of the agent obtained from exposure measurements, based on the same reference period as that used for the applicable limit value. Two types of exposure can be defined:

- **Short-term exposure:** is the average concentration of the chemical agent in the worker's breathing zone, measured or calculated for any 15-minute period throughout the working day, except for those chemicals for which a lower reference period is specified in the Limit Values list.

- **Daily exposure:** is the average concentration of the chemical agent in the worker's breathing zone, measured or calculated on a time-weighted basis, for the actual working day and referenced to a standard eight-hour working day.

Exposure: when this term is used without qualifiers, it always refers to the respiratory route, i.e. exposure by inhalation.

Handling of HD: any operation carried out with the aim of adapting a hazardous drug to the specific needs of a patient as well as its administration, use and transport. For example, personalising doses or reconstituting a drug so that it is ready for administration.

Cytotoxic drug: a drug that interferes with the growth and proliferation of cells or with DNA synthesis. Most of them bind directly to genetic material in the nucleus of cells, or affect the synthesis of cellular proteins. Cytotoxic drugs are chemotherapy drugs, antineoplastic drugs, some antivirals, antibiotics and biotechnology drugs. In some cases, the non-selective actions of these drugs disrupt the growth and function of both healthy and diseased cells, resulting in toxic side effects in the patients under treatment.

Hazardous drug (HD): any drug identified on the basis of one or more of the following characteristics: carcinogens, genotoxic, immunogens, teratogens, low-dose toxicants in animal models or treated patients. Hazardous drugs are also new drugs that mimic the existing hazardous drugs in their structure or toxicity. Antineoplastic and cytotoxic

agents, some hormonal agents, immunosuppressants, antiviral drugs and some monoclonal antibodies are considered to be hazardous drugs.

Until reference regulations are published at a national level, the principle of prevention will be adopted, considering as hazardous drugs all those that are included in the INSHT reference document (Available at http://www.insht.es/InshtWeb/Contenidos/Documentacion/FICHAS%20DE%20PUBLICACIONES/EN%20CATALOGO/Higiene/2016%20medicamentos%20peligrosos/Medicamentos%20peligrosos.pdf), and those not included in it but which are on the NIOSH list: List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings. (Available at https://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf).

Consultations regarding medications can be made through the Spanish Agency of Medicines and Medical Devices (AEMPS) at the following website: https://www.aemps.gob.es/cima/fichasTecnicas.do?metodo=detalleForm And also atINFOMEP:http://www.insht.es/portal/site/Insht/menuitem.1f1a3bc79ab34c578c2e8884060961ca/?vgnextoid=fb69bf9db7c13610VgnVCM1000008130110aRCRD&vgnextchannel=9f164a7f8a651110VgnVCM100000dc0ca8c0RCRD

Chemotherapy drugs: include all types of drugs that are used to destroy, inactivate microorganisms (bacteria, viruses, fungi) and cancer cells. Today, chemotherapy is the name given to the treatment with drugs for treating cancer. Chemotherapy is a generic expression that embraces many drugs that exhibit cancer cell destruction activity but also have other side effects of a wide variety and intensity.

Toxic medication: those that possess any of these characteristics: carcinogenicity, teratogenicity or other developmental toxicity, reproductive toxicity, low-dose organ toxicity, genotoxicity, toxicity structure and profiles of new drugs that mimic drugs classified as toxic according to the above criteria. ASHP [1990].

Genotoxic: a substance capable of interacting with genetic material (DNA), causing its modification and causing mutations or cancer.

Mutagens: substances and preparations that may cause hereditary genetic effects or increase their incidence.

Hazard due to chemical agent: the intrinsic ability of a chemical agent to cause harm (RD 374/2001, regarding the protection of the health and safety of workers against risks related to chemical agents at work).

Authorised personnel: a worker who has been authorised by the employer to carry out certain tasks on the basis of his or her ability to do them correctly, in accordance with the procedures set out in this guidance.

Reprotoxic drugs: substances and preparations that may produce negative effects on progeny, or increase their frequency, or affect male or female reproductive ability.

Chemical risk: the possibility of a worker suffering specific harm as a result of exposure to chemical agents. In order to evaluate a risk from the point of view of its severity, the probability of the damage occurring and the severity of the damage will be assessed together. (RD 374/2001, regarding the protection of the health and safety of workers against risks related to chemical agents at work).

Reproductive Risk/Fertile age:

Reproductive risk: (NTP 612: Protection and promotion of reproductive health, INSHT). The population susceptible to reproductive alterations will be identified as that made up of company workers exposed to the risk factors.

The recommendations for the handling of List 3 drugs are for personnel who are at reproductive risk (persons engaged in procreative activity, women who are pregnant or breastfeeding), not for personnel of fertile age (two different concepts: see definition). Response of the National Centre for Working Conditions-OT 279.17. Reference: 2225.15. Date 19/12/17.

Fertile Age: according to WHO, the average fertile age for women is 15 to 44 years of age, and for men it is 14 to 60 years of age.

Closed system: NIOSH (National Institute for Occupational Safety and Health, United States) gave the name CSTD (Closed System drug Transfer Devices) to the devices for the transfer of cytostatic drugs and, in general, for active substances of high potency or toxicity. They are defined as equipment that mechanically prevents the entry of contaminants into the system and the escape of dangerous active ingredients out of the same system.

Highly sensitive workers: those workers who, due to their personal characteristics or known biological condition, including those with a recognised mental, physical or sensory disability, are particularly sensitive to the risks arising from the work. These aspects will be taken into account in the risk assessment and the necessary preventive and protective measures will be adopted, as well as a possible change of post, when such adaptation is not possible (Art. 25 LPRL).

2.2. PURPOSE

To produce Guidelines for Action on the Risk of Exposure to HD for Health Service workers in Castile-La Mancha (SESCAM), including Safe Work Procedures and Preventive Measures; Personal and Collective Protective Equipment to be used; as well as Information and Training for workers on the risk arising from the handling of HD in the different Areas of activity throughout their life cycle.

2.3. SCOPE OF APPLICATION

This Guide applies to all personnel who may be exposed to HD in healthcare centres: from the reception and transport of the HD, through its preparation and administration in the centre or at home, the treatment of the excreta of treated patients, to its disposal as waste.

3. RISK FACTORS AND PERSONNEL EXPOSED TO HD.

3.1. RISK FACTORS

In general, the risks associated with the handling and use of HD are as follows:

USE STAGE	RISK
Reception and Storage	• Risk of exposure to chemical agents. • Liquid splashes/sprays.
Preparation	• Risk of exposure to chemical agents. • Liquid splashes/sprays. • Cuts. • Pricks. • Inhalation of aerosols
Transport	• Risk of exposure to chemical agents. • Liquid splashes/sprays.
Administration	• Risk of exposure to chemical agents. • Liquid splashes/sprays. • Cuts. • Pricks.
Segregation/removal of residues	• Risk of exposure to chemical agents. •Liquid splashes/sprays. • Cuts. • Pricks.
Removal of excreta from patients being treated with HD	• Risk of exposure to chemical agents. •Liquid splashes/sprays. • Inhalation of aerosols.
Cleaning of spills	• Risk of exposure to chemical agents. •Liquid splashes/sprays. • Inhalation of aerosols.
Cleaning and maintenance of installations and BSC	• Risk of exposure to chemical agents. •Liquid splashes/sprays. • Inhalation of aerosols.
Any other operation involving potential risk	• Risk of exposure to chemical agents. • Liquid splashes/sprays.

Risk factors.

3.2. PERSONNEL EXPOSED TO HD

The personnel exposed to HD are considered to be those health or non-health workers belonging to SESCAM who, during their work, may intervene in any of the phases or stages described in the previous section, in particular:

- Orderlies.
- Nursing Assistants.
- Pharmacy Technicians.
- Nursing Staff.
- Doctors and Residents in Training.
- Cleaning and Maintenance Staff.
- Any personnel carrying out other operations involving potential contact.

4. PROCEDURE TO BE FOLLOWED IN RELATION TO HAZARDOUS DRUGS.

The selection of drugs by the Pharmacy and Therapeutics Commission and the Commission for the Rational Use of Medicines will be carried out, to the extent possible, in such a way as to minimise the risk of handling HD in the centres within its scope. In other words, priority will be given to selecting the alternatives that avoid/minimise the risk for the personnel who have to handle them in the Centres of their competence.

Each Department will identify the Medicines considered as hazardous that are used in their Centres. To this end, this may be based on the list presented as ANNEX 1 to this Guide, which is based on the document drawn up by the INSHT (Hazardous Drugs: Prevention measures for their preparation and administration. September 2016), this list will be updated according to the needs of each Centre. In any case, all workers must know and have access to the full list of HD, regardless of whether or not they are included in their Pharmacotherapy Guide.

The recommendations are defined below, separating the actions into two parts: the "Procedure within the Pharmacy Service" and the "Procedure in other Services", indicating the different preventive measures to be taken into account when working with HD. Those centres in which specific Procedures or Instructions are available and which deal with the different activities (reception and transport, preparation and administration, cleaning, waste management, spillages, maintenance), will take the measures indicated here as complementary to those established in their technical documents.

4.1. PHARMACY SERVICE PROCEDURE

4.1.1. Selection criteria for commercial presentations.

In the selection of commercial presentations of HD, among other criteria, those with content that best adapts to the usual dosage will be considered, with the aim of minimising handling, considering those presentations that do not require reconstitution, clearly identified so as not to make mistakes, packed in unbreakable containers that do not have to be divided for dosage and presented in individual doses to avoid repackaging.

4.1.2. Reception and storage.

• The reception and storage of HD in the Pharmacy Services shall be carried out in the general storage area of the Pharmacy, and whenever possible there shall be a specific storage place, separate from the rest of the drugs, properly indicated and of restricted access, in accordance with the specific procedures approved in each Centre, guaranteeing at all times the effective control of the quality of these products.

• The personnel responsible for reception and storage will have received the necessary training in safe handling practices for this type of HD.

• A list of HD and a spill kit will be available at the place of reception and storage, with instructions for use by responsible personnel in case of an incident.

• The following procedure shall be followed when unpacking the HD in the Pharmacy Service:

Recommended PPE for reception and storage: gloves and gown (see section 6.2.2). However, the specific risk assessment carried out in the Centre will determine the protective equipment according to the working conditions.

• Carry out a visual inspection of the packaging to rule out signs of breakage or poor condition.

• If any damaged packaging is identified, proceed to its assessment according to the Protocol established by the Centre.

• The transport of the HD to the final storage area should be carried out immediately after receipt, with the least possible delay, using extreme caution so as to minimise the risk of breakage.

• Clinical research samples containing HD shall be stored in a specific location designated for this purpose, suitably identified.

• Group 1 HD should not be available as inpatient unit stock and should be dispensed individually per patient. Ex-

ceptionally, and after a documented risk assessment, a dispensation for stock replenishment may be granted in those cases in which it is deemed appropriate.

• All storage areas shall be clearly identified with specific warnings, and shall be areas of infrequent movement of material and persons. HD spill kits must be available, with precise instructions for use in the event of incidents (See ANNEX 6: Spill Kit Contents).

• The definitive HD storage areas shall be arranged in such a way as to minimise the risk of falling or breakage, preferably with shelves with non-slip surfaces and ledges to avoid accidents. This also applies to HD that require special storage conditions with regard to temperature and light exposure.

• In the case of thermolabile HD, a specific refrigerator will ideally be available for the exclusive storage of this type of drug.

• HD liable to cause spillage should not be stored in automated systems.

• In the case of storage in the handling area for dosage in a sterile area, the exterior part of the unit formats must be previously decontaminated by cleaning with a disinfectant solution in order to ensure the integrity of the identification label.

4.1.3. Preparation and handling.

• The preparation is the process by which, based on the commercial presentation of the HD, the prescribed doses are pre-packaged for its administration to patients. It is the phase of greater relative risk if adequate prevention and protection measures are not adopted.

• To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service, thus reducing the number of workers exposed.

• **Preparations of Group 1 HD and Group 2 parenteral HD must be carried out in the Pharmacy Services.** Other HD should preferably be prepared in that Service during its opening hours.

• In those cases in which the preparation needs to be performed in the clinical units: **Non-parenteral Group 2 HD, parenteral Group 2 HD (exceptionally) and Group 3 HD** and after verifying that there is no other possibility, this preparation must be carried out under strict control of the working conditions (outside passageways, away from air currents, on an easy to clean table, etc.) and with the **PPE recommended in Annex 3; in the case of parenteral HD2 always add eye protection and respiratory protection.**

THE DEPARTMENT WILL ESTABLISH THE ORGANISATIONAL MEASURES AND ADEQUATE TRAINING FOR THE COMPLIANCE WITH THIS POINT.

• Medication preparation activities should be carried out by trained and qualified personnel.
• All preparation activities should be carried out following clear, written instructions and should be recorded.
• The preparation area of these HD must guarantee both the safety of the preparation for the patient and the safety of the worker who prepares it.

4.1.3.1. Working rules in the Preparation Area of sterile HD.

• The area for the preparation **of sterile HD** is divided into different zones.
-Antechamber for storage and pre-packaging of material.
-Airlock: connects the other two areas. This is where products and people are transferred. There are mechanisms that prevent the simultaneous opening of the two doors. If possible, the PPE should be put on and removed in this intermediate zone to avoid both contamination with suspended particles in the preparation room and chemical contamination of the antechamber.

-PPE recommended for the preparation of sterile HD: Gown, shoe protectors, FFP3 face mask, cap and double sanitary gloves.

-Sterile drug preparation area: This area will meet the specifications of a "clean room" controlled environment room. The Class II Biological Safety Cabinet (BSC) is located within this preparation area.

1. Antechamber and airlock.

Working rules:

- Aseptic washing of hands and forearms.
- Once equipped with the corresponding PPE, do not leave the antechamber.
- The products needed for each preparation will be prepared, checking possible defects such as expiration date, particles in suspension or changes in colour. Once checked, they will be decontaminated with 70º alcohol and placed on a tray that will be taken to the clean area.

2. Preparation area.

This is where the biological safety cabinet (BSC II) is located. It is classified as a clean area.

Working rules in the preparation area:

• The professional will always wash their hands before entering and after leaving the BSC.

• The professional will not wear jewellery, mobile devices, cosmetics and will not eat or drink in the place.

• Working rules in the Class II BSC are established in accordance with the Centre's Standard Operating Procedure (SOP) for handling cytostatic drugs, however, the following recommendations are generally established:

- Work with the front of the BSC down and avoid sudden movements inside the cabin that could cause turbulence in the laminar flow.
- While working, avoid any contact of gloves with areas susceptible to contamination, particularly the face.
- Check that the ultraviolet light is off before introducing any drug and before starting work.
- Place a sterile, impermeable and non-slip absorbent mat, absorbent side up, on the work surface (without covering the cabinet grille), which will be changed in the event of spillages and at the end of each work session.
- Always keep the ventilation grilles uncovered.

• Only the necessary material should be inside the BSC, distributed in such a way that it does not obstruct the airflow.

• Place a waste container in such a way that it does not obstruct the airflow.

• Check that the medication prepared is the correct one and that it corresponds to what is detailed on the work order and on the identification label.

• Handling shall be carried out at 5-10 cm and in the central area of the BSC, never in the area close to the edges.

• Material: Use syringes and equipment with Luer lock connection and closed biosafety systems for all preparations.

• Placement of the administration apparatus in intravenous infusions, as well as the removal of bubbles ("purging") must be performed before the drug is added to the intravenous solution.

• Specific recommendations on ergonomics (in particular regarding repetitive movements, forced postures, environmental comfort) will be made for working with in the BSC, depending on the structure and organisation of the Pharmacy Services.

• At the end of each day's work, clean the BSC according to the cleaning procedure, switch off the cabinet and close the front panel.

• In the event of a power cut, close the front panel immediately, communicate and document the incident.

• If there is accidental exposure or spillages in the BSC, act according to the corresponding procedure.

Working procedures according to presentations:

HD in vial:

The preparation from vials will be carried out with closed systems and in a Class II BSC.

Certain studies have shown that some HD can change to a gaseous form under normal working conditions. With regard to cytostatic drugs, most of them, with the exception of Carmustine, have extraordinarily low vapour pressures of less than 5 mPa. HEPA filters retain approximately 99.9% of particles greater than or equal to 0.3 microns in size providing ultra-clean air, however they are not effective in retaining volatile drugs or vapours. Filters with a pore diameter of 0.22 microns do not retain volatile drugs either. Therefore, the use of closed drug transfer systems during preparation is recommended to prevent the environmental transfer of contaminants (aerosols and vapours) both inside and outside the cabinet.

HD in ampoules:

The preparation from ampoules will be carried out in a Class II BSC following the technique below:

- The ampoules will be opened when there is no product left on the neck and head.

- They will be opened with sterile gauze impregnated with 70° alcohol to avoid possible injuries.

- It should be opened in the opposite direction to the operator, keeping the gauze between the hand and the ampoule.

- Use a 5 µm particle retention filter to load the contents into the syringe.

4.1.3.2 Working rules in the Preparation Area of non-sterile HD.

Circumstances may arise in health centres that require the handling or preparation of non-sterile HD:

• Reconstitution of extemporaneous oral suspensions of commercially available HD.

• Adjustment of doses (fractionation) or pulverisation of solid pharmaceutical products to facilitate administration.

• Preparation of non-sterile HD Master Formulas (MF).

• In the Pharmacy Services (PS) for the handling or preparation of non-sterile HD, at least one class I BSC will be required. This may be located in a separate area of the sterile drug preparation area, or in another area that is prepared for this purpose.

• Access to the non-sterile drug preparation area must be restricted to the personnel involved in the preparation and the standard operating procedures (SOPs) of each centre must be followed.

PPE recommended in the handling or preparation of non-sterile HD: for working in a Class I BSC use double gloves, gown and face mask. However, the specific risk assessment carried out in the Centre will determine the protective equipment according to the working conditions.

Preparation of unitary doses of oral suspensions of commercialised HD:

As a general rule, HD commercialised in liquid oral pharmaceutical form do not require a preparation process as such. Therefore, once dispensed from the PS, follow the recommendations established for their safe administration.

If the dispensation is carried out in unitary doses, they will be prepared in the Pharmacy Service in the Class I BSC and with at least double gloves, gown and face mask. The risk assessment will determine the additional protective equipment, depending on the working conditions and the types of preparations carried out.

If it is necessary to reconstitute solutions, suspensions and emulsions of commercialised HD, this shall always be done following the instructions provided in the technical specifications and information pamphlet and assigning the validity period indicated in the product information.

To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service, thus reducing the number of workers exposed.

When the drug must be prepared on the ward (stability, specific use, etc.), and after verifying that there is no other option, this preparation must be carried out under strict control of the working conditions (outside passageways, away from air currents, on an easy to clean table, etc.) and with the following PPE:

PPE recommended for the preparation of unitary doses of oral suspensions of commercialised HD: Group 2 HD and only for personnel with reproductive risk for Group 3 HD: double gloves, FFP3 face mask, gown and eye protection.

Fractionation or pulverisation of solid pharmaceutical products:

Fractionation or pulverisation of tablets is sometimes necessary to meet a given dosage or to facilitate administration of the drug. Alternatives to the HD should be sought in order to avoid such handling (change of medication, commercialised liquid pharmaceutical forms, adaptation of doses to commercial presentations, etc.). If this is not possible, as a general rule, the handling of group 1 and 2 HD will be carried out in the Pharmacy Service in the Class I BSC following the procedures established to guarantee the quality of the process and the protection of personnel.

In the case of Centres that do not have a Pharmacy Service (Public Health Residences, Primary Care, etc.), the preparation and handling of HD will be carried out in accordance with the technical and protection recommendations of the SPRL and the relevant technical instructions given by the Pharmacy Service, which must be accessible and easily located in any workplace.

Preparation of non-sterile HD Master Formulas.

The preparation of HD MF will be carried out in the PS in the non-sterile drug preparation area.

Oral solids (capsules, sachets, etc.), solutions, suspensions, emulsions, topical pharmaceutical forms (creams, gels, ointments, etc.), suppositories, etc. can be prepared in the PS. For the preparation of these MF it is possible to start from commercialised drugs or raw materials.

In order to classify a non-sterile MF as a HD, it is necessary to take into account not only the level of danger of the commercial medicine being used, but also the hazard classification of the raw materials (chemical products, not active ingredients) being used. The hazard classification of raw materials is given in the REACH (https://www.boe.es/doue/2006/396/L00001-00852.pdf) and CLP (https://www.boe.es/doue/2008/353/L00001-01355.pdf) regulations, and are reflected in the safety specifications of raw materials. If these regulations establish a hazard classification for any of these substances used as an active ingredient, that classification should be considered.

The preparation of non HD MF must be carried out in at least a Class I BSC, following the SOPs by pharmaceutical type and the safety and PPE recommendations established by the PRL Service once the risks in the preparations and materials used have been assessed.

The PS must specify the protection measures to be established in the standardised preparation procedures of each MF once the risks have been assessed by the PRL Service. This will allow all personnel who create the MF to have comprehensive information on the means of protection to be used during preparation. Also, once pre-packaged, the MF should be identified as HD with the labels or pictograms established by the centre.

4.1.4. Identification.

HD must be identified throughout the entire process of their use.

1. MODIFY THE DESCRIPTION OF THESE DRUGS IN THE COMPUTERISED MANAGEMENT SYSTEM.

The symbol "HD" shall be added to the description of these medicines in the Pharmacy Services management software. This will allow these drugs to be identified from the time the order is placed and the delivery note is printed, and the Pharmacy Service staff will then be aware upon receipt that the drug is hazardous and that appropriate measures must be taken.

2. MODIFY THE DESCRIPTION OF THESE DRUGS IN THE ELECTRONIC ADMINISTRATION AND COMPUTERISED PRESCRIPTION SYSTEM.

This will ensure that all healthcare workers are aware of the type of medicines they are using during prescription, pharmaceutical validation, preparation and administration. The list of HD and the recommendations to be implemented during preparation, handling and administration will be accessible to all healthcare personnel and will be available on the intranet so that staff can refer to it and be informed of the measures to be taken in each case.

3. PLACE IDENTIFICATION SYMBOL IN STORAGE AREAS

HD stored in the Pharmacy Service will be properly identified.

HD prepared in the Pharmacy Service must be identified with the acronym "HD". (see Annex 3, general recommendations for preparation according to the HD classification).

REPACKAGING .

This is the procedure by which a medicine is packed in unit doses to allow the dose prescribed by the doctor to be administered to the patient, providing an easy and complete identification, without the need for handling.

The repackaging should be performed for oral solid or liquid drugs, the dispensing of which requires presentation in unitary doses, as there is no single dose format available. As a general rule, it will be preferable to purchase HD that are already in single-dose format.

All personnel involved in the HD repackaging process should have the qualifications and experience necessary to perform the tasks involved in this area. It will be permanently supervised by a pharmacist.

The use of automatic repackaging systems that are not for the exclusive use of the handler and under environmental conditions of protection is not recommended, and the repackaging must always retain the original blister. Type I HD will not be automatically repackaged

The type of medication (HD1, HD2, HD3) shall be clearly identified on the repackaging.

Types of HD repackaging:

a) **Solid pharmaceutical products:**

a.1) **Re-labelling of industry blister packs.**
It is considered the method of choice for HD as it does not require handling by personnel.

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It consists of re-labelling the blister packs of medicines by placing printed stickers with the drug information and that allows the blister to be cut later, leaving each unit of medicine correctly identified for subsequent dispensing in single units. For this, the templates created for each medicine and self-adhesive paper will be used. Medicines that are packaged in blister packs and that comply with the following requirement will be repackaged in this manner: adequate size and distribution so that once the label has been applied they can be cut out while maintaining all the drug information on each unit.

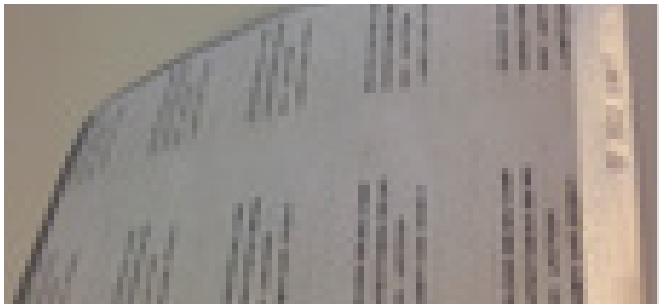

Figure 1.-Re-labelling of industry blister packs.

a.2) **Repackaged in blister packs.**

This method will be used for HD that cannot be relabelled, either because the distribution of each pharmaceutical form does not allow it or because they are packaged in industrial bottles.

The process consists of filling the blisters with the drugs and sealing them with self-adhesive stickers previously printed with the description of each drug.

The Pharmacy Service should limit the repackaging of these medicines only when strictly necessary, e.g. dispensation to hospitalised patients.

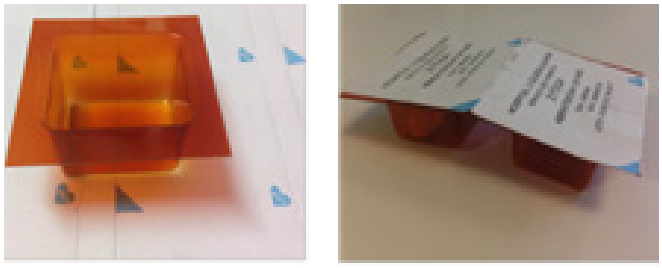

Figure 2.-Re-packaging in blister packs.

• HD packaged in industry blister packs: The blister shall be cut and each unit shall be placed in an appropriate sized blister. The appropriate label shall then be attached.

• HD packaged in a bottle: These drugs pose the greatest risk to staff as they require handling and contact. For this reason, it is essential to comply with the established protection and preventive measures.

PPE recommended for the repackaging of solid HD: this must be carried out following the recommendations of the Prevention of Occupational Risks Service with regard to the PPE that are necessary, in general: **a pair of gloves, gown and FFP3 respiratory protection mask must be used.**

a.3) **Repackaging in a repackaging machine.**

It is possible to carry out the repackaging of HD 2 and 3 using automatic systems:

• If the automatic systems are used exclusively for the repackaging of HD.

• Always maintaining the original blister of the medicine.

• Adequate protection of the operator following the recommendations of the Prevention of Occupational Risks Service.

• Do not use this repackaging method for oral cytostatic drugs.

• Have an action protocol in case of any alteration of the drug during the repackaging process (breakage or crushing of the drug).

b) **Liquid pharmaceutical types:**

Avoid the use of automatic repackaging systems for liquid HD.

PPE recommended for the **repackaging of liquid HD:** this must be carried out following the recommendations of the Prevention of Occupational Risks Service. With regard to the environmental conditions of the operator's protection, in general: **Double pair of gloves, gown, eye protection if a closed system is not used and respiratory protection if a closed system is not used.**

4.1.5 Transport and distribution.

Group **1 and 2 HD** must be transported in such a way as to prevent breakage or spillage. In addition, they must be correctly identified to facilitate their processing at the destination unit. For this reason, the following recommendations will be followed, differentiating fundamentally between the possibility or not of breaking them during this process.

Group 1 and 2 HD intended for the restocking of first-aid kits that are not likely to cause spillage should be packed in a bag, box, etc., separated from the rest of the medicines in the order and correctly identified as hazardous.

Group 1 and 2 HD that are packaged in pharmaceutical forms that can break during transport (vials, ampoules, parenteral administration bags, pre-filled syringes, etc.) should be in separate containers. These containers must meet the following requirements:

- Be used exclusively for transporting HD.
- Be of a specific colour and with a recognisable symbol.
- Be made from hard material, both robust and resistant to impacts and external pressure during transport.
- Be watertight to prevent spillage or breakage.
- Be closed during transport.
- Be opaque and easy to clean.

Group 1 and 2 HD intended for the restocking of first-aid kits that may cause spillage and individualised HD treatments of these groups should be packed in such a way as to minimise the risk of breakage. They shall also be in a perfectly identified bag which must be able to contain spillages from the primary container. This bag should be heat-sealed whenever possible.

The smaller the distance travelled by the preparations, the lower the risk of errors and incidents. For this reason, the transport of group 1 and group 2 HD susceptible to spillage will be carried out directly, without carrying out adjacent tasks or stopping at other services, and whenever possible, through an independent circuit.

For the transport of HD that may break or spill, transport methods that cause stress to the contents or packaging should not be used. Therefore, no pneumatic tubes or other mechanical systems should be used. These medicines should not be transported together with other materials or unrelated medicines.

The personnel responsible for transportation should know the procedure to be followed in the event of a spillage and the location of the nearest spill kit. (See ANNEX 6).

If any medicine is not administered, it will be returned to the Pharmacy by the same procedure and in the same packaging.

PPE recommended during transport: Use a single pair of gloves.

4.1.6. Cleaning and disinfection.

Cleaning and disinfection are basic preventive measures to avoid exposure and include several stages:

- **Deactivation:** transforms the HD into an inert or inactive compound.
- **Decontamination:** eliminates residues of HD from surfaces.
- **Cleaning:** remove contaminants from surfaces.

Any person in charge of cleaning the work area must be properly trained in the correct procedures to protect themselves and avoid contamination of the environment.

Each Centre will establish in its procedures the type and dilutions of the different cleaning products it considers most suitable, as well as the frequency of cleaning and disinfection of the work areas.

Disinfection will be carried out on previously clean and dry surfaces.

Products.

The selection of cleaning and disinfection products must be appropriate for the type(s) of contaminant(s), location and material of the surfaces to be cleaned. They must not alter the surface and walls of the cabinet, nor the floors and walls of the rooms. For cleaning equipment, follow the recommendations of the manufacturer.

There is no single accepted method for deactivating all HD. Cleaning systems using sodium hypochlorite, detergent and thiosulfate (chlorine neutraliser) have been shown to be effective in decontaminating and deactivating surfaces. New agents such as high-level disinfectants containing hydrogen peroxide and peracetic acid may provide an alternative to bleach in cleaning procedures involving HD.

On the other hand, products used for cleaning clean rooms should adhere to the following recommendations:

- Cleaning and disinfection agents should be free of viable microorganisms and those used in grade A and B rooms should be sterile and free of spores.

• Sporicidal products should be used periodically to reduce contamination of spore-forming microorganisms.

• Virus-specific cleaning agents should be used to decontaminate areas where blood or viral products are handled.

4.1.6.1. Cleaning of floors and surfaces.

Recommended PPE: double gloves, FFP3 face masks, gowns and shoe protectors are recommended for cleaning surfaces, materials, and packaging containing HD residues.

Wet cleaning of floors and walls. Floors must not be swept in order not to raise dust.

- Floor cleaning: with water and detergent with 0.1% sodium hypochlorite.

- Horizontal and vertical surfaces: spray with water and detergent with 0.1% sodium hypochlorite and use quaternary ammonium solutions on metal areas.

Cleaning materials will be for exclusive use.
The surfaces to be disinfected must be previously cleaned, and once cleaned they must be left to dry.

4.1.6.2. Cleaning the biological safety cabinet.

It will be carried out in accordance with the Centre's cleaning SOP, however, the following recommendations are generally established:

PPE recommended for cleaning the BSC: gown, two pairs of gloves, shoe protectors, cap, safety goggles or face shield and FFP3 respiratory protection mask.

During cleaning operations, the cabinet fan must be running and moving parts must be cleaned without removing them from the interior.

Clean the metal interior with soapy water, rinse with sterile water, and then pass a single-use sterile fabric dampened with 70º alcohol.

• Do not pour liquids directly on the surfaces, nor use spray cleaners; apply with damp cloths or gauze.

• Wipe following the direction of the air flow and from the areas of most to least contamination:

1. Roof grill.

2. Rear wall.

3. Side walls from top to bottom and accessories (gas or vacuum valves and bars/hooks if any).

4. Working surface from the back to the outside.

5. Front aspiration grid.

6. Display window.

• Do not get the HEPA filter wet while cleaning the cabinet.

• Do not use 70º alcohol to clean the front if it is made of methacrylate, as it becomes translucent; ideally use a chlorhexidine solution.

• Cleaning and disinfection should be carried out in the following situations:
- Before starting any work in the BSC.
- Once the work in the BSC has been completed.
- Before performing sterile preparations if BSC has been used for non-sterile HD preparations.
- In case of spills.
- Before and after carrying out a mechanical or biological control or revision in the cabinet.

• The external part of the cabinet must be cleaned to avoid any contamination.

All material used for cleaning must be treated as contaminated waste. Cleaning carried out in the BSC must be documented.

4.1.6.3. Periodicity

Minimum cleaning and disinfection frequency:

Daily

• BSC.
• Floors.
• Work surfaces (antechamber and clean room).
• Transportation containers.

Weekly

• Preparation area trays and trolleys.
• External parts of the BSC and area under the removable BSC work tray.
• Ventilation equipment.

Monthly

• Walls, ceilings, clean room vents and ante-chamber storage shelves.

4.1.7. Procedure for accidental exposure or spillage.

Any phase related to the handling of HD throughout the circuit (reception and storage, preparation, pre-packaging, dispensing, transport, administration and disposal) may lead to an accident resulting in accidental exposure that may pose a risk to both the handlers and the environment. Therefore, **all personnel involved in each of the phases of the circuit where these agents are handled must be** suitably trained in the procedures to be followed when necessary, as well as in the handling of the spill kits (see Annex 5).

4.1.7.1. Procedure for spillages.

In the event of a spillage, action by suitably trained personnel should be immediate to minimise potential harm to other personnel or the environment.

Spill kits should be available in all areas where HD are stored and used, and should be available in a visible and easily accessible location.

There should be a spill log in the Work Centre to centrally collect all accidental spillage episodes.

The resulting waste must be treated as HD waste, therefore the disposal of all material used will be in accordance with the Centre's HD waste disposal procedure.

The location of the spill will determine the appropriate procedure for its cleaning, therefore two distinct zones are distinguished depending on the location of the spillage (see ANNEX 5.A. Procedure to be followed in the event of spillage of HD inside a Biological Safety Cabinet and ANNEX 5. B. Procedure to be followed in the event of spillage of HD outside a Biological Safety Cabinet).

4.1.7.2. Procedure for accidental exposure.

Any professional who has suffered accidental exposure must go to the corresponding department's Prevention of Occupational Risks Service (SPRL) for assessment and monitoring, after completing and registering the report of the work incident/accident, except in cases of urgent assistance, when it will be filled in and subsequently registered by the Middle Management or Service Manager, as appropriate (see Memo 3/2011: Procedure for reporting work-related accidents and incidents).

In the case of non-hospital personnel, they must go to the Emergency Department and inform their SPRL so that they can be monitored (as per the provisions of the Procedure for Coordination of Business Activities in preventive matters).

Within the SPRL working hours:

He/she will be clinically evaluated by the SPRL Occupational Physician, and interviewed by the SPRL Technician to determine the causes of the accident.

Action will be taken in accordance with the "Protocol in case of cytostatic accidents and spillages" of each Centre.

Outside the SPRL working hours:

- He/she will go to the Emergency Room or the On-call Internist (according to the protocol of each Hospital) for clinical assessment.

- On the first working day, he/she must go to the SPRL and follow the controls prescribed.

Record of accidents and incidents with HD.

In the SPRL there must be a record of accidental exposures to HD. These records must be filed.

(For more information, refer to ANNEX 7: procedure to be followed in the event of accidental exposure to Hazardous Drugs).

4.2. PROCEDURE IN OTHER SERVICES

The HD handling procedure outside the Pharmacy must consider aspects concerning both the protection of the environment and the worker as well as patient safety. The administration of HD requires specially trained people due to the risks that the patient may suffer and the possibility of contamination of the handler and/or the environment.

It is important to reduce the number of people handling HD as much as possible through organisational measures and the use of preparations that require as little handling as possible.

The affected Services will be ALL those in which HD are handled. The following are mentioned as a reference:

• Hospitalisation Ward.
• Day Hospital.
• Outpatient Consultations.

• Primary Care Centres.
• Emergency Services.
• Interventional Radiology.
• Public Health Residences

4.2.1. Reception and storage.

The reception and storage of HD outside the Pharmacy Services shall be carried out in accordance with the specific procedures approved in each centre, guaranteeing at all times the effective control of the quality of these products. In particular, the following shall be considered:

• Insofar as possible, there will be a distinct place in the corresponding Service for this type of drug, which will be suitably identified as HD in order to avoid confusion and minimise the risk of accidental contamination.

• The definitive HD storage areas shall be arranged in such a way as to minimise the risk of falling or breaking, preferably with shelves with non-slip surfaces and ledges to avoid accidents. This also applies to HD that require special storage conditions with regard to temperature and light exposure.

• Access to HD storage areas in the different rooms or day units must be limited to authorised personnel (see definitions section).

• All these HD storage areas shall be clearly identified, and shall be areas of infrequent movement of material and persons. Spill kits must be available, with precise instructions for use in the event of accidents. (See Annex 6: Spill Kit Contents).

4.2.2 Preparation and handling.

To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service, thus reducing the number of workers exposed.

• In those cases in which the preparation needs to be performed in the clinical units: **Non-parenteral Group 2 HD, parenteral Group 2 HD (exceptionally) and Group 3 HD** and after verifying that there is no other possibility, this preparation must be carried out under strict control of the working conditions (outside passageways, away from air currents, on an easy to clean table, etc.) and with the **PPE recommended in Annex 3; in the case of parenteral HD2 always add eye protection and respiratory protection.**

THE DEPARTMENT WILL ESTABLISH THE ORGANISATIONAL MEASURES AND ADEQUATE TRAINING FOR THE COMPLIANCE WITH THIS POINT.

• Medication preparation activities should be carried out by trained and qualified personnel.
• All preparation activities should be carried out following clear, written instructions and should be recorded.

• The preparation area of these HD must guarantee both the safety of the preparation for the patient and the safety of the worker who prepares it.

4.2.2.1. Preparation/handling area:

HD preparation areas in the Clinical Units should be separated and identified. If possible, it should be a room exclusively for this activity.

They should be away from draughts and have doors and windows that close properly and away from the traffic of patients and relatives.

HD considered by the institution that may be in stock in the Hospitalisation Unit will be stored in this area.

4.2.2.2. Preparation/handling stage:

Before starting to prepare, check that all the necessary material is available.

The work surface should be covered with an absorbent, disposable waterproof mat with non-slip backing.

The order of action will be: hat, wash hands with germicidal soap or hydroalcoholic solution, dry hands, put on first pair of gloves (aseptic technique) under the cuffs of the gown, gown, respiratory protection mask, safety goggles, second pair of gloves over the cuffs of the gown. Once dressed, do not leave the preparation area.

Do not eat, drink or chew gum in this area.
Do not wear jewellery or make-up.

Avoid contact of hands with uncovered areas of skin during handling.

Syringes must have a Luer-lock.

Use needle-free systems or, if this is not possible, the needles should be of high calibre to minimise the formation of aerosols.
Use closed drug transfer systems whenever possible.

If the HD is in vials, the dose will be prepared with the available closed system.

1) Ampoules:

a. Ensure the absence of medication in the neck of the ampoule.

b. Surround the neck of the ampoule with a gauze impregnated in 70º alcohol, to reduce the risk of projections and cuts at the time of opening.

c. Open the ampoule in the opposite direction to the handler, so that any aerosols are not directed towards the handler.

d. Insert the needle with the bezel facing upwards, without touching the edges of the neck or the bottom, and extract the contents.

e. Adjust the volume of the syringe on gauzes soaked in 70º alcohol.

f. If the ampoule contains the solid drug, to reconstitute it, slide the solvent down the walls and, with gentle rotary movements, dissolve completely.

2) Oral solutions:

a. Commercial presentation in the form of a solution and with extraction device. Follow manufacturer's safety instructions.

b. Commercial presentation in the form of a solution and without an extraction device.

1. Attach a cannula of sufficient length and calibre to a Luer-lock syringe of the desired size.

2. With the bottle resting in a vertical position, insert the cannula connected to the syringe and fill with the necessary volume of the solution.

3. Extract cannula + syringe from the bottle.

c. Commercial presentation in powder for reconstitution.

1. Couple the dosage adapter to the mouth of the bottle (if the preparation has one) ensuring water tightness.

2. With the bottle resting in a vertical position, insert the syringe firmly into the dosage adapter.

3. Once the insertion has been secured, invert the bottle with the syringe and fill it with the necessary dose.

4. Return the bottle to its position and remove the syringe from the adapter.

3) Solid pharmaceutical products:

Avoid dose fractionation by adjusting the prescription dosage pattern where possible.

In the preparation of doses from oral solid forms such as tablets or capsules that require complex handling (crushing, opening of capsules, etc.) refer to the Pharmacy Service who will prepare them or indicate the possibility of using commercially available liquid forms, dispersible tablets or those formulated by their Pharmaceutical Department.

4.2.3. Administering HD to patients

HD should be administered by healthcare personnel who:

- Have proper training.
- Have sufficient experience in the handling of these medicines.
- Know the measures to be taken in the event of any spills, breakages or any other incident or accident.

The HD administration procedures must guarantee protection:

- Of the environment.
- Of the worker.
- Without altering the patient's safety.

MEANS OF ADMINISTRATION. GENERAL MEASURES FOR THE ADMINISTRATION OF HD.

Means of administration:

- Oral.
- Topical.
- Parenteral (subcutaneous, intramuscular, intravenous, etc.).

- Other methods (intrathecal, inhalation, intra-arterial and/or chemoembolisation, intracavitary).

General Measures.

The administration of **the HD** will be carried out following the recommendations of the technical specifications and always according to the protocols or guidelines of each centre:

• Wash hands before and after the procedure.

• Use of closed transfer systems for Group 1 and Group 2 drugs.

• Apply the maximum aseptic measures in the area where the handling is carried out to minimise contamination.

• Do not eat, drink or chew gum. Do not wear jewellery or make-up.
• After the administration of HD, discard all material used and waste generated in the appropriate container according to section 5.

• Have suitable furniture to place the drug before it is used. Use non-slip tables and surfaces with ledges to prepare the technique and armchair or bed to place the patient. All furniture shall be made of waterproof materials, easy to clean and shall be cleaned after use and whenever necessary.

• Have a Spill Kit and know the procedure to be followed in the event of a Spillage and the location of the Kit (see Annex 5 and 6).

• Use recommended PPE, according to the attached table.

4.2.3.1. ORAL ADMINISTRATION.

In the oral administration of HD, the choice of presentation will be made prioritising whole solid forms (tablets, pills and capsules) and liquid forms (syrups and drops). If an oral solid form requires fractionation or crushing, this should be done in the area adapted for this purpose.

- Adopt the general measures for all methods of administration of HD.

4.2.3.2. TOPICAL ADMINISTRATION OF HD.

Presentation in the form of creams, ointments, salves, balms, patches and other presentations.

Administration procedure:

In the topical administration of HD, the same general precautions shall be taken as for oral liquid pharmaceutical types.

• Use spatulas or other application aids that avoid contact with the product.

• Use mats that are absorbent on top and waterproof and non-slip beneath before administration. After application, cover the treated skin surface.

• Adopt the general measures for all methods of administration of HD.

4.2.3.3 PARENTERAL ADMINISTRATION OF HD (SUBCUTANEOUS (SC), INTRAMUSCULAR (IM), INTRAVENOUS (IV).

Administration procedure:

• Use intact pharmaceutical types, in single-dose vials with biosafety system. If not, pre-loaded presentations and purged with closed transfer systems will be required.

PERSONAL PROTECTIVE EQUIPMENT					
Pharmaceutical type	**Single glove**	**Double glove or specific for Group 1 HD**	**Eye protection**	**Respiratory protection FFP3**	**Waterproof protective gown**
Intact capsule/tablet	Yes	No	No[2]	No	No
Fractioned capsule/tablet	Yes	No[1]	No[2]	Yes	No
Oral solution/suspension	Yes	No[1]	No[2]	No[3]	No[2]
Local Methods	---	Yes	No[2]	No[3]	Yes
Parenteral forms (SC, IV, IM)	---	Yes	Yes	Yes	Yes
Solution for irrigation	---	Yes	Yes	Yes	Yes
Powder/Suspension for inhalation	--	Yes	No[2]	Yes	No[2]

1 Double glove or specific glove for Group 1 HD for frequent handling. **2** Required if there is risk of splattering. **3** Required if there is risk of inhalation.

• If purging is required, use sterile gauze soaked in 70º alcohol to prevent the formation of aerosols and surface contamination.

• To avoid contaminating bedding or armchairs when administering the drug, use a mat that is absorbent on top and waterproof and non-slip underneath.

• During parenteral administration, the needle or catheter should never be disconnected from the syringe; Luer lock connections should be used to prevent accidental disconnection.

• Parenteral HD will be prepared with a closed system in a syringe attached to the needle intended for this purpose in order to avoid handling during administration and not generate spills, aerosols or accidental punctures.

• Whenever possible, parenteral administration of HD should be performed in large, well ventilated spaces to minimise the concentration of aerosols and vaporisation.

• Take general measures for all methods of administration of **HD.**

INTRAVENOUS (IV) ADMINISTRATION

To minimise the risk of spills and any other incident or accident (punctures, breakage of bags, leaks, etc.) that may lead to inhalation, ingestion and/or splashing, the following must be used:

Material resources:

• Volumetric infusion pumps.

• Infusion equipment.

• Closed devices or closed perfusion systems.

• Spill kit (see Annex 6).

• Suitable and safe furniture.

Volumetric infusion pumps:

They allow treatments to be administered at the desired speed and with an alarm system that allows faults to be detected during infusion.

Infusion equipment:

These are known as drip equipment. They consist of:

• A piercing tool.

• Drip chamber.

• Tubing.

• Device that is inserted into the volumetric pump.

• Distal end with Luer lock connection.

There are many types on the market as they adapt to the characteristics of the volumetric pumps and to the needs of both the drug (low absorption equipment) and the patient (equipment with one or more access ports in its socket).

These infusion or drip devices are coupled to the closed drug administration systems.

Closed devices or perfusion systems:

NIOSH (National Institute for Occupational health and safety, United States) gave the name CSTD (Closed System drug Transfer Devices) to the devices for the transfer of cytostatic drugs and, in general, for active substances of high potency or toxicity. They are defined as equipment that mechanically prevents the entry of contaminants into the system and the escape of dangerous active ingredients out of the same system.

There are different types of closed systems for the administration of HD, which can be coupled to infusion pumps as required. These closed administration systems should as a minimum:

• Be free of latex, DEHP and other materials that may release particles in contact with this type of drug.

• Minimise the number of connection/disconnection manoeuvres.

• Have needle-free connection ports.

• Reduce the risk of leakage, spillage and aerosols by means of anti-reflux valves.

• Be a single-piece or compact system that reduces the number of products needed for its operation.

• There are closed systems **of continuous perfusion** with multiconnection made of a flexible and plastic material in **a single piece** and intermittent perfusion systems (bioconnectors), which are made of rigid plastic material in a single piece, provided with a female Luer lock connection compatible with syringe or standard perfusion system. The distal connection must be a male Luer lock type, adaptable to conventional needles, catheters and three-step valves.

Administration procedure:

Two techniques may be used; **continuous perfusion or bolus injection:**

- When the drug is administered using a bolus injection, it will be prepared in a syringe suitable for direct application, which requires the use of a closed system, specially designed for the administration of HD to avoid dripping, the creation of aerosols and accidental disconnection. At no time during administration should this system be disconnected from the syringe.
The administration will be made through a bioconnector, provided with safety valves closed both mechanically and microbiologically in such a way that the HD is administered by one stream, and by the other, clean serum to purge and wash the catheter. Once the infusion has been completed, the surface of the valve through which the HD has been infused is cleaned with the appropriate antiseptic to eliminate any residue that may remain, no matter how minimal it may be.

- For continuous **perfusion** of **HD,** closed perfusion systems are used, which guarantee the safety of both the worker and the patient.

The drug will reach the Service where it will be administered connected to an extension tube that has been previously purged in HPS with clean serum or with another innocuous solution, to avoid spilling the **HD** during transport or connection to the administration system. When it is time to administer the HD, the free end of the extension tube will be inserted into the needle-free access port of the closed infusion system. The system shall be disposed of as if it were a single piece **in the HD** container according to section 5. The drugs used should not be disconnected.

The staff involved in the technique must be trained to ensure the proper use of closed systems to achieve optimum performance, and minimise the risk of dripping, spilling or creation of aerosols.

4.2.3.4. ADMINISTRATION OF HD IN INFUSER.

• **Definition:**

Single-use device that allows the administration of medication in a continuous, safe and simple way, without the use of batteries or electric current. It is used for outpatients, at home.

• Fitting the infuser:

  • Preferably carried out in hospital.

  • Education to the patient wearing the infuser in order to avoid spillages, breakages.

  • Adopt the general measures for all methods of administration **of HD.**

  • Removing the infuser:

Can be carried out in: Hospital, home, medical centre, public health residence.

Before removing the infuser, clamp as close as possible to the connector using the clip intended for this purpose to prevent leakage of **HD.**

Dispose of Infuser with extension tube and needle in block and all the material used (gauze, syringes, etc.) in the **HD** waste container..

Adopt the general measures for all methods of administration **of HD.**

4.2.4. Cleaning and disinfection.

Cleaning and disinfection are basic preventive measures to avoid exposure and include several stages:

1. Deactivation: transforms the HD into an inert or inactive compound.

2. Decontamination: eliminates residues of HD from surfaces.

3. Cleaning: remove contaminants from surfaces.

Any person in charge of cleaning the work area must be trained in the correct procedures to protect themselves and avoid contamination of the environment and suitably qualified.

GENERAL RULES.

- Always clean with gloves suitable for the activity being carried out.

- Before starting the general cleaning, collect the organic matter (blood and other fluids).

- Clean whenever dirty.

- Never sweep, pick up dirt with a dry mop or cover the brush with a damp cloth or non-woven fabric.

- Clean surfaces with damp cloths.

- The cleaning material used must be specific.

- Do not create draughts that facilitate the movement of germs.

- Use products for hospital use approved by the Commission of Experts of each centre.

- Dispense the product according to the established guidelines.

- Do not mix incompatible products (e.g. sodium hypochlorite with aldehydes).

- Always carry the original containers of detergents and disinfectants in the cleaning trolley.

- Fumigation and spraying are not recommended.

- The material used to clean all types of surfaces (cloths, mops, dry mops, etc.) must be as well wrung out as possible. Let the disinfectant act on the surfaces, it is not necessary to rinse or dry.

- The material used for cleaning must be left clean, disinfected and well wrung out during each shift.

-During the handling of cleaning products, personnel should protect themselves to prevent possible risks (inhalation and/or splashes on skin or mucous membranes) with personal protective equipment (PPE).

-Cleaning personnel must use the same protective measures as health personnel, both in terms of clothing and for the disposal of waste generated, following the rules of each centre.

-Cleaning order: will always be from top to bottom, from inside to outside and from clean to dirty.

MATERIALS AND PRODUCTS.

MATERIALS.

- Suitable gloves for each activity.

- Waste bags.

- Transport trolley.

FOR CLEANING SURFACES.

Specific cloths and buckets for:

- Washbasin, bathroom.

- Rest of surfaces and tools.

Cloths:

- Reusable (washable).

- Cotton.

- Polyester and polyamide microfibres.

- Others.

- Single use (textile or cellulose).

FOR CLEANING PAVING.

According to the system of choice:

- Double bucket.

- Horizontal/flat system (interchangeable and reusable horizontal dry mop system).

- Others (automated systems, single broom, etc.).

PRODUCTS.

The Committee of Experts of each centre will recommend the type and dilutions of the different cleaning products, choosing the most suitable detergents and disinfectants for the health centre, which cause the minimum problems to staff and patients, minimising pollution of the environment as much as possible when disposed of as chemical waste. These products will also be subject to change as new products appear on the market that offer more advantages.

The safety data sheet of all the products used must be made available to the centre's personnel in accordance with Directive 91/155/EEC and R.D. 363/1995, 1078/1993 and 374/2001.

CLEANING FREQUENCY.

Cleaning should be programmed:

- Whenever required.

- 1 clean a day.

- And complementary cleans depending on the different areas of each healthcare centre.

In general, the cleaning services are responsible for all the internal and external parts of the building, as well as all those elements and/or devices that are not directly used by the health personnel in clinical practice.
Each health centre must agree with its own or external hygiene service the responsibilities assigned to each sector, and these must be protocolised.

CLEANING ASSESSMENT PROTOCOLS.

It is important to measure the degree of cleanliness in these areas. The Preventive Medicine and Microbiology Services should agree on evaluation protocols.

To measure the quality of cleaning we recommend:

- Periodic visual inspections.

- Microbiological cultures.

CONTINUOUS TRAINING.

- Own and/or external cleaning personnel.

- Healthcare personnel.

4.2.5. Handling excreta.

The excreta of patients who have received certain HD may contain traces of these drugs and/or their metabolites until several days after administration, so preventive measures should be taken during handling them.

The risk is variable and, among other factors, will be determined by the medication, method of administration, dose received, route of elimination, renal or hepatic function of the patient. In general, for the handling of excreta from patients treated with type 1 HD, the use of PPE is recommended for a minimum period of 48 hours.

The recommended PPE are: **gloves, waterproof gowns** with reinforcement at the front and arms, with tightened cuffs and tied at the back, disposable after use. Use mask and goggles, or face shield, if there is possibility of splashing. In the case of free pouring, transfer or similar handling of excreta that may generate aerosols in the workplace, **a FFP3 respiratory protection mask must also be worn.**

For other HD, refer to the information contained in the drug technical specifications.

General recommendations for the contact or handling of excreta or secretions of patients treated with HD:

• In the examination and normal contact with the patient, without handling or contact with medicines or secretions, no personal protection will be necessary, from the point of view of chemical risk.

• Generally recommended PPE should be used in all tasks, including cleaning of toilets and reusable items, and the handling of undergarments and sheets. Wash hands afterwards.

• When collecting excreta and body fluids (urine, pleural fluid, ascitic fluid, etc.), closed means with a drainage system (faucet type) that allows the subsequent safe disposal of fluids are advisable.

• The biological fluids and excreta that must be kept for later analysis or measurements must be stored in hermetically sealed containers to avoid the generation of vapours and the risk of splashing and/or spillage.

• The use of disposable items (mattress protectors, bedpans, etc.) is recommended instead of other reusable ones.

• Excreta waste should be managed according to point 5.

Specific recommendations for the contact or handling of excreta or secretions of patients treated with type 1 HD:

• Staff should use appropriate PPE for handling undergarments, excreta and cleaning toilets according to general recommendations. Its use is recommended for a minimum period of 48 hours after ending treatment, as most type 1 HD are excreted within this interval, although it can be reduced to 24 hours in some cases and extended to 1 week in others (Table 3 of Cytostatic drugs).

• Whenever possible, exclusive use of toilets is recommended for patients receiving type 1 HD.

•In men, seated urination should be indicated to minimise the risk of creating aerosols and contamination.

• It is recommended that children and pregnant women do not use the toilet moments after the patient has done so (instructions written on the recommendation sheet should be given to patients and family members).

• Pots, urinals and other reusable material should be washed twice with plenty of soapy water and decontaminated with bleach.

• In bedridden patients, the corresponding health personnel should be informed after urination in a bedpan or other container for immediate removal.

• If possible, these patients should use disposable underwear. If not, it is advisable to manage it specifically and separately from the rest of the hospital linens.

• The central part of the sheet (pelvic support area) and especially the pillowcase should be considered as potentially highly contaminated areas. Do not shake the sheets so as to avoid generating dust.

• If the patient needs to be washed in bed, the use of disposable wet wipes is recommended to minimise contamination. No water should be spilled.

• After the excreta have been disposed of via the sanitary sewer, the cistern must be flushed twice with the toilet lid closed. Subsequently, a small glass of bleach is added.

• In the case of outpatients, appropriate information will be provided to them and their relatives: handling with gloves and washing of hands after being in contact, separate washing of contaminated clothes, etc.

4.2.6. Procedure for accidental exposure or spillage outside the Pharmacy Service.

In the event of an accidental exposure or spillage outside the Pharmacy Service, act in accordance with section 4.1.7.

Medicamentos que requieren alargar el periodo de precaución para el manejo de excretas tras la quimioterapia (Periodo de precaución una vez finalizada la administración)

Citostático	Orina	Heces
Bleomicina	3 días	
Carmustina	4 días	
Cisplatino	7 días	
Ciclofosfamida	3 días	5 días
Dactinomicina	5 días	
Daunorubicina	6 días	7 días
Doxorubicina	6 días	7 días
Epirubicina	3 días	
Etopósido	3 días	5 días
Fludarabina	3 días	
Idarubicina	3 días	2 días
Melfalán	2 días	7 días
Mercaptopurina	2 días	5 días
Metotrexato	3 días	7 días
Mitoxantrona	6 días	7 días
Oxaliplatino	3 días	
Paclitaxel	3 días	3 días
Procarbazina	3 días	
Tenipósido	3 días	
Tiotepa	3 días	
Alcaloides de la Vinca	4 días	7 días

Table 3. Precaution period for excreta Source: Protocolo de Vigilancia Sanitaria Específica para Agentes Citostáticos (Protocol for specific health surveillance for cytostatic agents). Ministry of Health and Consumption.

5. WASTE MANAGEMENT

As defined by Law 22/2011, dated 28 July, on contaminated soil and waste, waste is any substance or object that its holder discards or intends or is obliged to discard.

The national legislation on waste does not specifically address health care waste. Its management is complex, with different types of waste (chemical, biosanitary, analogous to urban waste) which require treatment appropriate to their dangerousness. The Castile-La Mancha Health Service has the Protocol for the management of sanitary waste generated in the SESCAM dependent centres, in which it establishes guidelines for the management of the waste produced in its activity.

The term "sanitary waste" covers all waste generated in any establishment or service in which human health care activities are carried out. In this sense, sanitary material must be considered waste from the moment in which its utility or clinical management is definitively concluded.

Classification and segregation.

The SESCAM protocol establishes a series of groups to classify waste. In relation to the management of drug residues, Class IV is of interest. Residues of cytotoxic and cytostatic drugs, and the subgroup Expired drugs and medication waste, belonging to Class II, are of interest. In turn, cytotoxic and cytostatic drug waste from medical services, find their correspondence in code 180108* of the European waste list, while drug waste other than those specified in that section and also from medical services, receive code 180109, in accordance with the provisions of ORDER MAM/304/2002 of 8 February, which publishes the operations of recovery and disposal of waste and the European waste list.

Focusing on the management of HD waste, although those belonging to group 1 fit into the European waste list code 180108* Cytotoxic and cytostatic medicines, group 2 and 3 HD waste do not find an exact correspondence in this list, section 18 (Waste from medical or veterinary services or associated research), since it only offers a hazardous waste code for cytotoxic and cytostatic drugs, and another non-hazardous waste code for other medicines. Since it is not consistent to dispose of HD waste as non-hazardous waste for which special prevention measures will be recommended in its preparation, administration and disposal, given its hazardous nature, HD waste will be segregated as follows:

- **HD1 Waste.**

This group of wastes corresponds exactly with the one defined in the European list of waste as Waste of cytotoxic and cytostatic medicines (LER 180108*) and with Class IV of the SESCAM Protocol for the management of sanitary wastes generated in dependent centres, of the same name. It includes medical waste consisting of remains of HD1 and all material that has been in contact with them.

The following are considered cytostatic waste:

- Remains of cytostatic drugs generated in their preparation and administration.

- The material used to clean the areas where handled, particularly the preparation and administration of cytostatic drugs.

- The material used in the preparation and administration of cytostatic drugs (needles, syringes, bottles, bags and infusion systems).

- Protective equipment for handlers of cytostatic drugs (disposable protective clothing, gloves and protective breathing masks).

- Material stemming from the treatment of accidental spills, including those of excreta during the active life period of the cytostatic drug.

Its segregation will be carried out in official, rigid, single-use blue containers or the one designated by SESCAM, as the case may be. Containers are available with 30 and 60 litre capacity (Figure 3).

Figure 3-. Containers for cytostatic waste.

Sharp waste generated through the administration of this type of medicine should be disposed of in containers for sharp objects identified for cytostatic waste. Examples of available options are 3, 5 and 10 litre capacity (Figure 4).

Figure 4. Containers for cytostatic sharps waste.

- **HD2 and HD3 Waste.**

As a general rule, oral HD will be administered, whenever possible, in doses or presentations that avoid fragmentation and therefore the generation of HD residues.

Waste containing traces of HD2 and HD3 (vials, systems, ampoules, vials, syringes, etc.) will be disposed of in the blue container for hazardous drug waste (Figures 3 and 4), selecting the smallest possible container in order to adjust its capacity to the volume of waste production. In many cases, the use of 3 or 10 litre containers will be appropriate.

The PPE used for the administration of HD2 and HD3 will be disposed of as urban waste, except for evident contamination (splattering, spillage, etc.). The PPE used in preparation will be disposed of in the container for hazardous drug waste.

The material used for cleaning spillages (absorbent material, PPE, etc.) will be disposed of in the blue container for hazardous drug waste.

General precautions in waste management.

- It is important to correctly close the containers.

In the case of containers for sharp objects, it is necessary to assemble the lid properly before its first use (Figure 6).

Figure 6-. Assembly of the lid of the container for sharp objects.

During use, apply the temporary closure (by turning the lid when not in use) and the definitive closure once it is full (by pressing the tab) (Figure 7).

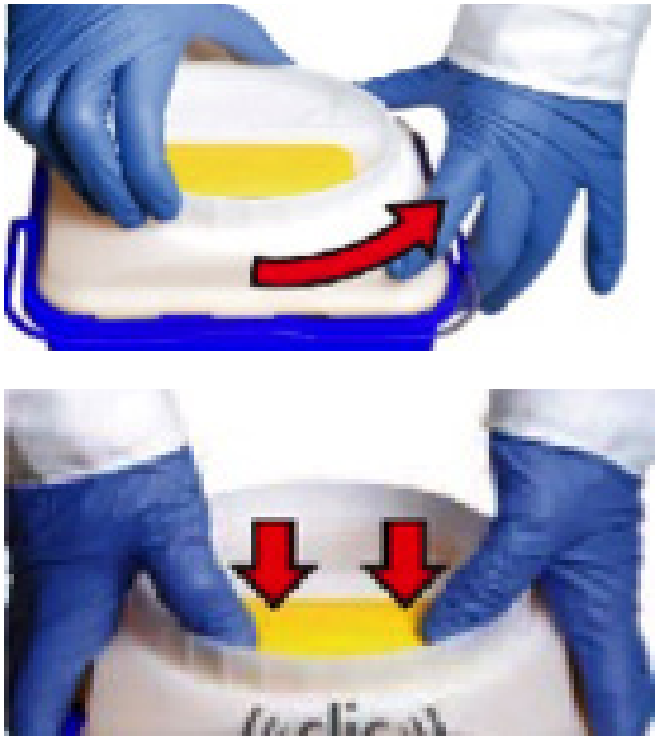

Figure 7-. Application of the provisional and definitive closures of the container for sharp objects.

- To avoid possible leakage of medicines, when disposing of the systems (e.g. infusers) they should be clamped as close as possible to the connector, using the device provided for this purpose (clamp) (Figure 8).

Figure 8.-. Infuser for administration of cytostatic drugs.

- As a general rule, containers should be closed when used to 2/3 of their capacity.

- The filling limit must not be exceeded so as to avoid accidents and difficulties in closing the containers.

- The capacity of the container should be adapted as much as possible to the amount of waste generated, so as to establish a reasonable balance between the frequency of removal and the efficient use of its capacity.

- Containers in use should never be left in areas of passage or places that could cause stumbling, and should always be kept away from any source of heat.
- It is very important that in all points where HD may be administered, infusion systems are removed, etc., those responsible for requesting the material provide for the supply of appropriate containers. The segregation of waste in designated containers minimises the risk of accident and ensures that it is managed according to its danger level.

- In any case, the high-efficiency filters of the safety cabinets used in the preparation of HD, when replaced, will be disposed of as such waste. To this end, they must be deposited in the established containers or, if they do not fit, in waste bags or sacks with a minimum gauge of 400, adequately sealed and labelled for identification.

Storage.

The waste storage facility should, to the extent possible, be isolated from the rest of the premises and used exclusively for the storage of the hazardous waste generated in the activity.

The storage shall be marked with the corresponding signs and located in an enclosure that meets the following minimum requirements:

- The upper cover must prevent rainwater from causing an increase in volume or drag-out of pollutants and must protect the waste from the effects of solar radiation.

- Floor covered with an impermeable material that is resistant to the physical-chemical characteristics of the stored waste.

- The storage shall have a ventilation system that ensures a minimum number of air renewals.

The maximum storage period for hazardous waste shall be 6 months from the time the waste is deposited at the storage site.

Disposal of excreta and other biological fluids

As a general rule and unless the information available in the drug datasheet makes a different practice advisable:

Coming from patients treated with HD1:

• Excreta and other biological fluids: disposal by sanitation system.

• Excreta and other biological fluids during the first 48 hours from the administration of the medicine, when they are contained in devices without the possibility of emptying: cytostatic waste.

• Disposable material contaminated with excreta and other biological fluids during the first 48 hours from the administration of the medicine (empty containers that have contained excreta, nappies, protector pads, etc.): disposed of as cytostatic waste.

• After 48 hours from the administration of the medicine, the waste will be disposed of as urban waste, except excreta and biological fluids contained in devices without the possibility of emptying that meet some criterion that determines its disposal as a specific biosanitary waste, according to the SESCAM waste protocol.

Coming from patients treated with HD2 and HD3:

• Excreta and other biological fluids: disposal by sanitation system.

• Excreta and other biological fluids contained in devices without the possibility of emptying and contaminated disposable material: treated as urban waste, except when meeting some criterion that determines its disposal as a specific biosanitary waste, according to the SESCAM waste protocol.

6. ACTIONS BY THE PREVENTION SERVICE.

6.1. RISK ASSESSMENT OF WORKERS EXPOSED TO HD.

An initial risk assessment, or re-assessment as appropriate, will be conducted in each Pharmacy Service and Areas with staff exposed to HD. Furthermore, and with the periodicity established by the corresponding Area SPRLs, the periodic risk assessment shall be carried out according to the classification of the workers.

6.1.1. Factors to be considered in order to carry out the Risk Assessment.

An assessment of the risk of exposure to HD shall be carried out in each Service.
An assessment of the risk of exposure through inhalation and dermal contact will be conducted for each of the three NIOSH drug groups in its 2014 publication:

Group 1: antineoplastic drugs.

Group 2: non-antineoplastic drugs that meet at least one of the criteria from Table 1.

Group 3: drugs which present a risk to the reproductive process and which may affect men and women who are actively trying to conceive, and women who are pregnant or breastfeeding, but which do not pose a risk to other staff.

The factors to be evaluated for each group are:

- Risk of exposure through inhalation: Hazard class of the medicinal products of that group, amount handled per day and frequency of use.

- Risk of dermal contact; hazard class of the drugs in that group, exposed body surface and frequency of exposure.

In addition, other aspects such as the following will be assessed for each group:

- Use of PPE.
- Training received in handling HD.
- Implementation of written work procedures.
- Facilities and equipment used.
- Instructions from manufacturers and suppliers for the operation and maintenance of equipment.
- Existing control measures.
- Sensitive workers.

6.1.2. Risk magnitude.

The risks to be assessed are classified as: high, moderate or low. An action priority will be established for each of them.

6.2. PERSONAL PROTECTIVE EQUIPMENT.

As a complement to the collective protection measures, which must always be adopted and on which it is necessary to act as a priority, it may be necessary to use the appropriate Personal Protective Equipment (PPE). The use of these PPE imply certain responsibilities on the part of both the worker and the employer:

The employer must:

- Provide PPE to the workers under their charge, according to the risks identified in the risk assessment.

- Provide information and training to workers. Each worker should receive sufficient information on: activities or occasions when PPE must be used, the risk against which it protects them and its limitations, the correct use, following the manufacturer's instructions and supplementing it where necessary with illustrative posters, and maintenance as a guarantee of its effectiveness.

The workers must:

- Make proper use and take proper care of the PPE assigned to them.

- Wash their hands with soap and water or an alcohol solution, before and after using the protective equipment.

- Perform a visual inspection of the PPE (gloves, gowns, face masks, etc.) before use to ensure that they have no defects that could affect their protective effectiveness.

The corresponding Area SPRL can be asked about the most suitable PPE in each case.

The PPE are for personal and non-transferable use and each user is responsible for their maintenance and preservation as well as their correct use, following the manufacturer's instructions.

6.2.1. Applicable markings.

The following is a general description of the mandatory marking of the PPE used for protection against HD depending on the risks to be covered:

- **The "CE" marking** will be MANDATORY for all PPE according to RD 1407/1992.

- If the PPE is intended to protect the user from any mortal danger or that could seriously and irreversibly damage health, without being able to discover in time its immediate effect, in application of RD 1407/1992, it will be classi-

fied in **category III.** PPE classified in this category must bear the CE marking and the **number identifying the Notified Body that carries** out the quality control of the production.

-When the purpose of the PPE is to prevent a disease in the patient, by transmission of biological agents carried by the user, as is the case with gloves, the equipment must also comply with the provisions relating to the commercialisation of medical products, as stated in RD 1591/2009.

6.2.2. Recommended PPE. Technical features.

GLOVES.

- Purpose:

To protect the hands of handlers by avoiding exposure by contact through the skin; to avoid particle contamination in the preparation and microbiological contamination in the preparation and administration.

- Materials and characteristics:

Nitrile, polychloroprene or similar. Vinyl gloves are not recommended because they are more permeable than other materials.
Gloves should be free of dust and traces of nickel as they may attract or disperse HD particles.

- Recommended certification:

- CE marking in accordance with Royal Decree 1407/1992. Replaced by Regulation (EU) 2016/425 of the European Parliament and of the Council, dated 9 March 2016, regarding personal protective equipment and replacing Council Directive 89/686/EEC (OJEU No L 81 dated 31/03/2016), which will be applicable as of 21 April 2018
-Medical product certificate in compliance with RD 1591/2009.

- Category III PPE certificate.

- UNE-EN 420:2004+A1:2010. Protective gloves. General requirements and test methods.

- UNE-EN 374-1,2:2016. Protective gloves against chemical products and microorganisms. EN-374-1 (Terminology and required features for chemical hazard), EN-374-2 (Determining resistance to penetration).

- UNE-EN 388:2016. Protective gloves against mechanical hazards.

- UNE-EN 16523-1:2015. Determining the resistance of materials to the permeability of chemical products. Part 1: Permeability by a liquid chemical under conditions of continuous contact. (Determination of minimum permeation resistance.) Minimum level 4.
- UNE-EN 455-1, 2, 3,4:2015. Single-use medical gloves.

- ASTM-3577 is recommended. Standard Specification for Rubber Surgical Gloves.

- Conditions of use:

- Washing of hands and drying.

- The handler should perform a visual inspection of the gloves before use to ensure that they are free from defects.

- Mandatory use in all HD handling processes, although the receipt, dispensing, transport and handling of waste containers does not require the protective gloves to be sterile.

- Obligatory use of sterile gloves in the elaboration of sterile HD in BSC.

- Frequency of replacement. Under normal working conditions, they will be changed whenever they become contaminated, broken or deteriorated, at the end of the procedure or when attending to another patient. During the preparation of HD it is recommended to change them after the time of permeation indicated by the manufacturer, or after a spill.

- They should be removed immediately whenever their integrity is in doubt.

- Avoid contact of gloved hands with face, mouth, nose and hair during handling of HD.

- Personnel must not leave the processing room with gloves on.

- In case of using double gloves:

  - They will be placed according to the aseptic technique, the first pair under the sleeve of the gown and the second on top.

  - The order of removal will be: glove, gown, glove.

  - They will be disposed of in the corresponding waste container.

GOWN.

- Purpose:

To protect from spillages, splashes and waste materials that may expose the handler by absorption through the skin; to avoid particle and microbiological contamination in the preparation.

- Materials and characteristics:

Disposable, made of polypropylene or covered with polyethylene, the front part will be reinforced (chest and abdomen) and the sleeves at least up to the elbow, with cuffs from 5 to 7 cm, elastic and adjustable and waterproof, with rear opening, highly breathable.

- Recommended certification:

- CE marking in accordance with (EU) Regulation 2016/425.

-Medical product certificate in compliance with RD 1591/2009.

- UNE-EN 6530:2005. Protective clothing. Protection against liquid chemical products. Test method for resistance of materials to penetration by liquids.

- UNE-EN 13688:2013. Protective clothing. General requirements.

- UNE-EN 13034:2005+A1:2009. Protective clothing against liquid chemical products. Performance requirements for chemical protective clothing offering limited protection against liquid chemicals (type 6 equipment).

- UNE-EN 13795:2011+A1:2013. Surgical cloths, gowns and clean air suits, used as medical products for patients, clinical staff and teams. General requirements for manufacturers, processors and products, test methods, performance requirements and performance levels.

- Recommended ASTM/F-99: Standard Test Method for Resistance of Protective Clothing Materials to Permeation by Liquids or Gases Under Conditions of Continuous Contact.

- Conditions of use:

- The handler should perform a visual inspection of the gown before use to ensure that it is free from defects.

- Replace the gown for each working session, and immediately when there is contamination or tissue breakage, or in case of accidental exposure.

- Obligatory use of sterile gown in the preparation of sterile HD.

- In the preparation of non-sterile HD, the condition of sterility is not necessary, unless the installations and equipment are used for the preparation of sterile HD, in which case it is recommended that the gown be sterile. In other processes such as administration, maintenance operations, cleaning of installations and equipment and containment of spillages outside the BSC, sterility is not necessary either.

- They should be changed according to the time recommended by the manufacturer, according to the SOP of each Centre, or in the event of contamination, spillage, breakage, or at the end of the procedure. Remove the gown being careful not to touch the outside.

- Personnel must not leave the preparation area with the gown on. It will be disposed of in the corresponding waste container.

RESPIRATORY PROTECTION: FACE MASK.

- Purpose:

To avoid the inhalation of particles, droplets, vapours and aerosols; to avoid the absorption by contact, and to prevent microbiological contamination.

- Materials and characteristics:

- FFFP3 particle self-filtration face mask.

- Recommended certification:

- CE marking in accordance with (EU) Regulation 2016/425.
- Certified as category III PPE.
- UNE-EN 149:2001+A1:2010. Respiratory protection devices. Filtration half masks to protect against particles. Requirements, tests, marking.

- Conditions of use:

- If working on a BSC, the respiratory protection mask is not necessary. However, the risk assessment will determine whether this PPE is required depending on the working conditions (suitability of the BSC, use of closed systems, characteristics of the preparation room, volume of preparations, etc.)

- It should be used by personnel working in the preparation area and all procedures where there is a risk of aerosol generation, such as BSC cleaning, spill containment and cleaning, and waste collection.

- It will also be used whenever there is a risk of splashing.
- Personnel must not leave the processing area with their masks on.

- The mask must be hermetically adjusted to the user's face in order to protect him/herself, checking it is air tight by covering the air inlet valve with one hand and breathing in to check that the mask collapses.

- It should not be worn over a beard, as it does not ensure protection.

- To be disposed of after use, unless the manufacturer indicates that it can be reused.

- They will be disposed of in the corresponding waste container.

- Masks with open exhalation valve should not be used in sterile environments.

EYE PROTECTION: GOGGLES.

- Purpose:

To avoid contact with vapours, vaporised droplets, aerosols and particles arising from the handling of HD.

- Materials and characteristics:

Full frame panoramic goggles
Safety goggles with side protection.

- Recommended certification:

-CE marking in accordance with (EU) Regulation 2016/425.
-Medical product certificate in compliance with RD 1591/2009.
-UNE-EN 166:2002. Individual eye protection. Specifications.

- Conditions of use:

-Personnel must not leave the processing area with the goggles on.

-They will be disposed of in the corresponding waste container.

-The safety goggles should be removed avoiding touching the external surface that could be contaminated, removing them from the back of the head, from back to front.
-From a chemical contamination point of view, it only makes sense to change them if there is evidence or suspicion that they may have been contaminated.

-Clean and maintain according to manufacturer's instructions.

CAP.

- Purpose:

To minimise the number of particles and to avoid the dispersion of contaminants from the preparation area.

- Materials and characteristics:

The material of these garments must not give off particles and it must be disposable and single-use.

- Unisex.

- Recommended certification:

- CE marking in accordance with (EU) Regulation 2016/425.

- Medical product certificate in compliance with RD 1591/2009.

- Conditions of use:

- It is a requirement of the "clean" rooms, so it is of obligatory use for all personnel entering the preparation room.

- It must completely cover hair and ears.

- Mandatory use in the production process of sterile preparations of any kind.

- The handler should perform a visual inspection of the cap before use to ensure that it is free from defects.

- Personnel must not leave the preparation area with the cap on. It will be disposed of in the corresponding waste container.

SHOE PROTECTORS.

- Purpose:

To minimise the number of particles and to avoid the dispersion of contaminants outside the preparation area.

- Materials and characteristics:

- It should not give off particles and it must be disposable and single-use.

- Waterproof and non-slip.

- Recommended certification:

-CE marking in accordance with (EU) Regulation 2016/425.
-Medical product certificate in compliance with RD 1591/2009.

- Conditions of use:

- It is a requirement of the "clean" rooms, so it is of obligatory use for all personnel entering the preparation room.

- The handler should perform a visual inspection of the shoe protectors before use to ensure that they are free from defects.

- Medical footwear does not replace the obligation to use shoe protectors.

- When access to the preparation room in which the BSC is located is from a room that is also classified as clean, which is accessed after putting on shoe protectors, another pair of shoe protectors must be added in the airlock prior to accessing the HD preparation room.

- Personnel must not leave the processing area with the shoe protectors on.

6.2.3. Sequence for putting on and removing personal protective equipment for handling sterile HD.

Clothing for preparing sterile HD will be put on in the airlock in the following order, unless a second pair of gloves is used, in which case they are put on in the preparation room:

1. Hand-washing with common soap before antisepsis if hands are visibly soiled.
2. Protection of medical footwear with standard shoe protectors.
3. Put on standard cap and safety goggles (if applicable).
4. Put on the specific mask.
5. Antiseptic hand washing with germicidal soap, followed by complete drying.
6. Put on the first pair of specific gloves, following the aseptic technique.
7. Put on the specific/gown, taking special care to ensure that the sleeves are correctly positioned with the cuffs over the gloves.
8. Put on of the second pair of specific gloves, being placed over the cuffs of the gown, inside the preparation area, once the handler is seated at the BSC.

The PPE should always be removed before leaving the processing room, as possible contaminants adhering to the mask, gloves, gown, shoe protectors or cap could spread. This can be done in the airlock if the environment is classified and the minimum negative differential pressure between the areas is guaranteed.
Regardless of the activity carried out handling HD, it is imperative that all clothing used be disposed of in the corresponding waste containers.

Sequence for removing PPE:

1. Remove the shoe protectors and put them in the bag.
2. Remove the outer gloves.
4. Carefully remove the gown, turning it inside out so that the clean part is on the outside. Put it in the bag.
6. Remove the elements that cover the head: goggles, face mask and cap, and discard in the bag as appropriate. If the goggles are going to be reused, store them in a separate bag marked "contaminated" so that they can be washed later.
7. Remove the second pair of gloves.
8. Wash hands, face and neck.

6.3. INFORMATION AND TRAINING

6.3.1. Information.

All workers must be informed of the risks inherent to their positions. The occupational risk assessment and any preventive measures derived from it shall be available to the worker.

It is convenient to have a poster with all the HD sorted into lists, not only with those included in the Pharmacotherapy Guides, since patients sometimes have prescribed medicines not included in the Pharmacotherapy Guides.

Initiatives will be developed to add the protective measures to the nursing administration sheets.

They will also be able to refer to the Safe Work Standards, available on the SESCAM website, through the following link:http://sescam.castillalamancha.es/profesionales/atencion-al-profesional/prevencionriesgoslaborales

(See ANNEX 3: Action to be taken in relation to the risk of exposure to HD and ANNEX 4: Exposure to HD. Specific information for pregnant or breastfeeding workers).

6.3.2. Training.

Those workers who, as a result of their work activity, have to carry out tasks involving HD must be trained in the Handling of Hazardous Drugs.

The training must be given, whenever possible, within working hours or, failing that, at other times, but discounting the time invested in the training from work time.

The Service Manager and Middle Managers are responsible for verifying that the professional is properly trained in those aspects determined in the risk assessment to be related to HD, for conveying the appropriate indications as well as for facilitating the procedures and instructions that may affect the personnel under their charge.

Theoretical and practical training in the handling of HD must be given by the Middle Managers of the respective Services or Units, although specific training on the risks and preventive measures of said activities must be given by the corresponding Area Prevention Services; such training must be coordinated.

The training must be aimed at ensuring that the work activity is carried out in a safe manner, therefore the proposed contents must be geared towards the tasks performed in each job. Each Department must consider its particularities and adapt the contents of the training to its needs.

The proposed contents are explained in Annex II.

6.4. HEALTH SURVEILLANCE.

Occupational health surveillance (OHS) is one of the tools of occupational medicine that includes the set of health actions, referring both to individuals (individual OHS) and collectives (collective OHS) that are carried out with the aim of knowing the state of health of the worker, to apply this knowledge to the prevention of risks at work (avoiding the appearance of occupational disease and occupational accidents, favouring, insofar as this is possible, a comfortable working environment and promoting health at work).

When we talk about HD, and taking into account the potential risk to which we refer (hypersensitivity, toxicity to different organs, carcinogenicity and mutagenicity) and that in many cases the exposures to these risks are multiple and combined, we must adopt health protection measures for exposed workers. Health surveillance must be part of the prevention procedures to be adopted.

In any case, for the detection and control of health effects related to work activity, and in accordance with the provisions of Art. 22 of Law 31/1995 on Prevention of Occupational Risks (LPRL) and Art.37.3 of Royal Decree 39/1997, which approves the Regulation of Prevention Services, health surveillance will be subject to specific protocols regarding the risk factors to which the worker is exposed. The aim of health surveillance is twofold: expertise (suitability for the position) and prevention (detecting workers particularly sensitive to the risk of exposure to HD) and adopting in each case the pertinent measures for the prevention of said risk, according to Art. 25 of the LPRL.

Health surveillance may be: initial (when entering the workplace), periodic (see table), following acute accidental exposure, risk assessment during pregnancy, breastfeeding or any other situation that may make the worker especially sensitive, after prolonged temporary incapacity.

In general, the periodicity will be established according to the following outline:

Probability or risk of exposure	Periodicity
Very high High	**Annual**
Moderate	**Biennial**
Low Very low	**Triennial**

Annex 8 deals specifically with the Health Surveillance of workers exposed to HD.

6.5. EMERGENCY MEASURES.

In accordance with article 20 "Emergency Measures", (Law 31/1995 of 8 November on the Prevention of Occupational Risks) and in application of Royal Decree 393/2007, SESCAM will analyse possible emergency situations and adopt the necessary measures in matters of first aid, fire fighting and evacuation of workers, designating for this purpose the personnel in charge of putting these measures into practice and periodically checking, where appropriate, their correct application. Such personnel must have the necessary training, be sufficient in number and have the appropriate means available. It is also the obligation of SESCAM to draw up, implement and ensure the operation of Self-Protection Plans or Emergency Measure Plans based on the characteristics of each Centre.

6.6. COORDINATION OF BUSINESS ACTIVITIES IN MATTERS OF PREVENTION OF OCCUPATIONAL RISKS.

Coordination of business activities will be carried out in accordance with the provisions of the SESCAM Memo 5/2011 Coordination Procedure for Business Activities in preventive matters, which establishes the obligation to implement the necessary means of coordination regarding the protection and prevention of occupational hazards when there are workers from several companies in the same work centre. Through the coordination of business activities, the aim is to achieve an effective control of the risks generated and aggravated as a result of business concurrence in a single workplace.

Both in the Pharmacy Area and in the rest of the Areas, there may be concurrence of SESCAM's own personnel and contracted personnel, such as for example:

- Cleaning companies.
- Periodic maintenance of specific installations.
- Occasional maintenance repairs.
- Research institutions or companies.
- Waste management.

In addition to the provisions of Memo 5/2011, given that these are pharmaceutical products not included within the scope of application by REGULATION (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the registration, evaluation, authorisation and restriction of chemical substances and preparations (REACH); information must be requested on the risks to the safety or health of workers arising from their storage or use, as well as the measures to be adopted in relation thereto, in particular:

"Manufacturers, importers and suppliers of products and chemical substances used at work are obliged to package and label them in such a way as to permit their safe storage and handling and to clearly identify their contents and the risks to the safety or health of workers that their storage or use entails".

They must also provide information indicating the correct way of use by the workers, the additional preventive measures to be taken and the occupational hazards arising from normal use, handling or improper use.

Manufacturers, importers and suppliers must provide employers, and employers must collect from them, the information necessary to ensure that the use and handling of machinery, equipment, products, raw materials and tools is carried out without risks to the health and safety of workers, as well as to enable employers to comply with their obligations to inform workers.

The employer shall ensure that such information is provided to the workers in terms that are understandable to them (Art. 41 LPRL: Obligations of manufacturers, importers and suppliers).

This information must be included in the foreseen communications regarding the coordination of business activities in accordance with the provisions of the aforementioned Memo.

7. INSTALLATIONS AND EQUIPMENT IN THE PREPARATION OF HD. MONITORING AND CONTROL: PERIODIC MAINTENANCE AND REVISIONS OF INSTALLATIONS AND EQUIPMENT.

Reference standards will be followed in terms of installations, equipment and maintenance to ensure that the preparation, distribution, administration and disposal of HD is carried out with the maximum guarantees as regards safety for personnel and the quality of the prepared HD.

With respect to the rooms of controlled environment (Pharmacy) "clean rooms", the concentration of particles contained in the air will be controlled and both their construction and their use will be carried out in such a way that the number of particles introduced or generated and existing in the interior of the premises is as low as possible and in which other important parameters such as temperature and pressure can be controlled. In particular, the air conditioning requirements in PHARMACY will be the following:

Hospital area	Type of premises	Minimum flow of external air $m^3/(h*m^2)$ (1)	Environmental conditions		Maximum sound pressure dB(A) (2)a
			Minimum temperature	Maximum temperature	
Pharmacy					
Sterile premises	**I**	**10**	**24**	**26**	**40**
Corridors	**II**	**10**	**24**	**26**	**40**

(1) In specific cases, higher air flow rates may be required. (2) These values can be reduced at the discretion of the hygienist.

A confined and exclusive area must be available to ensure safe handling and minimise the risks of preparing HD. Class II BSC is recommended and Class I BSC can be used for non-sterile preparations. All BSC used in the preparation of HD must be certified, have "CE marking", and comply with international standards. Maintenance activities may only be carried out by qualified personnel and must be documented.

As for the rest of the HD handling Areas, when selecting the type of installations required, we will comply with the provisions of Royal Decree 1027/2007, of 20 July, which approves **the Regulation on Thermal Installations in Buildings (RITE**) and develops the standards that must be met by the air-conditioning (heating, cooling and ventilation) and hot water production (DHW) installations of a building to meet the needs of well-being and thermal comfort, people's hygiene and rational use of energy.

In particular, the requirements will be, category of air quality inside the hospitals: IDA 1 (air of optimum quality). Technical Instruction IT.1 design and dimensioning will also be complied with: IT 1.1. Well-being and hygiene requirement. IT 1.1.4.2. Indoor air quality requirement: in buildings for hospitals and clinics the valid values are those of Standard UNE 100713: "Air conditioning installations in hospitals".

The modification of the RITE **(Royal Decree 238/2013)** also specifies that the licensee of the facility shall be responsible for the following actions:

– Maintenance of the thermal installation by a qualified maintenance company.

– Mandatory inspections.

– The conservation of the documentation of all actions, whether maintenance, repair, renovation or inspections carried out on the thermal installation or its equipment, by recording them in the Building Book.

There are different specific standards applicable to the design, control and maintenance of air conditioning systems in health centres, including **UNE-100713:2005**, on air conditioning installations in hospitals and **UNE-EN ISO 14644**, on clean rooms and annexed premises.

Royal **Decree 238/2013** on Modifications of the RITE includes in the Preventive Maintenance section, as obligatory on an annual basis, the revision of indoor air quality according to the **UNE 171330** and **UNE 100012 standards.**

This modification affects all buildings with installations with a output power greater **than 70 Kw** (hospitals and most health centres would be included in this section).

In addition to the general requirements detailed above, in hospitals and health centres indoor environmental quality in "critical areas" will be governed by **UNE 171340:2012.**

- Validation and qualification of controlled environment rooms in Hospitals. The purpose of this standard is to establish fundamental control principles, with a formalised system, application criteria and a testing methodology, including its periodicity, to validate the correct operation of controlled environment rooms located in health centres. To this end, it describes the tests to be carried out according to the parameters to be evaluated, the results of the tests

Controlled environment room	Validation prior to commissioning	Post maintenance validation (including filter changes)	Annual "on standby" validation
Validation body	**EXTERNAL**	**EXTERNAL OR INTERNAL**	**EXTERNAL**
Environmental parameters	Differential pressure Validation fitting absolute filter Flows and renewals/h Direction of air flow Analysis of air flow configuration Recovery of the room	Differential pressure Classification of the operating theatre As per reach of the renovation	Differential pressure Validation fitting absolute filter Flows and renewals/h Direction of air flow Recovery test of the room
Technical conditions from table A.1 from Standard UNE 100713			
Hygiene conditions from Standard UNE 100012			

to be recorded, the presentation of the results obtained by means of reports, as well as the criteria for evaluating the results.

According to this standard, **a controlled environment room** is defined as those rooms with specific structures and facilities to control biocontamination and the appropriate environmental parameters.

The types of validation, periodicity and criteria for the evaluation that must be carried out in order to know the air quality in controlled environment rooms are shown in the following table:

8. REVISIONS OF THIS DOCUMENT.

As a result of the implementation of this Guide and in accordance with scientific/regulatory progress, it may be decided to repeal, amend or extend one or more of the sections contained herein.

These revisions will be updated and included in the format shown on the cover page of the document.

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must ensure that each worker receives **sufficient and adequate theoretical and practical training in preventive matters**, both at the time of hiring, whatever the modality or duration of the contract, and when there are changes in the duties performed or when new technologies or changes in work equipment are introduced. The training must be specifically focused on the job or function of each worker, adapted to the evolution of risks and the appearance of new ones, and repeated periodically, if necessary."

Moreover, art. 9 on Information and training of workers, of R.D. 374/2001, of 6 April concerning the protection of the health and safety of workers against risks related to chemical agents at work establishes that:

• "In accordance with articles 18 and 19 of the Law on the Prevention of Occupational Hazards, the employer must ensure that workers and workers' representatives receive adequate training and information on the risks arising from the presence of hazardous chemical agents in the workplace, as well as on the prevention and protection measures to be adopted in application of this Royal Decree.

• In particular, the employer must provide the workers or their representatives, following the criteria established in section 1 of article 18 of the aforementioned Law:
– The results of the risk assessment contemplated in article 3 of this Royal Decree, as well as any changes in those results that occur as a result of significant alterations in working conditions.
– Information on hazardous chemical agents present in the workplace, **such as their name, health and safety risks, occupational exposure limit values and other applicable legal requirements**.
– Training and information on appropriate precautions and measures to be taken in order to protect themselves and other workers at the workplace.
– Access to any technical specifications provided by the supplier in accordance with the regulations on the classification, packaging and labelling of dangerous substances and preparations.

• The information shall be provided in an appropriate form, taking into account the volume, complexity and frequency of use, as well as the nature and level of risks identified by the assessment; depending on these factors, individual instructions and training supported by written information may be necessary or verbal communication may suffice. The information shall be updated whenever it is necessary to take account of new circumstances."

• The workers will be provided with the SWS (Safe Work Standard) applicable to for them. The SWS referring to Administration of HD (SWS No. 35) and to Preparation of HD (SWS No. 36) are included at the end of this document. In addition, art. 11 on information and training of workers, of RD 665/1997, of 12 May, on the protection of workers against risks related to exposure to carcinogens at work.

• "In accordance with articles 18 and 19 of the Law on the Prevention of Occupational Hazards, the employer shall adopt appropriate measures so that workers and workers' representatives receive training and are informed of the measures to be adopted in application of this Royal Decree. Furthermore, the employer shall take appropriate measures to ensure that workers receive sufficient and adequate training and accurate information based on all available data, in particular in the form of instructions, in relation to:
– Potential health risks, including additional risks due to use of tobacco.
– Precautions to be taken to prevent exposure.
– Personal hygiene provisions.
– The use of protective equipment and clothing.
– The consequences of the selection and use of protective equipment and clothing.
– The measures to be taken by workers, in particular intervention personnel, in the event of an incident and for the prevention of incidents.

• Such training must:
– Adapt to changes in knowledge regarding risks and the appearance of new risks.
– Repeat periodically if necessary.

• The employer must inform workers of installations and their annexed containers containing carcinogens or mutagens.

• The workers' representatives and the workers concerned shall also be informed of the causes of the accidental exposures and non-regular exposures referred to in Article 7 and of the measures taken or to be taken to remedy the situation.

• Workers shall have access to the information contained in the documentation referred to in Article 9 when that information concerns them. Similarly, the workers' representatives or, failing that, the workers themselves, shall have access to any anonymous collective information.

3. TRAINING CHARACTERISTICS:

• The personnel who handle or may handle HD must receive adequate training prior to exposure to the risk and periodically depending on the professional category, job position and risk of the HD that are usually handled in that plant, service, etc.

• The trainers in the Risks and Preventive Measures to be adopted in the workplace in relation to HD will be the Technical and Sanitary personnel of the Prevention of Occupational Risks Service.

• The training for workstation operations and other tasks shall be conducted by the line managers of the workers.

• Each Department must have a manual with Standard Operating Procedures (SOPs) for the proper preparation and administration of hazardous drugs, reconstitution, administration, cleaning, dealing with spillages, and transportation. These will include a detailed description of the individual protective equipment (PPE).

• The training should address:
– The risks of the work place, the evolution of the knowledge of the risks and the appearance of new ones.
– The specific tasks to be carried out.
– Previous training level of the workers.
– Level of responsibilities of the workers in relation to the handling of hazardous drugs (cytostatic, etc.).

• The accredited courses that exist on this topic will be delivered.

• Attendance must be documented.

• They must be accredited courses with an allocation of hours of continuous training.

• The competences acquired must be assessed upon completion of the training programme.

• It is recommended that the training course be repeated as often as required according to Services, professional category and/or Work Procedures, in order to cover new procedures, include new techniques, work equipment or new HD or as a consequence of the observation of an inadequate application of the techniques, procedure, etc. or the generation of risks for the worker himself or the other workers, during the work.

AIMED AT:
All personnel related to:
1. Reception and storage.
2. Preparation.
3. Transport.
4. Administration.
5. Segregation/elimination of waste.
6. Removal of excreta from patients being treated with HD.
7. Cleaning of spillages.
8. Cleaning and maintenance of installations and BSC.
9. Any other operation that implies a potential risk descried in the Risk Assessment.

PERSONNEL EXPOSED TO HD:
- Orderlies.
- Nursing Assistants.
- Pharmacy Technicians.
- Nursing Staff.
- Doctors and Residents in Training.
- Cleaning and Maintenance Staff.
- Any personnel carrying out other operations involving potential contact.

OBJECTIVES:
1. To avoid/minimise risk by developing updated technical skills and attitudes for the correct execution of tasks related to exposure to HD.
2. To provide workers with adequate information and training on the risks to which they are exposed and the preventive measures.

CONTENTS:
• Introduction (definitions: HD, carcinogenic, mutagenic, toxic for reproduction, etc. Existing classifications, regulations, etc.).

• Sources of exposure. Personnel exposed to HD.

• Risks and/or effects on workers' health.
- Potential risks of exposure to hazardous drugs.
- Specific treatment for pregnancy.

• Procedures for taking action. Preventive measures to be adopted:
- Use of Closed Systems.
- Means of collective protection. Containment and barrier devices.
- Rules and procedures of each hospital on handling hazardous drugs (protocols and safe work procedures).
- Transport of hazardous drugs.
- Personal hygiene provisions.

• Use of Personal Protective Equipment (PPE), depending on the case, method of fitting and removal, selection criteria, etc.

• Handling excreta.

• Action in case of spillages and accidental exposure, basic use of the spillage KIT, access and availability.

• Cleaning procedures.

• Emergency procedures.

• Waste management.

• Maintenance procedures.

• Notification of incidents and accidents

• Health surveillance.

• Additional contents: Directed at and focused on workers depending on their place of work:
- Pharmacy Service:

  • Specific work (work in a clean room, work in booths, handling drugs).

  • Work organisation: Identification, handling, location, distribution circuit of drugs.

  • Specific protocols for internal operation in each Pharmacy Service.

- Preparation and administration in Hospitalisation Units. Specific protocols for internal use in each Hospital.
- Transport and storage.
- Cleaning (take into account the coordination of business activities).
- Specific protocols on maintenance of installations for internal use in each Hospital.

Each Department must consider its particularities and adapt the contents of the training to its needs.

This general training may be complemented by more specific training according to the risks of exposure to HD at the different workstations.

It is important to coordinate the training actions; the different actors involved (middle managers, heads of Services, Pharmacy Service, Prevention Service, etc.) must establish mechanisms for joint action in the dissemination of the courses and in their delivery.

SAFE WORK STANDARDS. ADMINISTRATION OF HAZARDOUS DRUGS. SWS No. 35

(Art. 18 Law 31/1995 on Prevention of Occupational Hazards. Duty to inform).

The most common health and safety risks, as well as the preventive measures you should take to avoid risks in the administration of hazardous drugs, inter alia, are the following:

INTRODUCTION

HAZARDOUS DRUGS (hereinafter HD) are those that present one or more of the following six characteristics in humans or animals:
1. Carcinogenicity.
2. Teratogenicity or other developmental toxicity.
3. Reproductive toxicity.
4. Evidence of severe organ toxicity or other low-dose toxicity in animal specimens or in treated patients.
5. Genotoxicity.
6. Structure and toxicity profiles of new drugs that have been determined to be dangerous according to the above criteria.

NIOSH (National Institute for Occupational Safety and Health) classifies HD into:
Group 1: antineoplastic drugs.
Group 2: non-antineoplastic drugs that meet at least one of the above criteria.
Group 3: drugs which present a risk to the reproductive process and which may affect men and women who are actively trying to conceive, and women who are pregnant or breastfeeding, but which do not pose a risk to other staff.
In September 2016, the National Institute for Occupational Health and Safety and Welfare (INSHBT) published the Technical Document: Hazardous drugs. Preventive Measures for their preparation and administration; the aforementioned document specifies recommendations on handling, associated preventive measures and individual protection equipment to be used. This information is also available since May 2018 on the following link **http://infomep.inssbt.es/.**
"Guidelines for action on the risk of exposure to hazardous drugs for SESCAM health service workers" includes specific actions in this respect in our field.

This SWS is applicable for HD types 1 and 2.
Type 3 HD present a **risk** to the reproductive process, therefore **only for certain workers**, those who are actively trying to conceive, and women who are pregnant or breastfeeding (these people should contact their Prevention Supervisor), **but not to other staff**.

PRECAUTIONS IN THE ADMINISTRATION OF HAZARDOUS DRUGS

The administration of HD must be carried out by qualified and properly trained healthcare personnel who have sufficient experience in the handling of these drugs and who know the measures to be taken in the event of spillage, breakage or any other incident or accident.

HD administration procedures must guarantee the protection of the environment and the worker without altering patient safety.
It is recommended to have stable and adequate surfaces in the work area to place the drugs and material needed for the correct administration to the patients.

Means of administration.
Any: Oral, topical, parenteral (subcutaneous, intramuscular, intravenous, etc.), other methods (intrathecal, inhalation, intra-arterial and/or chemoembolisation, intracavitary).

General Measures.
The administration of the HD will be carried out following the recommendations of the technical specifications and always according to the protocols or guidelines of each centre:
– Wash hands before and after the procedure.
– Use recommended PPE, according to the attached table.
– Use of closed transfer systems for Group 1 and Group 2 drugs.
– Apply the maximum aseptic measures in the area where the handling is carried out to minimise contamination.
– Do not eat, drink or chew gum and do not wear jewellery or make-up during administration.
– After the administration of HD, discard all material used and waste generated in the appropriate bin according to SESCAM waste protocol.
– Have suitable furniture to place the drug before it is used. Use non-slip tables and surfaces with ledges to prepare the technique and armchair or bed to place the patient. All furniture shall be made of waterproof materials, easy to clean and shall be cleaned after use and whenever necessary.
– Have a Spill Kit and know the procedure to be followed in the event of a Spillage and the location of the Kit.

HIGHLY SENSITIVE WORKERS

It is recommended that hazardous drugs not be administered by workers in the following groups:
- Women who are pregnant or breastfeeding.
- Allergic to cytostatic agents and/or with dermatological pathology .

PERSONAL PROTECTIVE EQUIPMENT

Pharmaceutical type	Single glove	Double gloves or Glove specific for Group 1 HD	Eye protection	Respiratory protection FFP3	Waterproof protective gown
Intact capsule/tablet	Yes	No	No[2]	No	No
Fractioned capsule/tablet	Yes	No[1]	No[2]	Yes	No
Oral solution/suspension	Yes	No[1]	No[2]	No[3]	No[2]
Local Methods	---	Yes	No[2]	No[3]	Yes
Parenteral forms (SC, IV, IM)	---	Yes	Yes	Yes	Yes
Solution for irrigation	---	Yes	Yes	Yes	Yes
Powder/Suspension for inhalation	--	Yes	No[2]	Yes	No[2]

1 Double glove or specific glove for Group 1 HD for frequent handling.
2 Required if there is risk of splattering.
3 Required if there is risk of inhalation.
In the case of pregnant workers or workers who are breastfeeding, contact the Prevention of Occupational Risks Service.

- Women with a history of miscarriages at childbearing age
- Personnel professionally exposed to ionising radiation (more than 1 mSv/year).
- Personnel who have previously received cytostatic or immunosuppressive treatments.
- Staff with a previous history of neoplasia.
- Immunodeficiencies.

DISPOSAL OF GENERATED WASTE

HD Waste 1.
This group of wastes corresponds exactly with the one defined in the European list of wastes as cytotoxic and cytostatic medicinal waste and with Class IV of the SESCAM Protocol for the management of sanitary wastes generated in dependent centres, of the same name.
The following are considered type I HD waste.
- Remains of cytostatic drugs generated in the administration.
- The material used in the administration (needles, syringes, bottles, bags and infusion systems).
- Protective equipment for handlers (disposable protective clothing, gloves and masks).
- Material stemming from the treatment of accidental spills.

Its segregation will be carried out in official, rigid, single-use blue containers or the one designated by SESCAM, as the case may be. There are bins of various capacities available. Sharp objects generated as a result of the administration of this type of medicine must be managed in the sharp objects bins specifically identified for this type of waste.

Regarding HD2 and HD3 waste.
- As a general rule, oral HD will be administered, whenever possible, in doses or presentations that avoid fragmentation and therefore the generation of HD residues.
- Waste containing traces of HD2 and HD3 (vials, systems, ampoules, vials, syringes, etc.) will be disposed of in the blue container for hazardous drug waste (Figures 3 and 4), selecting the smallest possible container in order to adjust its capacity to the volume of waste production. In many cases, the use of 3 or 10 litre containers will be appropriate.
- The PPE used for the administration of HD2 and HD3 will be disposed of as urban waste, except for evident contamination (splattering, spillage, etc.). The PPE used in preparation will be disposed of in the container for hazardous drug waste.
- The material used for cleaning spillages (absorbent material, PPE, etc.) will be disposed of in the blue container for hazardous drug waste.

HANDLING EXCRETA

Patients' excreta (basically urine and faeces) should be considered potentially dangerous at least 48 hours after administration (although it may last up to a week for some drugs).
As a general rule and unless the information available in the drug datasheet makes a different practice advisable:

Coming from patients treated with HD1:

• Excreta and other biological fluids: disposal by sanitation system.
o Excreta and other biological fluids during the first 48 hours from the administration of the medicine, when they are contained in devices without the possibility of emptying: cytostatic waste.

• Disposable material contaminated with excreta and other biological fluids during the first 48 hours from the administration of the medicine (empty containers that have contained excreta, nappies, protector pads, etc.): disposed of as cytostatic waste.

• Personnel who may come into contact with or handle the blood, vomit or excreta of patients who have received cytostatic medication in the past 48 hours should wear gloves (double pair) and a waterproof gown.

• They should wash their hands after removing gloves and after contact with excreta.

• After 48 hours from the administration of the medicine, the waste will be disposed of as urban waste, except excreta and biological fluids contained in devices without the possibility of emptying that meet some criterion that determines its disposal as a specific biosanitary waste, according to the SESCAM waste protocol.

Coming from patients treated with HD2 and HD3:

• Excreta and other biological fluids: disposal by sanitation system.

• Excreta and other biological fluids contained in devices without the possibility of emptying and contaminated disposable material: treated as urban waste, except when meeting some criterion that determines its disposal as a specific biosanitary waste, according to the SESCAM waste protocol.

PROCEDURE FOR SPILLAGE

• Isolate and mark off the affected area identifying that it is a HD spillage.

• Open the spill kit and put on the complete PPE in the kit

• Put the personal protective equipment on in the following order: shoe protectors, first pair of gloves, cap, waterproof gown, high filtration face mask, protective goggles, second pair of gloves on top of the gown.

• If there are pieces of glass, collect them with the tweezers or dustpan and brush, but never with your hands, and place them inside the sharp objects container in the kit, which will then be disposed of in the cytostatic waste bin.

• In case of liquid spillage, cover it with absorbent cloths and let them soak it up. Also use pads or absorbent material to prevent the spillage from spreading.

• In the case of solid waste, damp cloths or pads should be used to help with collection.

• When cleaning floors and surfaces, proceed from the least polluted areas to the most polluted, always without extending the spillage.

• Wash with detergent solution and rinse 3 times (detergent - water - detergent - water - detergent - water).

• Remove PPE in the following order: shoe protectors, outer gloves, gown (turning it inside out, the clean part must be on the outside), goggles, face mask, cap, discard in the bag as appropriate; if you are going to reuse the goggles, store in another bag marked as contaminated, and lastly remove the second pair of gloves.

• Wash hands, face and neck.

• All waste and material used must be treated as contaminated material for disposal purposes.

• Refill spill kit.

• Complete spillage data collection sheet.

PROCEDURE FOR ACCIDENTAL EXPOSURE

Any professional who suffers accidental exposure as a result of a spill, accidental puncture or any other accident with HD must go to the corresponding Prevention of Occupational Risks Service (SPRL) for their department for assessment and monitoring. They shall also fill in and register the work accident/incident report, except in urgent cases, in which case the middle manager or Head of Service, as appropriate, shall do so afterwards.

In the case of non-hospital personnel, they must go to the Emergency Department and inform their SPRL so that they can be monitored (as per the provisions of the Procedure for Coordination of Business Activities in preventive matters).

Inhalation exposure/ingestion exposure:
– Monitor possible symptoms.
– Notify the immediate superior and the SPRL of any abnormal symptoms.

Non-contact exposure to skin or mucous membranes:
• Avoid exposure of skin and mucous membranes when the protective equipment is impregnated, removing them immediately, without exposing the skin to contaminated PPE and disposing of them in the corresponding container.

• Wash hands with soap and plenty of water for ten minutes.

Exposure in contact with undamaged skin:
• Immediately remove contaminated PPE and/or clothing.

• Wash affected skin area immediately with mild, non-antiseptic soap and plenty of water for at least ten minutes. Shower if necessary.

• If the affected area is lacerated or irritated, it should be examined by a doctor, in any case medical monitoring of the affected area should be carried out.

• Dispose of contaminated PPE in the corresponding container and/or store clothes in a bag and dispose of them according to the Centre's Cleaning Protocol.

Exposure in contact with eyes or mucous membranes:

• If the injured person wears contact lenses, remove them immediately.

• If substance has splashed in eyes, wash the conjunctiva with plenty of warm water for fifteen minutes and then apply 0.9% saline solution. Do not rub eyes.

• Seek immediate medical attention from the corresponding doctor and monitor the affected area.

Cuts or punctures with contaminated needle or glass:

• Immediately remove contaminated PPE and/or clothing.

• Rinse the area with plenty of warm water. Let the blood flow freely. Do not press on the wound area.

• Clean the area thoroughly with warm water and mild soap for at least ten minutes.

• If contact occurs by accidental inoculation (needle puncture): do not remove the needle, remove only the syringe and with a new syringe aspirate the contents of the injected HD. If the needle has been moved, insert a new one at the point of injection and aspirate the medication.

• Seek immediate medical attention from the corresponding doctor and monitor the affected area.

• In the case of cuts or punctures with contaminated material, it must always be assessed whether the accident also involves exposure to biological material with blood or haemoderivative, in which case the centre will act according to its protocol.

Signature

Received by

Name and surnames: .....

Date: .....

SAFE WORK STANDARDS. PREPARATION OF HAZARDOUS DRUGS. PHARMACY SERVICE. SWS No. 36

(Art. 18 Law 31/1995 on Prevention of Occupational Hazards. Duty to inform).

The most common health and safety risks, as well as the preventive measures you should take to avoid risks in the preparation of hazardous drugs in the Pharmacy Service, among others, are the following:

INTRODUCTION

HAZARDOUS DRUGS (hereinafter HD) are those that present one or more of the following six characteristics in humans or animals:

1. Carcinogenicity.
2. Teratogenicity or other developmental toxicity.
3. Reproductive toxicity.
4. Evidence of severe organ toxicity or other low-dose toxicity in animal specimens or in treated patients.
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Group 3: drugs which present a risk to the reproductive process and which may affect men and women who are actively trying to conceive, and women who are pregnant or breastfeeding, but which do not pose a risk to other staff.

In September 2016, the National Institute for Occupational Health and Safety and Welfare (INSHBT) published the Technical Document: Hazardous drugs. Preventive Measures for their preparation and administration; the aforementioned document specifies recommendations on handling, associated preventive measures and individual protection equipment to be used. This information is also available since May 2018 on the following link **http://infomep.inssbt.es/.**

"Guidelines for action on the risk of exposure to hazardous drugs for SESCAM health service workers" includes specific actions in this respect in our field.

RECEPTION AND STORAGE OF HAZARDOUS DRUG PRODUCTS

• The reception and storage of HD in the Pharmacy Services will be carried out in the general storage area of the Pharmacy, adapted for this purpose. A list of HD and a spill kit with instructions will be available in a visible place. The PPE recommended by the SPRL will be used

• The transport of the HD to the final storage area should be carried out immediately after receipt, with the least possible delay, using extreme caution so as to minimise the risk of breakage.

• Clinical research samples containing HD shall be stored in a specific location designated for this purpose, suitably identified.

• All storage areas shall be clearly identified with specific warnings, and shall be areas of infrequent movement of material and persons.

PREPARATION OF HAZARDOUS DRUGS

• The preparation is the process by which, based on the commercial presentation of the HD, the prescribed doses are pre-packaged for its administration to patients. It is the phase of greater relative risk if adequate prevention and protection measures are not adopted.

• To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service, thus reducing the number of workers exposed.

• Preparations of Group 1 HD and Group 2 parenteral HD must be carried out in the Pharmacy Services. Other HD should preferably be prepared in that Service during its opening hours.

• Medication preparation activities should be carried out by trained and qualified personnel.

• All preparation activities should be carried out following clear, written instructions and should be recorded.

• The preparation area of these HD must guarantee both the safety of the preparation for the patient and the safety of the worker who prepares it.

Working rules in the Preparation Area of sterile HD.
PPE recommended for the preparation of sterile HD: gown, shoe protectors, FFP3 face mask, cap and double sanitary gloves.

• Antechamber and airlock.
- Aseptic washing of hands and forearms.
- Once equipped with the corresponding PPE, do not leave the antechamber.
- The products needed for each preparation will be prepared, checking possible defects such as expiration date, particles in suspension or changes in colour. Once checked, they will be decontaminated with 70º alcohol and placed on a tray that will be taken to the clean area.

• Preparation area.
This area will meet the specifications of a "clean room" controlled environment room. The Class II Biological Safety Cabinet (BSC) is located within this preparation area.

General work rules in the biological safety cabinet.
1. If the cabinet is not in operation 24 hours continuously, it must be put into operation at least 15 to 20 minutes before any handling is carried out so as to stabilise the air circulation. During this time the UV light will be on. Some texts recommend that the cabinet should remain in operation with the fan running 24 hours a day, 7 days a week.

2. When the cabinet is in operation, activity inside the room should be kept to a minimum in order to avoid drafts that could influence the flow of the exhaust duct. The opening and closing of the access door to the room should be avoided as much as possible; in any case, when this is necessary, the pre-cabinet door should be closed.

3. The work surface shall be covered with a sterile cloth absorbent on top and laminated underneath to collect any accidental spills that may occur. The cloth should be changed after each work session or when a spill occurs.

4. All material needed for the task should be carefully cleaned with antiseptic solution (70° alcohol) before being introduced into the cabinet.

5. All material will be inside the cabinet before beginning the task and there will be a waiting time of 2 to 3 minutes to restore flow conditions.

6. Do not block the air inlet or outlet with paper or objects

7. A sharp object container for cytostatic waste and an empty vial or closed bottle should be placed inside the cabinet, where the excess solutions generated during preparation will be placed.

8. Do not work or place objects less than 8 cm from the sides and 10 cm from the front of the cabinet. All handling must be carried out in the area where there is a flow current.

9. Distance must be kept between the products to be handled in order to maintain a relative flow current, with sterile products in the centre and non-sterile products on the outer side.

10. The movements of the operator's arms, inside and outside the cabinet, must be minimal to maintain the integrity of the negative pressure in front of the operator trying to follow the air flow.

11. Prepared and ready to use medicines must be perfectly identified, indicating on the label, at least, the format and dose prepared, and the method of administration, expiry and storage conditions and the patient for whom it is intended.

General rules for cleaning and disinfection of the biological safety cabinet.
Cleaning and disinfection should be carried out in the following situations:
• before starting any work in the cabinet,
• once the work in the cabinet has been completed,
• whenever the work programme changes,
• in case of spills,
• before carrying out a mechanical or biological control test in the work area.

1. The cabinet fan will be running.

2. Use disposable sterile cloths slightly dampened with disinfectant solution (70° alcohol).

3. Clean with soapy water and immediately apply a disinfectant (70° alcohol)

4. Do not get the HEPA filter wet while cleaning the cabinet.

5. While cleaning the contaminated area, the above-mentioned protective equipment must be worn.

6. All material used for cleaning must be treated as contaminated waste.

Rules for working in the Preparation Area of non-sterile HD.
PPE recommended for the Work Centre Specific Risks Assessment.

Preparation of unitary doses of oral suspensions of commercialised HD:
If the dispensation is carried out in unitary doses, they will be prepared in the Pharmacy Service in the Class I BSC and with at least double gloves, gown and face mask. The risk assessment will determine the additional protective equipment, depending on the working conditions and the types of preparations carried out.

To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service, thus reducing the number of workers exposed.

Fractionation or pulverisation of solid pharmaceutical products:
As a general rule, the handling of group 1 and 2 HD will be carried out in the Class I BSC of the Pharmacy Service following the procedures established to guarantee the quality of the process and the protection of personnel.

Preparation of non-sterile HD Master Formulas
The preparation of non HD MF must be carried out in at least a Class I BSC, following the SOPs by pharmaceutical type and the safety and PPE recommendations established by the PRL Service once the risks in the preparations and materials used have been assessed.
The PS must specify the protection measures to be established in the standardised preparation procedures of each MF once the risks have been assessed by the PRL Service.

HIGHLY SENSITIVE WORKERS

It is recommended that HD 1 and 2 not be handled by workers in the following groups:

- Women who are pregnant or breastfeeding.
- Allergic to cytostatic agents and/or with dermatological pathology.
- Women with a history of miscarriages at childbearing age
- Personnel professionally exposed to ionising radiation (more than 1 mSv/year).
- Personnel who have previously received cytostatic or immunosuppressive treatments.
- Staff with a previous history of neoplasia
- Immunodeficiencies.

It is recommended that HD3 not be handled by workers at risk to the reproductive process (men and women who are actively trying to conceive), and women who are pregnant or breastfeeding; there is no risk to other staff.

DISPOSAL OF GENERATED WASTE

HD1 Waste.
This group of wastes corresponds exactly with the one defined in the European list of wastes as Waste of cytotoxic and cytostatic medicines and with Class IV of the SESCAM Protocol for the management of sanitary wastes generated in dependent centres, of the same name.
The following are considered cytostatic waste:
- Remains of cytostatic drugs generated in their preparation and administration.
- The material used to clean the areas where handled, particularly the preparation and administration of cytostatic drugs.
- The material used in the preparation and administration of cytostatic drugs (needles, syringes, bottles, bags and infusion systems).
- Protective equipment for handlers of cytostatic drugs (disposable protective clothing, gloves and protective breathing masks).

- Material used in cleaning up accidental spills.
Its segregation will be carried out in official, rigid, single-use blue containers or the one designated by SESCAM, as the case may be. Containers are available with 30 and 60 litre capacity and containers for sharp objects.

HD2 and HD3 Waste.
Waste containing traces of HD2 and HD3 (vials, systems, ampoules, vials, syringes, etc.) will be disposed of in the blue container for hazardous drug waste, selecting the smallest possible container in order to adjust its capacity to the volume of waste production.
The PPE used for the administration of HD2 and HD3 will be disposed of as urban waste, except for evident contamination (splattering, spillage, etc.). The PPE used in preparation will be disposed of in the container for hazardous drug waste.
The material used for cleaning spillages (absorbent material, PPE, etc.) will be disposed of in the blue container for hazardous drug waste.

PROCEDURE FOR ACCIDENTAL EXPOSURE

Any professional who suffers accidental exposure as a result of a spill, accidental puncture or any other accident with HD must go to the corresponding Prevention of Occupational Risks Service (SPRL) for their department for assessment and monitoring. They shall also fill in and register the work accident/incident report, except in urgent cases, in which case the middle manager or Head of Service, as appropriate, shall do so afterwards.
The health care worker may be accidentally exposed to HD in a number of ways:

1. Exposure by inhalation or ingestion.
In case of exposure by inhalation and/or ingestion, possible symptoms should be monitored and any abnormal symptoms should be reported to the immediate superior and to the SPRL.

2. Exposure without contact to skin or mucous membranes:
Wash hands with soap and plenty of water for ten minutes and put on new PPE.

3. Exposure in contact with undamaged skin:
- Immediately remove contaminated PPE and/or clothing.
- Wash affected skin area immediately with mild, non-antiseptic soap and plenty of water for at least ten minutes. Shower if necessary.
- If the affected area is lacerated or irritated, it should be examined by a doctor.
- The affected area should be monitored by a doctor. Do not use hand cream or moisturisers, as they may increase the absorption of the drug.
- Dispose of contaminated PPE in the corresponding container and/or store clothes in a bag and dispose of them according to the Centre's Cleaning Protocol.

4. Exposure in contact with eyes or mucous membranes:
- If the injured person wears contact lenses, remove them immediately.
- If substance has splashed in eyes, wash the conjunctiva with plenty of warm water for fifteen minutes and then apply 0.9% saline solution. Do not rub eyes.
- Seek immediate medical attention from the corresponding doctor.
- The affected area should be monitored by a doctor.

5. Cuts or punctures with contaminated needle or glass:
In the event of an accidental cut or puncture wound:
- Immediately remove contaminated PPE and/or clothing.
- Rinse the area with plenty of warm water. Let the blood flow freely. Do not press on the wound area.
- Clean the area thoroughly with warm water and mild soap for at least ten minutes.
- If contact occurs by accidental inoculation (needle puncture): do not remove the needle, remove only the syringe and with a new syringe aspirate the contents of the injected HD. If the needle has been moved, insert a new one at the point of injection and aspirate the medication.
- Seek immediate medical attention from the corresponding doctor.

PROCEDURE IN EVENT OF SPILLAGE OF HD INSIDE BSC

- Any spillage in the cabinet must be cleaned immediately.

- If the volume of the spillage exceeds 30 ml or the contents of a vial or ampoule of medicine, the spillage kit will be used.

- For larger spills, additional decontamination of the cabinet is required after initial cleaning.

- Open windows and immediately mark out the area, maintaining airflow.

- Put the personal protective equipment on in the following order: shoe protectors, first pair of gloves, cap, waterproof gown, high filtration face mask, protective goggles and a second pair of gloves on top of the gown.

• If there are pieces of glass, collect them with the tweezers (or dustpan and brush), and place them inside the sharp objects container, which will then be disposed of in the cytostatic waste bin.

• In case of liquid spillage, cover it with absorbent cloths and let them soak it up. Also use pads or absorbent material to prevent the spillage from spreading.

• In the case of solid waste, damp cloths or pads should be used to help with collection.

• If the spill affects the HEPA filter, the use of the cabinet must be interrupted and the cabinet sealed with plastic until the HEPA filter is replaced by authorised, suitably equipped personnel, the filter being treated as contaminated material and placed in the cytostatic waste container.

• Wash hands and dispose of gloves after cleaning.

Signature

Received by
Name and surnames: .....
Date: .....

ANNEX 3. SUMMARY OF MEASURES TO BE TAKEN IN RELATION TO THE RISK OF EXPOSURE TO HAZARDOUS DRUGS

1. PURPOSE

To establish the rules to be followed so the preparation and administration of HD is carried out in suitable health and safety conditions for the workers involved.

2. SCOPE OF APPLICATION

All personnel related to the handling of hazardous drugs.

3. SAFETY RULES

In the handling of HD, as in other activities in the health field, it is necessary to consider both the aspects regarding the protection of the product and the minimisation of the risks that affect the handling personnel, the patient and the environment.

In the case of occupational exposure, the combination of adequate technical facilities (collective protection) with personal protective equipment (personal protective equipment and clothing) is the best form of protection against different contamination possibilities.

Through the Management, Medical and Nursing Directorates, the Prevention of Occupational Risks Services and the Pharmacy Services, the Department must:

• Distribute the Safe Work Standards to workers administering the HD, with proof of receipt. It is also recommended that it be available on the Intranet.

• Provide training and information regarding the actions to be carried out in relation to the risk of exposure to HD. As well as periodically explain to workers the need to comply with rules.

• Visibly display the rules in the place where the preparation and administration is carried out.

The following document includes prevention measures and PPE for the preparation and administration of HD. Must be completed in each case.

HAZARDOUS DRUGS. PREVENTION MEASURES PPE FOR PREPARATION AND ADMINISTRATION CLOSED SYSTEMS FOR SAFE ADMINISTRATION		
GROUP 1	PREPARATION IN PHARMACY	GROUP 2
	ADMINISTRATION WITH CLOSED SYSTEMS	
	ELIMINATION IN BLUE CONTAINER	
ANTINEOPLASTIC DRUGS		NON-ANTINEOPLASTIC DRUGS THAT MEET AT LEAST ONE OF THE DANGER CRITERIA
TO BE FILLED OUT BY EACH DEPARTMENT		TO BE FILLED OUT BY EACH DEPARTMENT

GROUP 3					
TOXIC TO THE REPRODUCTIVE PROCESS DRUGS WHICH PRESENT A RISK TO THE REPRODUCTIVE PROCESS AND WHICH MAY AFFECT MEN AND WOMEN WHO ARE ACTIVELY TRYING TO CONCEIVE, AND WOMEN WHO ARE PREGNANT OR BREASTFEEDING, BUT WHICH DO NOT POSE A RISK TO OTHER STAFF					
To be filled out by each Department					
PPE for PREPARATION, Group 2 not parenteral and parenteral as an exception and Group 3 only in case of reproductive risk and for the ADMINISTRATION of hazardous drugs in CLINICAL UNITS.					
Pharmaceutical type	**Single glove**	**Double gloves or Glove specific for Group 1 HD**	**Eye protection**	**Respiratory protection FFP3**	**Waterproof protective gown**
Intact capsule/tablet	Yes	No	No[2]	No	No
Fractioned capsule/tablet	Yes	No[1]	No[2]	Yes	No
Oral solution/suspension	Yes	No[1]	No[2]	No[3]	No[2]
Local Methods	---	Yes	No[2]	No[3]	Yes
Parenteral forms (SC, IV, IM)	---	Yes	Yes	Yes	Yes
Solution for irrigation	---	Yes	Yes	Yes	Yes
Powder/Suspension for inhalation	--	Yes	No[2]	Yes	No[2]

1 Double gloves or specific glove for Group 1 HD for frequent handling./2 Required if there is risk of splattering./3 Required if there is risk of inhalation

CLOSED SYSTEMS FOR SAFE ADMINISTRATION
HD shall be administered by means of a closed system of watertight connections with safety valves to avoid the risk of accidental disconnection. The bag extension must be connected to the conventional infusion system by means of a universal connection. The infusion bag extension will be purged with clean saline solution from the pharmacy. After purging the system with clean saline solution, the male valve of the extension will be connected to the female valve of the infusion bag. After the administration is finished, the IV must be washed.

ANNEX 4. EXPOSURE TO HAZARDOUS DRUGS. SPECIFIC INFORMATION FOR PREGNANT OR BREASTFEEDING WORKERS

The different risk factors (physical, chemical, biological, ergonomic) to which the worker is exposed in her working environment, can influence the physiology of human reproduction causing alterations in conception, in the development of the embryo or foetus, or in the newborn. The consequences will depend on the stage of reproduction in which they act, as well as on the characteristics of the harmful agent (carcinogenic, mutagenic or reprotoxic) and the amount of exposure, apart from the fact that other risk factors may interact (occupational/non-occupational).

Human reproduction can be altered by different factors (personal, environmental, occupational). Within the workplace, the protection of the occupational health and safety of pregnant workers, workers who have recently given birth or workers who are breastfeeding is provided for in many general provisions, as well as specific regulations in this area, adapted to European legislation (Directive 92/85/EEC). The purpose of the Law on the Prevention of Occupational Hazards (LPRL) is the protection of the health and safety of all workers, and in addition, it especially protects maternity (Art. 26 LPRL), and even the reproductive function (Art. 25.2 LPRL, Highly Sensitive Workers (HSW).

Following criteria of maximum protection of pregnancy, RD 298/2009 amending RD 39/1997 (Regulation of Prevention Services) in relation to the application of measures to promote the improvement of occupational health and safety of pregnant workers, workers who have given birth or workers who are breastfeeding, it is specified that, in the risk assessment (RA), the existence of agents, work procedures and conditions which may adversely affect the health of pregnant workers or of the foetus or of the child during the breastfeeding period shall be taken into account and the worker may not engage in certain activities where, according to the conclusions drawn from the risk assessment, their safety, health or that of the foetus during pregnancy or while breastfeeding may be compromised.

In this sense, RD 298/2009 contemplates an ANNEX VIII with a "non-exhaustive list of agents and working conditions to which there may be no risk of exposure by pregnant or breastfeeding workers" to carcinogenic and mutagenic substances for which there is no exposure limit value assigned. That is to say, the cytostatic agents in general, although not all of them are cancerigenic (RD 665/1997 would apply), nor are they all teratogens. RD 374/2001 on the risks of exposure to chemical agents at work will apply to those for which the carcinogenic or mutagenic nature is not established. The INSHT published in September 2016 the Guidance "HD. Preventive measures for their preparation and administration", which can be of great help in dealing with these issues.

In the RA, the employer must take into account the risk factors that may affect the reproductive function of workers, in particular exposure to physical, chemical and biological agents that may exert mutagenic effects or toxicity for procreation, in the aspects of both fertility and the children's development, in order to adopt the necessary preventive measures (Art. 25.2 LPRL). In the event that possible risk situations are detected, the following measures may be established:

- Adaptation of the Workstation, with the employer proceeding to adapt the working conditions or work time of the employee affected by the risk situation.

- Change of Workstation, if the adaptation is not technically or objectively possible, the employee will be offered another position with duties compatible with her condition.

- Suspension of the employment contract and application for benefits due to risk situations during pregnancy and/or breastfeeding (RD 1251/2001), only if the adaptation or change of position was not technically or objectively possible (Art. 26 of the LPRL). The "Equality Law" (Organic Law 3/2007) establishes that situations of risk for pregnancy and breastfeeding have the nature of professional contingencies.

Decision-making in the health surveillance of workers exposed to dangerous drugs, including HSW (risk to procreation, pregnant women, breastfeeding or recent birth), will be based on the estimation of the level of possible health consequences in unwanted exposures (NICOSEND), or magnitude of possible health damage that could occur during unwanted exposure.

All of these issues are dealt with extensively in the Best Practices Guidelines for Workers Exposed to Cytostatic Substances, and the procedures set out in the guidelines will therefore be taken into account before decisions are made about actions to protect the reproductive function of workers exposed to hazardous drugs or to issue suitability reports regarding the protection of workers in situations of pregnancy or breastfeeding.

With regard to the measures to be adopted, the provisions of SESCAM Memo 3/2012 on Procedure for adaptation/ change of workstation for workers in a situation of recent childbirth and during the breastfeeding period shall also be taken into account.

ANNEX 5. PROCEDURE TO BE FOLLOWED IN THE EVENT OF ACCIDENTAL SPILLAGE OF HD.

The location of the spill will determine the appropriate procedure for its cleaning, so two distinct zones are distinguished accordingly:

A. Procedure to be followed in the event of spillage of HD inside a Biological Safety Cabinet.

B. Procedure to be followed in the event of spillage of HD outside a Biological Safety Cabinet.

A. PROCEDURE TO BE FOLLOWED IN THE EVENT OF SPILLAGE OF HD INSIDE A BIOLOGICAL SAFETY CABINET

1. PURPOSE

To establish a protocol for swift action in the event of a spillage of Hazardous
Drugs (HD) inside the BSC.

2. LIMITS OF THE PROCEDURE

Commencement: with the breakage or spillage of a HD.
Completion: with the elimination of the waste.

3. STEPS OF THE PROCEDURE

The procedure is as follows:

1. Contain the spillage without shutting off the laminar airflow from the cabinet.

2. Remove contaminated gloves and personal protective equipment and dispose of them in a specific container for chemically contaminated waste.

3. In case of contact with skin and/or mucous membranes, proceed to immediate decontamination before starting to clean any surface.

4. Restrict the movement of personnel near the biological safety cabinet so that the air flow is optimal and thus minimise the possibility of part of the contaminated air escaping from the cabinet into the room.

5. Before decontaminating cabin surfaces, the operator involved must be protected with full personal protective equipment.

FITTING THE PERSONAL PROTECTIVE EQUIPMENT (PPE).

Before entering the area of the spillage and prior to the fitting of personal protective equipment (PPE), the following checks shall be made for the person who is to enter the contaminated area:

Never wear any accessories such as watches, earrings, rings, bracelets, mobile phones, etc. that could fall off or damage the PPE.

If the person collecting the spillage has long hair, it must be tied up.

Next, **PUT ON THE PPE** in the following order:

1. Waterproof shoe protectors.
2. First pair of gloves.
3. Cap.
4. Waterproof gown. Ensure that the wristbands cover the gloves properly and that they reach the wrists.
5. Put on the face mask, making sure that it covers the area under the jawbone.
6. Put on the safety goggles.
7. Put on the second pair of gloves, fitting them over the cuff of the waterproof gown.

6. Remove all fungible material (cloth, gauze, syringes and others) located inside the laminar flow duct and dispose of it in the specific container for chemically contaminated waste.

7. If there are glass fragments, collect them with the tweezers from the kit, and place them in the rigid container for HD sharp or pointed objects.

8. Clean the spillage, taking care not to increase the contaminated surface. Use disposable absorbent cloths. If it is a liquid, collect with dry cloths, soaking up with absorption movements. If it is a solid, clean with a cloth dampened with water in order to avoid the formation of aerosols.

9. Clean all surfaces with disposable cloths and soapy solution three times and rinse with water, always from the least to most contaminated area, from top to bottom and from inside to outside. Cleaning solutions should be applied to the cloth and never in spray form inside the cabin to avoid damaging the HEPA filter.

10. Lift the protective front and working surface of the cabinet to access the base. Remove the waste and clean in the same way as described above.

11. Lastly, clean all cabinet surfaces with 70º alcohol, following the same technique (from top to bottom and from inside to outside). Avoid the excessive use of alcohol inside the cabinet where the air flows, as the vapours can concentrate inside and damage the HEPA filter.

12. If the HEPA filter is affected, the use of the cabinet must be interrupted until the filter is replaced. The cabinet should remain off and with the front opening sealed until the filter is changed.

13. Dispose of all decontamination material in the appropriate specific waste container.

14. Remove the PPE in the following order:
1. Remove the shoe protectors and put them in the bag.
2. Remove the outer gloves.
3. Carefully remove the gown, turning it inside out so that the clean part is on the outside. Put it in the bag.
4. Remove the elements that cover the head: goggles, face mask and cap, and discard in the bag as appropriate. If the goggles are going to be reused, store them in a separate bag marked "contaminated" so that they can be washed later.
5. Remove second pair of gloves.
6. Wash hands. It is also recommended to wash the face and neck because the PPE leaves part of the skin in these areas exposed.

15. Once the cabinet has been decontaminated, purge for 20-30 minutes before making any mixture.

16. Report the incident to the corresponding Middle Manager or Head of Service.

17. Complete the form for work incidents/accidents and register in the Area, informing the Prevention of Occupational Risks Service.

B. PROCEDURE FOR ACTION IN THE EVENT OF A SPILLAGE OF HD OUTSIDE A BIOLOGICAL SAFETY CABIN

1. PURPOSE.
To establish a protocol for swift action in the event of a spillage of Hazardous Drugs (HD) outside the BSC.

2. LIMITS OF THE PROCEDURE.
Commencement: with the breakage or spillage of a HD.
Completion: with the elimination of the waste.

3. STEPS OF THE PROCEDURE.

The procedure is as follows:

1. Isolate and mark off the affected area identifying that it is a HD spillage.

2. Notify personnel in that area so that they do not extend the spillage and inform the person designated by the centre.

3. If a worker has been exposed, the personal decontamination procedure takes precedence over the spill collection procedure, first decontaminating the worker and then collecting the spillage. This shall be done in accord In the case of a large spill, or one of special risk for the handler (cytostatic substances), for the placement and subsequent removal of the PPE, the professional who is going to access the area of the spillage must be accompanied by a person to assist (OBSERVER).

4. In the case of a large spill, or one of special risk for the handler (cytostatic substances), for the placement and subsequent removal of the PPE, the professional who is going to access the area of the spillage must be accompanied by a person to assist (OBSERVER).

5. Open the spill kit and put on the complete PPE in the kit.

Bef ore entering the area of the spillage and prior to the fitting of PPE, the worker will check that:

- He/she is not wearing any accessories such as watches, earrings, rings, bracelets, mobile phones, etc. that could fall off or damage the PPE.
- Hair is tied back in a ponytail or bun.
- Put on the PPE in the following order:

1. First, put on the shoe protectors.
2. Put on first pair of gloves.
3. Put on the cap.
4. Put on the waterproof gown, ensuring that the wristbands cover the gloves properly and that they reach the wrists.
5. Put on the face mask, making sure that it covers under the jawbone and adjusting it to you nose.
6. Next put on the safety goggles so that they slightly overlap the face mask on the bridge of the nose. To avoid them misting, you can apply a demisting product or dampen them with hot water.
7. Put on the second pair of gloves, fitting them over the cuff of the waterproof gown.

6. Remove any pieces of glass using tweezers or a scoop and a dustpan, but never with your hands. They will be disposed of in the sharp material container from the kit.

7. Then collect the spillage using the kit material as appropriate:

- For liquids, dry with cellulose or dry absorbent cloths. For liquids, dry with absorbent material from the kit (cellulose, dry cloths, polymer, etc.).
- For solids, clean with cellulose or absorbent cloths dampened with water, limiting dust dispersion and the formation of aerosols.
- The waste will be placed in the hermetically sealed bag provided in the kit. Do not close the bag yet.

8. Clean, taking care not to increase the contaminated surface. Clean with disposable cloths making a spiral movement from the least contaminated areas to the most contaminated. Wash with detergent solution and rinse 3 times (detergent - water - detergent - water - detergent - water).

9. Remove the PPE. To do so, proceed as follows:

1. Remove the shoe protectors and put them in the bag.
2. Remove the outer gloves.
3. Carefully remove the gown, turning it inside out so that the clean part is on the outside. Put it in the bag.
4. Remove the elements that cover the head: goggles, face mask and cap, and discard in the bag as appropriate. If the goggles are going to be reused, store them in a separate bag marked "contaminated" so that they can be washed later.
5. Remove the second pair of gloves.
6. Wash hands, face and neck.

10. All waste and material used must be treated as contaminated material for disposal purposes. Therefore, both the material used and the PPE will be disposed of in the bag provided in the kit. Once closed, this bag will then be placed in the nearest container as established according to the Protocol for the management of sanitary waste generated in the SESCAM dependent centres. Dispose of gloves and tweezers.

11. Refill spill kit. The kit must be refilled at the same time as it is used so that it is always available, and therefore the person in charge of the affected area must request that the appropriate service refill the kit.

Since action in the event of a spillage must be immediate, it is recommended that spillage kits be available in all areas where HD are usually handled. The guidance content of this kit is included in Annex 4 "Composition of the Spill Kit".

SPILLAGE DATA COLLECTION SHEET

DATE, TIME AND LOCATION OF SPILLAGE

Date: _____ **Location:** _____
Time spent on cleaning spillage (start time - end time):
_____

CIRCUMSTANCES RELATED TO SPILLAGE

Name of the persons involved in the spillage (accidentally or those appointed to clean it):

_____

_____

_____

_____

Drugs involved in spillage:

_____

_____

_____

_____

Approximate volume: _____

_____

Cause of spillage: _____

_____

OTHER COMMENTS (optional)

Include any observation, problem or incident found.

_____

_____

_____

_____

Signed (person cleaning spillage):

_____

_____

_____

_____

Signed (area manager):

_____

_____

_____

_____

_____

ANNEX 6. PROCEDURE TO BE FOLLOWED IN THE EVENT OF ACCIDENTAL SPILLAGE OF HD.

Accidental spills can occur in any process in which a HD is present (reception, transport and storage, preparation, administration, collection, disposal, cleaning of waste and excreta, as well as maintenance operations), so the protocols and materials necessary for collection must be established.

These spillages must be cleaned up immediately by trained personnel (informed of the protection to be used and the procedures to be carried out).

The protective equipment will consist of:

- Personal Protective Equipment (PPE):

- Low permeability protective gown.
- Two pairs of nitrile gloves with adequate mechanical resistance.
- Shoe protectors.
- Cap.
- Safety goggles or face mask.
- FFFP3 Respiratory protection face mask.

- Material for cleaning:

- Absorbent material in sufficient quantity (cellulose, dry cloths, polymer, etc.)...
- Rigid container for sharp objects.
- Large, resistant plastic waste bag (at least 0.1 mm thick), preferably hermetically sealed.
- Tweezers.
- Small, disposable scoop and dustpan.
- Soapy solution or equivalent commercial preparation for decontamination, and water.
- Hazard sign.

- Documents

- Copy of spillage protocol.
- Spillage data collection sheet.

ANNEX 7. PROCEDURE TO BE FOLLOWED IN THE EVENT OF ACCIDENTAL EXPOSURE TO HD.

Any professional who suffers accidental exposure as a result of a spill, accidental puncture or any other accident with HD must go to the corresponding Prevention of Occupational Risks Service (SPRL) for their department for assessment and monitoring. They shall also fill in and register the work accident/incident report, except in urgent cases, in which case the middle manager or Head of Service, as appropriate, shall do so afterwards.

In the case of non-hospital personnel, they must go to the Emergency Department and inform their SPRL so that they can be monitored (as per the provisions of the Procedure for Coordination of Business Activities in preventive matters).
An accident can occur at any stage of the HD circuit, so all personnel involved must be properly trained on the procedures of action if necessary.

The professional's exposure depends, fundamentally, on the personal working technique and the precautions taken during

handling. Exposure during preparation and administration can be minimised by using closed systems, although they will only be effective if a good technique is used.

In all cases of accidental exposure, the following should be done:
- Make note of the agent involved.
- Seek specialised medical attention.
- Notify the area manager and/or supervisor.
- Go to the SPRL for assessment and monitoring.

The health care worker may be accidentally exposed to HD in a number of ways:

1. Exposure by inhalation.
This is greatest when aerosol or vaporised particles are released into the environment when a vial or infusion bag is punctured, a syringe or system is purged, an ampoule is broken, etc.

Respiratory protection masks are necessary when collecting an accidental spillage, cleaning and decontamination of the BSC when the protective screen needs to be lifted, in operations where aerosols may be generated, etc. (see section 3.1. of the Guidelines on HD : Risk factors).

If exposure occurs by inhalation, proceed as follows:
– monitor possible symptoms.
– notify the immediate superior and the SPRL of any abnormal symptoms.

2. Exposure by ingestion.
This may occur when particles or droplets of hazardous drugs enter the body through the oral cavity. Therefore, personnel working in contact with these drugs should not introduce food, gum, beverages, cigarettes or medication for personal use into the area where these agents are being handled.

If exposure occurs by ingestion, proceed as follows:
- Monitor possible symptoms.

- Notify the immediate superior and the SPRL of any abnormal symptoms.

3. Exposure without contact to skin or mucous membranes:
- Avoid exposure of skin and mucous membranes when the protective equipment is impregnated, removing them immediately, without exposing the skin to contaminated PPE and disposing of them in the corresponding container.

- Wash hands with soap and plenty of water for ten minutes.

- Put on new PPE.

4. Exposure in contact with undamaged skin:

- Immediately remove contaminated PPE and/or clothing.

- Wash affected skin area immediately with mild, non-antiseptic soap and plenty of water for at least ten minutes. Shower if necessary.

- If the affected area is lacerated or irritated, it should be examined by a doctor.

- The affected area should be monitored by a doctor. Do not use hand cream or moisturisers, as they may increase the absorption of the drug.

- Dispose of contaminated PPE in the corresponding container and/or store clothes in a bag and dispose of them according to the Centre's Cleaning Protocol.

5. Exposure in contact with eyes or mucous membranes:

- If the injured person wears contact lenses, remove them immediately.

- If substance has splashed in eyes, wash the conjunctiva with plenty of warm water for fifteen minutes and then apply 0.9% saline solution. Do not rub eyes.

- Seek immediate medical attention from the corresponding doctor.

- The affected area should be monitored by a doctor.

6. Cuts or punctures with contaminated needle or glass:
These occur when a contaminated needle or piece of glass pierces through the skin. Punctures can occur when a needle is "uncovered" or "covered," during insertion or removal, etc. In order to avoid accidental injections, it is essential to acquire good working techniques (see sections 4.1.3 and 4.2.2 of the Guidelines on HD) and to handle with caution.

In the event of an accidental cut or puncture wound:

- Immediately remove contaminated PPE and/or clothing.

- Rinse the area with plenty of warm water. Let the blood flow freely. Do not press on the wound area.

- Clean the area thoroughly with warm water and mild soap for at least ten minutes.

• If contact occurs by accidental inoculation (needle puncture): do not remove the needle, remove only the syringe and with a new syringe aspirate the contents of the injected HD. If the needle has been moved, insert a new one at the point of injection and aspirate the medication.

• Seek immediate medical attention from the corresponding doctor.

• The affected area should be monitored by a doctor.

• In the case of cuts or punctures with contaminated material, it must always be assessed whether the accident also involves exposure to biological material with blood or haemoderivative, in which case the centre will act according to its protocol.

• See table below for "Specific recommendations for action in case of exposure to cytostatic drugs".

CYTOTOXIC DRUG	ACTION
AMSACRINE	Wash with soap and water.
ASPARAGINASE	Wash with water.
BLEOMYCIN	Wash with soap and water.
BCG	Wash with soap and water.
CARBOPLATIN	Wash with water.
CARMUSTINE	Wash with water. If irritation appears, apply a bicarbonate solution.
CISPLATIN	Wash with water.
CYCLOPHOSPHAMIDE CYTARABINE DACARBAZINE	Wash with water, or soap and water.
DACTINOMYCIN	Wash with water.
DAUNORUBICIN DOXORUBICIN EPIRUBICIN	Wash with water, soap and water or bicarbonate soda solution.
ETOPOSIDE FLUOROURACIL IDARUBICIN IFOSFAMIDE MELPHALAN	Wash with soap and water.
METHOTREXATE	Wash with water.
MITOMYCIN	Wash with 1M bicarbonate soda, then with soap and water.
MITOXANTRONE	Wash with water.
MECHLORETHAMINE	Wash with water.
THIOTEPA VINBLASTINE VINCRISTINE VINDESINE	Wash with water.

Table: Specific recommendations for action in case of exposure to cytostatic drugs.
Source: Best Practices Guidelines for Workers Exposed to Cytostatic Substances. AMMTAS Monographs.

Record of accidents and incidents with HD. In the SPRL there must be a record of accidental exposures to HD. These records must be filed.

EXPOSURE IN THE HANDLING OF AN EXTRAVASATION

Extravasation is defined as the outflow of intravenous fluid into the perivascular space due to factors specific to the vessel or accidental reasons derived from the displacement of the cannula outside the venepuncture site. This is a side effect that affects the patient and is therefore not contemplated in these Guidelines.

The risks to which the worker is exposed in the handling of an extravasation are the same as those derived from the administration of drugs (see sections 4.1.3 and 4.2.2 of the Guidelines on HD).

However, there are certain HD belonging to group 1 (cytotoxic) which, in addition to their mutagenic and carcinogenic potential, present an added type of toxicity: (local toxicity) which is necessary to be aware of because of its implications for the worker.

Based on their aggressiveness to the tissue, group 1 HD can be classified into 3 groups:

- Vesicant: capable of causing tissue necrosis.
- Irritant: capable of producing pain and/or venous inflammation during administration, phlebitis, etc.
- Not irritant or vesicant.

The level of exposure to the drug influences the tissue damage that can occur, and this in turn depends on several factors such as: the penetration or absorption capacity of the drug, concentration, amount, and duration of exposure.

In order to treat the possible effects of the local toxicity of these drugs, several actions can be carried out:

1. Use of specific antidotes. There is no unanimity in the use of antidotes. The fundamental reason is that, given the absence of controlled studies, most of the available data come from more or less isolated individual experiences. In general, the most admitted specific antidotes are:

- Sodium thiosulphate (1/6 M): apply from 1 to 3 ml via subcutaneous infiltrations around the affected area. Used for mechlorethamine and cisplatin.

- Hyaluronidase: 150 I.U. for vinca alkaloids, etoposide

VESICANT	IRRITANT	NOT IRRITANT OR VESICANT
Dactinomycin	Carmustine (BiCNU)(*)	L-asparaginase
Amsacrine	Dacarbazine (DTIC)(*)	Bleomycin
Daunorubicin	Docetaxel(*)	Cyclophosphamide(*)
Doxorubicin	Etoposide (vp-16)	Carboplatin (*)
Epirubicin	Mitoxantrone(*)	Cisplatin (*)
Streptozocin	Paclitaxel(*)	Cytarabine
Idarubicin	Teniposide (vm-26)	Fluorouracil (5-FU)(*)
Mechlorethamine		Gemcitabine
Mitomycin C		Floxuridine
Vinblastine		Ifosfamide(*)
Vincristine		Irinotecan
Vindesine		Methotrexate
Vinorelbine		Thiotepa (*)
		Topotecan

(*) Controversial classification, certain authors may place them in a more aggressive group

and teniposide by subcutaneous application around the affected area.

• Dimethylsulfoxide (DMSO) 99%: for anthracyclines and mitomycin. Topical application every 6 hours on the affected area letting it air dry, followed by hydrocortisone cream and cold for 30 minutes in the first 24 hours. In the following 14 days the applications will be made every 24 hours.

2. General measures. These can be applied if deemed appropriate, after exposure to vesicant and irritant drugs always after physical and pharmacological treatment:

• Raise the limb to the height of the heart to encourage venous return.

• Apply cold for 15-20 minutes every 4-6 hours for a period of 72 hours except with vinca alkaloids, etoposide, teniposide, cisplatin and taxanes, in which case dry heat will be applied.

• Avoid photoexposure of the affected area if the drug is dacarbazine, fluoruracil or mitomycin.

• Do not apply any pressure to the area. Avoid bandages.

• If there is inflammation or pain, topical or systemic corticosteroids (hydrocortisone, dexamethasone) can be administered.

• If there is a significant peeling of the skin or ulceration that could cause an infection, antibiotic treatment can be started bearing in mind that the most frequent causative microorganisms are the Gram (+) cocci.

The material mentioned above can be found in the extravasation kit of each centre.

ANNEX 8. HEALTH SURVEILLANCE OF WORKERS EXPOSED TO HD.

1. INTRODUCTION

As determined in section 3 of article 37 of the Royal Decree approving the Regulation of Prevention Services, the employer shall ensure adequate and specific monitoring of the health of workers in relation to the risks of exposure to carcinogens and mutagens, carried out by competent health personnel, as determined by the health authorities in the Guidelines and protocols issued.

The Law on the Prevention of Occupational Hazards configures health surveillance as a right of the worker and an obligation of the employer, the general rule being its voluntary nature. Therefore, it provides for the establishment of adequate and specific medical surveillance in relation to exposure.

Currently there is no Protocol of the Interterritorial Council of the National Health System for specific health surveillance of personnel exposed to dangerous drugs. Bearing this in mind, the present health surveillance protocol is derived from the regulatory framework regarding the Prevention of Occupational Hazards, which assumes that the health examinations carried out on workers must be periodic, specific to the risks derived from work, with the informed consent of the worker and must not be used for discriminatory purposes or to the detriment of the worker. It is carried out to give coherence and homogeneity to the objectives and contents of this health activity within the context of a certain occupational risk, with the aim of implementing a health surveillance model at work carried out in exposure to HD, so that it is effective in prevention.

By having uniform criteria, the Prevention of Occupational Risks Service will not only be able to achieve the objective defined in the General Health Law, "to monitor the health of workers in order to ensure early detection and individualisation of risk factors and deterioration that may affect their health", but will also have a positive impact on the prevention of illness and the promotion of workers' health.

Monitoring the health of personnel in contact with these medicines not only aims to control their health condition, but also to assess compliance with preventive measures (use of gloves, face masks, gowns, cabinets, etc.) and encourage their application.

Health workers who prepare, administer, transport HD, or dispose of related waste, face risks to their own health such as skin disorders, reproductive disorders, and others. International and national institutions related to Occupational Health and Safety recommend that employers establish a medical surveillance program as part of a comprehensive prevention program that also minimises worker exposure through engineering controls, good work practices and personal protective equipment (PPE), and that educates about working with HD.
This surveillance includes the collection and interpretation of data to detect changes in the health of workers exposed to hazardous substances. The elements of a medical surveillance programme are used to establish an initial baseline of workers' health in order to provide proper monitoring of their health in relation to possible exposure to hazardous agents. This information can be used to identify and correct possible defects in prevention procedures leading to disease. Early identification of health problems can also benefit the workers individually.

Therefore, the workers who should be included in the health surveillance program are those who through their work may be directly exposed to HD and/or with hazardous waste or waste from a patient treated with these medications.

The exposure to HD can occur via inhalation, contact or absorption through the skin, ingestion or injection, with the most likely avenues of exposure being inhalation and contact/absorption through the skin, although other ways such as accidental ingestion by hand-to-mouth contact and accidental injection through needle pricks or injuries with sharp objects must also be considered.

The exposure of workers to HD has been assessed by studying biological markers of exposure, not having found any that is an indicator of exposure or a prognostic factor of health effects.

The symptoms that could affect workers are potentially all those that affect patients undergoing treatment with these drugs, some of which deserve special mention:
- Hypersensitivity to these drugs.
- Pulmonary toxicity.
- Alterations in platelet function.
- Cardiotoxicity.
- Neurotoxicity.
- Miscarriages, foetal malformations and infertility.
- Leukaemia.
- Neoplasms.
- Hepatotoxicity.

2. PERSONNEL FOR WHICH IT IS INTENDED

All workers who may be exposed to HD throughout their life cycle, including from its reception and transport to its disposal as waste, including its preparation and administration in the centre or at the patient's home, and the treatment of the excreta of treated patients, will be subject to Health Surveillance in accordance with this protocol.

All personnel in the field of action of the SESCAM SPRL who, through RA, have been identified as at risk of exposure to hazardous drugs are considered exposed personnel. For the employees of contracted companies it is necessary to apply art. 24 of the LPRL in relation to Coordination of Business Activities.

3. CONTENTS OF THE HEALTH SURVEILLANCE

Correct monitoring of the health of exposed workers is essential.

The objective of Health Surveillance is to avoid/minimise adverse effects on workers exposed to hazardous substances. By identifying and correcting possible failures in exposure prevention (identified through health surveillance), exposures can be limited and adverse health outcomes can be prevented in other workers (primary prevention).

Identifying the first reversible biological effects will help reduce or eliminate exposure and limit other negative side effects on the health of individual workers (secondary prevention).

Health surveillance is a second line of defence by increasing the protection offered by engineering controls, other administrative controls, work practice controls, personal protective equipment (PPE), and worker education about the hazards posed by the materials with which they work or with which they may come into contact in the course of their work.

3.1 Elements of a health surveillance programme.

Different issues should be considered when developing a health surveillance programme for workers exposed to HD. The first is to identify workers who are potentially exposed to HD based on their duties.

The second is how to apply health surveillance that is appropriate for the exposure because different types of HD differ in their ways of acting and may affect specific organs.

Since health workers are generally exposed to many, no single biological indicator is appropriate for all of these substances. Companies and organisations should use the information obtained through health surveillance to assist affected workers, and to identify and correct any system failures that may result in harmful exposures.

It should be indicated whether it is an initial health examination (when entering the workplace), periodic (recommended every one, two or three years depending on the probability of risk of exposure), following acute accidental exposure, risk assessment during pregnancy, breastfeeding or any other situation that may make the worker especially sensitive or after prolonged temporary incapacity.

3.2 Clinical History:

- Work centre details:
  - Job name and seniority.
  - Products used.
  - Number of hours of exposure per day.
  - Means of prevention used (gloves, face masks, gowns, cabinets, etc.)

- Family background:
  - History of neoplasms.
  - Liver alterations.
  - History of disabilities related to chromosomal alterations.
- Personal background:
  - Previous radio or chemotherapy treatments.
  - Recent radiological tests.
  - Drug allergies.
  - Impaired liver or kidney function.
  - Congenital or acquired immunodeficiencies.
  - Reproductive background: pregnancies, miscarriages, foetal alterations and congenital malformations in children.
  - Habits: tobacco consumption, consumption of other stimulants (medications, caffeine, stimulant drinks, drugs), sun exposure, hobbies (DIY), use of cosmetic products or hairdressing (nail polish, dyes, etc.).
- General questions by organs and systems:

a/ General symptoms:
- Asthenia.
- Anorexia.
- Weight loss.
- Night sweats.
- Fever.
- Others:

b/ E.N.T.
- Vertigo.
- Nasal obstruction.
- Dysphagia.
- Odynophagia.
- Others:

c/ Ophthalmology.
- History of eye injuries.
- Use of intraocular lenses or contact lenses.
- History of ocular paralysis.
- History of retinal detachment.
- Colour blindness.
- Cataracts
- Others:

d/ Cardiorrespiratory.
- Cough.
- Chest pain.
- Palpitations.
- Dyspnea.
- Orthopnea.
- Others:

e/ Gastrointestinal.
- Pyrrhosis, reflux.
- Intestinal habit: Diarrhoea/constipation.
- Abdominal pain.
- Blood in faeces.
- Others:

f/ Genitourinary.
- Dysuria.
- Hematuria.
- Polyuria.
- Nocturia.
- Others:

g/ Gynaecological and Obstetric.
- Menarche.
- Date of last period.
- Menstrual periodicity.
- Duration.
- Vaginal discharge.
- Menopause, treatment with HRT.
- Obstetric history: Pregnancy and lactation (specify previous and current, if any).
- Others:

h/ Locomotive.
- Joint pain.
- Swelling.
- Others:

i/ Skin and mucous membranes.
- Injuries with/without pruritus.
- Rashes.
- Others (skin hyperpigmentation, skin or mucous irritation):

j/ Neurological.
- Paresthesias.
- Dysesthesias.
- Motor impairments/limitations.
- Headaches.
- Loss of consciousness.
- Others:

- Clinical examination.

a/ Physical examination.
- Attitude, (anxiety and overall observation data).
- Race, height and weight.

b/ Exploration.
- Skin, hair, nails, mucous membranes.
- Eyes.
- Ears, mouth, pharynx.
- Neck: thyroid.
- Adenopathies.

c/. Cardiorrespiratory examination:
- Cardiovascular:
  - · Blood pressure.
  - · Auscultation: Murmurs, rubs, others.
  - · Arterial: Peripheral pulses, carotid pulses.
  - · Venous: Varicose veins.
  - · Others:
- Respiratory: Auscultation.

h/ Abdominal examination: with special interest win liver alterations.

i/. Examination of the locomotor system:
- Spinal column.

- Extremities: deformities/atrophy, asymmetry, amputations.
- Joints: limited movement, deformity.

j/ Neurological examination: gait, reflexes, sensitivity.

- Complementary tests:

a/ Blood test: Blood analysis includes haematological and biochemical parameters:

- Haematological parameters:
  - · Haematids.
  - · Haematocrit.
  - · Haemoglobin.
  - · Mean corpuscular volume.
  - · Mean corpuscular haemoglobin.
  - · Mean corpuscular haemoglobin concentration.
  - · Platelets.
  - · Mean platelet volume.
  - · Leukocytes.
  - · Leukocyte formula and count.
  - · Sedimentation rate (1st hour).
- Biochemical parameters.
  - · Glucose.
  - · Alkaline phosphatase.
  - · LDH.
  - · Glutamic oxalacetic transaminase.
  - · Glutamic pyruvic transaminase.
  - · Gammaglutamyltransferase.
  - · Total bilirubin.
  - · Direct bilirubin.
  - · Cholesterol.
  - · Cholesterol-HDL.
  - · Triglycerides.
  - · Urea.
  - · Creatinine.
- Serology: (Biological Agents Protocol):
  - · Hepatitis B.
  - · Hepatitis C.
  - · HIV.

b/ Urine analysis: biochemical and morphological.

According to medical criteria, and in order to assess exposure with more parameters (always taking into account the information provided by the RA) the following are determined:

- TSH.
- Albumin/Globulins Coefficient.
- Total proteins.
- Albumin.
- Proteinogram.
- Immunoglobulins.

and the additional parameters deemed appropriate in each case (e.g.: Reticulocytes, Granulocytic Alkaline Phosphatase, etc.)

c/ Complementary tests: generally the following will be carried out:

- Electrocardiogram.
- Spirometry, the first time the worker comes to perform Health Surveillance, and as long as the hazardous drug handled can affect lung function.
- Vision Control.

If considered necessary, in the presence of dermal lesions, interconsultation with the Dermatology Service will be carried out.

d/ Specific biological indicators: no particular biological indicator is appropriate for all hazardous drugs. It is necessary to obtain information from the safety specifications and to select those specific studies that provide information on the toxicity of the drug to which staff is exposed, medical criteria and depending on the type of exposure.

3.3 Evaluation of results

All results of the health surveillance programme should be examined for trends that may indicate changes in health due to exposure to HD. If changes in the worker's health are found during follow-up examinations, the following measures should be taken, through and with the support of the appropriate Services and, where appropriate, with the outsourcing of measures or actions:

1. Analyse the current protection measures that have already been established:

• Engineering controls (biological safety cabinets of the class or type necessary to prepare drugs, robotic systems, ventilation, transfer apparatus in closed systems and closed intravenous systems).

• Compare the practice of controls with recommended standards.

• Perform environmental sampling if analytical methods are available.

• Standards for the use of personal protective equipment (PPE) and that employees comply with these standards and use PPE.

• Availability of suitable PPE such as gloves for use with HD, waterproof gowns and respiratory protection.

2. Verify that all controls are in adequate working condition and check that the worker complies with existing standards or new ones that come into force.

3. Develop an action plan to prevent further exposure of workers.

4. Ensure mutual confidential communication between the worker and his or her occupational health unit regarding notifications:

• by any worker who wants to talk to the occupational health unit about changes in his or her health condition such as pregnancy or a chronic illness; or

• by the occupational health unit when workers are informed of the finding of an adverse health effect and follow-up instructions.

5. Provide continuous health surveillance to all workers at risk in order to ascertain whether the new plan is effective.

In the prevention of workers exposed to antineoplastics or any other hazardous drug, although, from the point of view of Industrial Hygiene, the incorporation of regulated methods of sampling techniques and analysis for the assessment of certain cytostatics (Cisplatin, 5 fluoracil, etc.) is a step forward in risk assessment and the adoption of preventive measures, the Occupational Physician does not have BEIs or sufficiently sensitive and specific indicators for the biological control of workers.

Therefore, the following considerations should be taken into account when assessing the individual risk of each worker:

The description of the specific procedure to be carried out (systemic or local use and application technique, work equipment, etc.) that could generate exposure to certain drugs (specific pharmacodynamics of each product).
In most of the studies published so far, there are no reference values (no assigned exposure limit value, ELV) to establish safe situations.

In general, there are no regulated methods of sampling and analysis techniques available.
The various drugs can penetrate through different avenues. Complementary tests are aimed at detecting risk factors or health conditions that may increase the risk for the worker exposed to these medicines (HSW), as no specific tests are available.

4. PERIODICITY OF THE HEALTH SURVEILLANCE

Health Examinations of workers exposed to dangerous drugs should be performed (Art. 37 RSPRL):

• At the beginning, after hiring and incorporation into the job (initial health examination).

• Periodically, during the working life in that job position (periodic health check). The regularity will depend on the magnitude of the worker's risk of exposure.

In general, the periodicity will be established according to the following outline:

In general, it will not be less than three years, and will always be ANNUAL in the workers in fertile age with VERY HIGH or HIGH risk of exposure, except for individual situations at the discretion of the occupational physician. It is not considered that a lower periodicity (greater frequency of health surveillance) implies a better coverage of the health risk, provided that the basic measures of collective and individual protection are strictly complied with and the worker has adequate technical training in the handling of hazardous drugs.

The risk has been considerably reduced since the implementation of measures that reduce environmental

PROBABILITY OR RISK OF EXPOSURE	PERIODICITY
Very high	Annual
High	
Moderate	Biennial
Very high	Annual
High	

pollution, fundamentally the use of closed systems and Luer lock connections, as well as the implementation of other measures, such as waste disposal systems with thermosealing.

• After acute accidental exposure to a hazardous drug (HD1 HD2), the severity and type of exposure (route of entry), the presence of acute respiratory or skin symptoms, and the need for therapeutic and/or aftercare measures will be assessed.

– The most common acute effect is local irritation (skin, eyes and mucous membranes). Some cases with allergic reactions and/or blistering effect have also been observed.

– The symptoms derived from acute exposure (either by direct contact or inhalation) described in the literature are: abdominal pain, nausea and vomiting, cough, dizziness, headaches and dermatitis.

– It is important to declare and record any type of incident or accident (see table).

• After prolonged absence from work for health reasons, in order to detect Highly Sensitive Workers (HSW) in relation to the illness that caused the absence from work.

• At the time of leaving the handling work (by dismissal, retirement or change of position), with a report by the Occupational Physician.

HANDLING FREQUENCY/PROBABILITY	High Risk of Danger to OHS	Moderate Risk of Danger	Low Risk of Danger
HIGH FREQUENCY	• Preparation of drugs in safety cabinet by Nurses and Hospital Pharmacy Technicians (manual, intensive and habitual task, consider rotation of tasks). • IV/Parenteral administration of drugs by Day Hospital Nurses. Very High NICOSEND	• Parenteral IV administration by Nurses with safe work equipment that prevents aerosols (use of closed systems, safe connections, waste collected in thermosealed containers., etc.) High NICOSEND	• Robotic preparation controlled by Nurses and Hospital Pharmacy Technicians (usual robotic task) Moderate NICOSEND
MODERATE FREQUENCY	• Auxiliary staff (Pharmacy Nursing Auxiliary Care Technician, Pharmacy Technicians) in the preparation and cleaning of cabinets (intensive and habitual task, although they tend to rotate tasks within the Pharmacy Service). • IV/parenteral administration by hospitalisation nurses (oncology, haematology, etc.). • Maintenance staff, actions regarding exhaust duct (changing of HEPA filters) High NICOSEND	• Auxiliary staff (Pharmacy Nursing Auxiliary Care Technician) in the reception and storage of hazardous drugs. (They usually rotate tasks). • IV/Parenteral Administration by hospitalisation nurses by means of Closed Systems (avoiding aerosols, but not splashes if the cycle has to be interrupted). • Operating room personnel (Nurses, Surgeons) who work in the surgical field (closed) in the HIPEC or where dangerous drugs are used. • Urology nurses who perform bladder instillations with Mitomycin C or similar. • Nursing Auxiliary Care Technicians from ICU and oncohaematological hospitalisation units or other hospitalisation units (patients with systemic CTX) that carry out excreta collection without anti-splash systems (splitting bags in order to empty as an example of bad practice, etc.). Moderate NICOSEND	• Orderlies or porters in charge of transport and/or storage. • Auxiliary personnel (Pharmacy Nursing Auxiliary Care Technician) in the handling and counting of hazardous oral drugs (in tablets) (single dose). They usually rotate tasks. • Cleaning personnel in charge of the collection of accidental spillages in wards, operating theatres, day hospital and areas where dangerous drugs are administered. • Nursing Auxiliary Care Technicians from ICU and oncohaematological hospitalisation units or other hospitalisation units that collect excreta from patients with systemic CTX, with anti-splash systems (bags with cap/valve for emptying, etc.). Low NICOSEND

HANDLING FREQUENCY/PROBABILITY	High Risk of Danger to OHS	Moderate Risk of Danger	Low Risk of Danger
LOW FREQUENCY	• Midwives who administer MTXT in treatment of ectopic pregnancy or any other hazardous drug. • Personnel from Interventional Radiology that intervenes in techniques with HD1 or 2. Moderate NICOSEND	• Hospital pharmacists who may occasionally handle cytostatic/hazardous drugs when performing quality controls. • Operating room personnel (anaesthetists, other staff) who remain in the operating room during HIPEC or any other technique with hazardous drugs. • Nurses from public health care homes/Primary Care and/or Rheumatology/dermatology offices that administer MTXT in PRELOADED SYRINGE (without aerosolisation). High NICOSEND	• Pathological A. Autopsies personnel (Orderly or porter, PCT, Specialists, etc.) in case of autopsy of an oncology patient with systemic CTX in the last 72h. • Personnel in Services where cytostatic/dangerous drugs are handled (Hospital Pharmacy, Daytime Pharmacy, Ophthalmology and CTX eye drops) that very rarely can be exposed incidentally (Oncologists, Administrative personnel, Other personnel). Very Low NICOSEND

• Workers at reproductive risk should contact the health area of their Prevention Service.

Specific measures in relation to the level of exposure:

The handling of hazardous drugs (HD1, HD2) shall be considered as potentially dangerous and if it cannot be replaced by another less dangerous product, measures must be taken to avoid exposure.

RD 665/1997 on the protection of workers against risks related to occupational exposure to carcinogens applies in the case of most cytostatic compounds (HD1), since their mutagenic and carcinogenic potential is perfectly established. However, not all antineoplastic agents (HD1) have a proven mutagenic and/or carcinogenic effect, which is why decisions regarding the health surveillance of exposed workers (frequency of health examinations, suitability, etc.) are made based on the magnitude of the risk of exposure. We consider the same criterion applicable to exposure to other hazardous drugs (HD2).

Estimation of the Level of Health Consequences in the event of Unwanted Exposures (NICOSEND):

NICOSEND: Estimation of the magnitude of possible health damage that could occur during unwanted exposure, and which is directly proportional to two factors: the frequency of manipulation of antineoplastics in the workplace and the degree of complexity of the task/s performed.

Following the INSHT risk level assessment methodology, the authors of the "Best Practices Guidelines for Workers Exposed to Cytostatic Substances."(AMMTAS 2014) established a model for estimating the LEVEL OF HEALTH CONSEQUENCES IN THE EVENT OF UNWANTED EXPOSURE (NICOSEND), which is directly proportional to the FREQUENCY OF HANDLING of antineoplastics in the workplace, and to the POSSIBILITY OF HARM according to the complexity of the task, generically considering that zero risk does not exist and these exposures are not always well controlled and reported. We consider that this risk estimation model is applicable to the exposure to hazardous drugs, since the objective is the same.

The objective is to obtain an assessment model that allows decisions to be made in Health Surveillance (in terms of periodicity of health examinations, suitability and recommendations for adaptation).

This model is not intended to replace the method of Risk Assessment (RA) particular to each workplace (its purpose is to prioritise prevention measures in terms of collective and individual safety), which should always be consulted (per job position) when assessing the worker, as it will clarify the frequency of exposure and the dangerousness in each particular case.

For this reason, and so as to avoid confusion, the authors did not use the Risk Level (RL) nomenclature that is used in the RA that follow the INSHT assessment method (Trivial, Tolerable, Moderate, Important and Intolerable RL), as they did not intend to correct avoidable safety risk situations, but, assuming that all collective and individual prevention measures are applied in each case, they considered the hypothetical danger

of unwanted accidental exposure, and always estimating the most unfavourable situation, especially in HSW. It is the same situation in which we find ourselves, so we consider that the procedure should be the same.

There are 5 NICOSEND variables:
- Very High.
- High.
- Moderate
- Low.
- Very Low.

The magnitude of the NICOSEND has been estimated in a simplified manner to facilitate health surveillance, but in reality it depends on multiple factors:

- Frequency of use (time and intensity of exposure).
- Danger associated with the task (probability of accidental exposure).
- Toxicity of the drug/s being handled (carcinogenic and/or teratogenic effects).
- Ways of exposure (airborne by inhalation or cutaneous by direct accidental contact with skin and mucous membranes).
- Possibility of environmental contamination (practically non-existent with the use of closed systems).
- Biological and pathological conditions of the worker.

5. SUITABILITY AND DERIVED ACTIONS

"Work suitability": to make a medical judgement of suitability between a person's health conditions and the characteristics of a particular job (specific protocols). This judgement must be based on the non-existence of psychophysical deficiencies that prevent the normal performance of the work, and on the detection of individual characteristics that pose a risk to the worker or others. These values must be taken into account when determining whether the post has adequate working conditions. The following conclusions can be drawn from the results of the health examination carried out according to this specific protocol for workers exposed to hazardous drugs:

Suitable:
The worker presents no limitation or contraindication to fully perform all the tasks assigned to his/her position, complying with collective and individual regulatory protection measures and with adequate technical training in the handling of dangerous drugs. Sometimes it is necessary to make a specific recommendation on additional protection or precautionary measures: Suitable with recommendations..

Suitable with limitations:
The worker has a limitation/contraindication and/or is under medical study and surveillance in order to determine his/her ability to fully perform all the tasks assigned to the job position, but in general can perform his/her activity, with limitations to specific tasks. This would include, inter alia, workers with significant dermatological pathology (with difficulty in occlusion of lesions in exposed areas, worsening of lesions by repeated hand washing and use of PPE, etc.) or with severe hepatopathies or chronic nephropathies, in workplaces with moderate or low NICOSEND, according to the criteria of the occupational physician.
The action to be taken involves adapting the job to avoid those tasks that involve the risk of inhalation or contact with hazardous drugs during unwanted exposure (e.g. cleaning up spillages).

Not suitable:
A worker who has health conditions that incapacitate him/her for work, either because it is impossible for him/her to perform the work due to the health condition, or because of a special sensitivity (Highly Sensitive Worker -HSW- due to specific risks of the job) that makes the worker vulnerable even in the safest working conditions, and the severity of an undesired exposure is significant, should that person remain in the job position.

- Allergic to hazardous drugs (if there may be a risk of inhalation or contact with them, during unwanted exposure). Moderate, high or very high NICOSEND (for the rest, a task limitation would suffice).

- Workers with severe, extensive dermatological pathology (with difficulty in occlusion of lesions in exposed areas, worsening of lesions by repeated hand washing and use of PPE, etc.) in positions with a high or very high NICOSEND.
- Women with a history of recurrent miscarriages, of childbearing age and with an effective willingness to have children (with a report from their gynaecologist responsible for their treatment) should avoid the risk of inhalation or contact with dangerous drugs during unwanted exposure, moderate, high or very high NICOSEND (in the rest, a limitation or adaptation of tasks could be considered).

- People with high exposure to ionising radiation (personnel working regularly with cytostatic agents should not be exposed to ionising radiation exceeding 15 mSv per year). Workers with recent exposure to ionising radiation through treatment (radiotherapy) or diagnostic tests (gammagraphy with radioactive isotopes, etc.) should be avoided, with individual assessment of received doses, risk of inhalation or contact with dangerous drugs, during unwanted exposure in moderate, high or very high NICOSEND (in the rest, a limitation or adaptation of tasks could be considered).

- Employees who are immunosuppressed and/or who have received previous cytostatic or immunosuppressive treatments: individually assess the current state of immunosuppression and the risk of inhalation or contact with HD during unwanted exposure. Not suitable for moderate, high or very high NICOSEND (for the rest, an adaptation or limitation of tasks could be considered).

- Other situations of high sensitivity, at clinical criteria, to be assessed individually.

The action to be followed will be the CHANGE OF JOB POSITION, either permanently or temporarily (when the duration of the process that gives rise to the non-suitability, is limited or of an evolutionary nature and a health recovery is expected, as well as any person who presents any other situation of susceptibility of a temporary nature, such as, for example, the situation of pregnancy or breastfeeding).

Safe work standard no. 15
Preparation of hazardous drugs

INTRODUCTION

Hazardous drugs (hereinafter HD) are those that present one or more of the following six characteristics in humans or animals:

1. Carcinogenicity.
2. Teratogenicity or other developmental toxicity.
3. Reproductive toxicity.
4. Evidence of severe organ toxicity or other low-dose toxicity in animal specimens or in treated patients.
5. Genotoxicity.
6. Structure and toxicity profiles of new drugs that have been determined to be dangerous according to the above criteria.

The National Institute for Occupational Safety and Health (NIOSH) classifies HD into:

- Group 1: antineoplastic drugs.
- Group 2: non-antineoplastic drugs that meet at least one of the above criteria.
- Group 3: drugs which present a risk to the reproductive process and which may affect men and women who are actively trying to conceive, and women who are pregnant or breastfeeding, but which do not pose a risk to other staff.

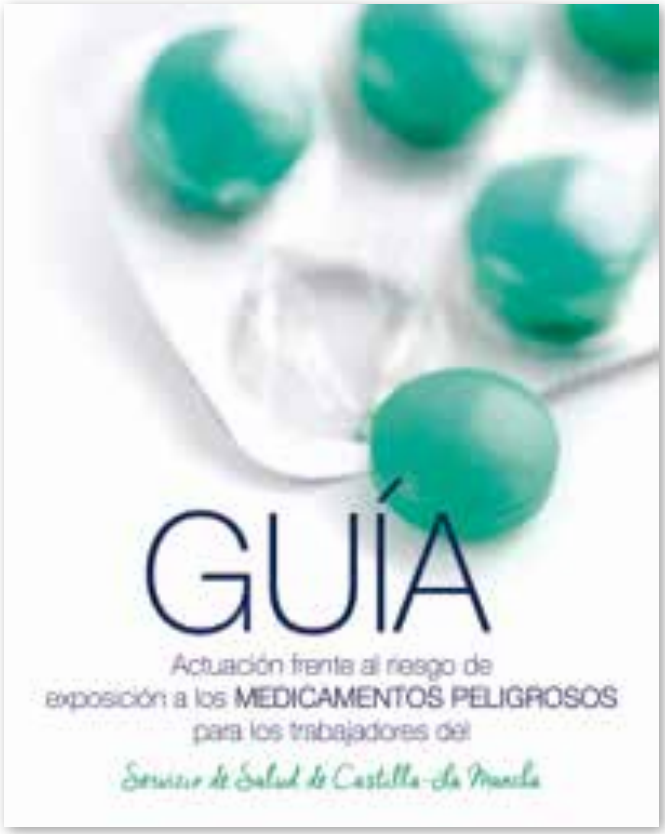
In September 2016, the National Institute for Occupational Health and Safety published the Technical Document: Hazardous drugs. Prevention measures for their preparation and administration.

This document specifies recommendations on handling, associated preventive measures and individual protection equipment to be used (information available at http:/ infomep.inssbt.es)

The "Guidelines for action on the risk of exposure to hazardous drugs for health service workers in Castile-La Mancha" includes specific actions in this respect in our field.

RECEPTION AND STORAGE OF HAZARDOUS DRUGS

Personal Protective Equipment (PPEs) to be used for the reception and storage of HD: gown and sanitary gloves.



- The reception and storage of HD in the Pharmacy Services will be carried out in the general storage area of the Pharmacy (adapted for this purpose).

- A list of HD and a spill kit will be available in a visible place with instructions for use for personnel in case of an incident.

- The transport to the final storage area should be carried out immediately after receipt, with the least possible delay, using extreme caution so as to minimise the risk of breakage.

- The HD should be stored, whenever possible, in a specific place separated from the rest of the drugs and clearly marked in areas of infrequent movement of material and people.

- The HD storage areas shall be arranged in such a way as to minimise the risk of falling or breakage (preferably with shelves with non-slip surfaces and ledges).

PREPARATION OF HAZARDOUS DRUGS

The preparation is the process by which, based on the commercial presentation of the HD, the prescribed doses are pre-packaged for its administration to patients. It is the phase of greater relative risk if adequate prevention and protection measures are not adopted.

To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service in order to reduce the number of workers exposed.

- Preparations of Group 1 HD and Group 2 parenteral HD must be carried out in the Pharmacy Services. Other HD should also preferably be prepared in that Service during its opening hours.

- HD preparation activities should be carried out by trained and qualified personnel.

- All preparation activities should be carried out following clear, written instructions.

- The preparation area of these HD must guarantee both the safety of the preparation for the patient and the safety of the worker who prepares it.

Working rules in the Preparation Area of sterile HD.

PPE recommended for the preparation of sterile HD: gown, shoe protectors, FFP3 face mask, cap and double sanitary gloves.

Antechamber and airlock:
• Aseptic washing of hands and forearms.
• Fitting of corresponding PPE (once on, do not leave the antechamber).
• The products needed for each preparation will be prepared, checking possible defects such as expiration date, particles in suspension or changes in colour. Once checked, they will be decontaminated with 70º alcohol and placed on a tray that will be taken to the clean area.

Preparation area:
• This area will meet the specifications of a "clean room" controlled environment room. The Class II Biological Safety Cabinet (BSC) is located within this preparation area.

General work rules in the biological safety cabinet.

1. It is recommended that the cabinet should remain in operation with the fan running 24 hours a day, 7 days a week. If the cabinet is not in operation 24 hours continuously, it must be put into operation at least 15 to 20 minutes before any handling is carried out so as to stabilise the air circulation. During this time the UV light will be on.

2. When the cabinet is in operation, activity inside the room should be kept to a minimum in order to avoid drafts that could influence the flow of the exhaust duct. The opening and closing of the access door to the room should be avoided as much as possible.

3. The work surface shall be covered with a sterile cloth absorbent on top and laminated underneath to collect any accidental spills that may occur. The cloth should be changed after each work session or when a spill occurs.

4. All material needed for the work should be carefully cleaned with antiseptic solution (70° alcohol) before being introduced into the cabinet.

5. All material will be inside the cabinet before work begins and there will be a waiting time of 2 to 3 minutes to restore flow conditions.

6. Do not block the air inlet or outlet with paper or objects

7. A sharp object container for cytostatic waste and an empty vial or closed bottle should be placed inside the cabinet, where the excess solutions generated during preparation will be placed.

8. Do not work or place objects less than 8 cm from the sides and 10 cm from the front of the cabinet. All handling must be carried out in the area where there is a flow current.

9. Distance must be kept between the products to be handled in order to maintain a relative flow current, with sterile products in the centre and non-sterile products on the outer side.

10. The movements of the operator's arms, inside and outside the cabinet, must be minimal to maintain the integrity of the negative pressure in front of the operator trying to follow the air flow.

11. Prepared and ready to use HD must be perfectly identified, indicating on the label, at least, the format and dose prepared, and the method of administration, expiry and storage conditions and the patient for whom it is intended.

General rules for cleaning and disinfection of the biological safety cabinet.

Cleaning and disinfection should be carried out in the following situations:

- Before starting any work in the cabinet.
- Once the work in the cabinet has been completed.
- Whenever the work programme changes.
- In case of spills.
- Before carrying out a mechanical or biological control test in the work area.

- The cabinet fan will be running.
- Use disposable sterile cloths slightly dampened with disinfectant solution (70° alcohol).
- Clean with soapy water and immediately apply a disinfectant (70° alcohol).
- Do not get the HEPA filter wet while cleaning the cabinet.
-While cleaning the contaminated area, the above-mentioned protective equipment must be worn.
- All material used for cleaning must be treated as contaminated waste.

Rules for working in the Preparation Area of non-sterile HD.

PPE to be used for the preparation of non-sterile HD: as a minimum, double loves, gown and FFP3 face mask (the risk assessment will determine the additional protective equipment, depending on the working conditions and the types of preparations).

To the extent possible and depending on the functional capacity of the Pharmacy Service, attempts will be made to centralise the activities of greatest risk (preparation and fractionation) in the Pharmacy Service, thus reducing the number of workers exposed.

Preparation of unitary doses of oral suspensions of commercialised HD.

If the dispensation is carried out in unitary doses, they will be prepared in the Pharmacy Service in the Class I BSC and with the specified PPE.

Fractionation or pulverisation of solid pharmaceutical products.

The fractionation or pulverization of HD tablets should be avoided, so alternatives should always be sought (change of medication, commercialised liquid pharmaceutical forms, adaptation of doses to commercial presentations, etc.). If this were not possible, the handling of group 1 and 2 HD will be carried out in the Pharmacy Service in the Class I BSC with the appropriate PPE.

In the case of centres that do not have a Pharmacy Service, the handling will be carried out with the PPE and always taking into account the recommendations of the Prevention of Occupational Risks Service.

Preparation of non-sterile HD Master Formulas.

Preparation of non-sterile HD Master Formulas will be carried out in the Pharmacy Service. They will be prepared at least in Class I BSC following the Standardised Preparation Procedures.

The Pharmacy Service must specify in the Standardised Preparation Procedures of each master formula the protection guidelines established once the risks have been assessed by the Prevention of Occupational Risks Service.

HIGHLY SENSITIVE WORKERS

It is recommended that HD 1 and 2 not be handled by workers in the following groups:

- Women who are pregnant or breastfeeding.
- Allergic to cytostatic agents and/or with dermatological pathology.
- Women with a history of miscarriages at childbearing age.
- Personnel professionally exposed to ionising radiation (more than 15 mSv/year).
- Personnel who have previously received cytostatic or immunosuppressive treatments.
- Staff with a previous history of neoplasia.
- Immunodeficiencies.

It is recommended that HD3 not be handled by workers at risk to the reproductive process (men and women who are actively trying to conceive), and women who are pregnant or breastfeeding; there is no risk to other staff.

DISPOSAL OF GENERATED WASTE

HD1 Waste.

This group of wastes corresponds exactly with the one defined in the European list of wastes as cytotoxic and cytostatic medicinal waste.

The following are considered cytostatic waste:

- Remains of cytostatic drugs generated in their preparation and administration.
- The material used to clean the areas fro handling, particularly the preparation and administration of cytostatic drugs.
- The material used in the preparation and administration of cytostatic drugs (needles, syringes, bottles, bags and infusion systems).
- Protective equipment for handlers of cytostatic drugs (disposable protective clothing, gloves and protective breathing masks).
- Material stemming from the treatment of accidental spills, including those of excreta during the active life period of the cytostatic drug.

Its segregation will be carried out in official, rigid, single-use blue containers or the one designated by SESCAM, as the case may be.

HD2 and HD3 Waste.

Waste containing traces of HD2 and HD3 (vials, systems, ampoules, vials, syringes, etc.) will be disposed of in the blue container for hazardous drug waste, selecting the smallest possible container in order to adjust its capacity to the volume of waste production.

The PPE used for the administration of HD2 and HD3 will be disposed of as urban waste, except for evident contamination (splattering, spillage, etc.). The PPE used in preparation will be disposed of in the container for hazardous drug waste.

The material used for cleaning spillages (absorbent material, PPE, etc.) will be disposed of in the blue container for hazardous drug waste.

PROCEDURE FOR ACCIDENTAL EXPOSURE

Any professional who suffers accidental exposure as a result of a spill, accidental puncture or any other accident with HD must go to the corresponding Prevention of Occupational Risks Service (SPRL) for their department for assessment and monitoring. They shall also fill in and register the work accident/incident report, except in urgent cases, in which case the middle manager or Head of Service, as appropriate, shall do so afterwards.

The health care worker may be accidentally exposed to HD in a number of ways:

1. Exposure by inhalation or ingestion.
In case of exposure by inhalation and/or ingestion, possible symptoms should be monitored and any abnormal symptoms should be reported to the immediate superior and to the SPRL.

2. Exposure without contact to skin or mucous membranes:
Wash hands with soap and plenty of water for ten minutes and put on new PPE.

3. Exposure in contact with undamaged skin:
- Immediately remove contaminated PPE and/or clothing.
- Wash affected skin area immediately with mild, non-antiseptic soap and plenty of water for at least ten minutes. Shower if necessary.
- If the affected area is lacerated or irritated, it should be examined by a doctor.
- The affected area should be monitored by a doctor. Do not use hand cream or moisturisers, as they may increase the absorption of the drug.
- Dispose of contaminated PPE in the corresponding container and/or store clothes in a bag and dispose of them according to the Centre's Cleaning Protocol.

4. Exposure in contact with eyes or mucous membranes:
- If the injured person wears contact lenses, remove them immediately.

- If substance has splashed in eyes, wash the conjunctiva with plenty of warm water for fifteen minutes and then apply 0.9% saline solution. Do not rub eyes.
- Seek immediate medical attention from the corresponding doctor.

5. Cuts or punctures with contaminated needle or glass:

In the event of an accidental cut or puncture wound:
- Immediately remove contaminated PPE and/or clothing.
- Rinse the area with plenty of warm water. Let the blood flow freely. Do not press on the wound area.
- Clean the area thoroughly with warm water and mild soap for at least ten minutes.
- If contact occurs by accidental inoculation (needle puncture): Do not remove the needle, remove only the syringe and with a new syringe aspirate the contents of the injected HD. If the needle has been moved, insert a new one at the point of injection and aspirate the medication.

PROCEDURE IN EVENT OF SPILLAGE OF HD INSIDE BSC

- Seek immediate medical attention from the corresponding doctor.
- Any spillage in the cabinet must be cleaned immediately.
- If the volume of the spillage exceeds 30 ml or the contents of a vial or ampoule of medicine, the spillage kit will be used.
- For larger spills, additional decontamination of the cabinet is required after initial cleaning.
- Open windows and immediately mark out the area, maintaining airflow.
- Put the personal protective equipment on in the following order: shoe protectors, first pair of gloves, cap, waterproof gown, high filtration face mask, protective goggles and a second pair of gloves on top of the gown.
- If there are pieces of glass, collect them with the tweezers (or dustpan and brush), and place them inside the sharp objects container, which will then be disposed of in the cytostatic waste bin.
- In case of liquid spillage, cover it with absorbent cloths and let them soak it up. Also use pads or absorbent material to prevent the spillage from spreading.
- In the case of solid waste, damp cloths or pads should be used to help with collection.
- If the spill affects the HEPA filter, the use of the cabinet must be interrupted and the cabinet sealed with plastic until the HEPA filter is replaced by authorised, suitably equipped personnel, the filter being treated as contaminated material and placed in the cytostatic waste container.
- Wash hands and dispose of gloves after cleaning.

Signature

Received by
Name and surnames:.....
Date:.....

For any queries or additional information please contact the Prevention Service or manager.

Safe work standard nº 16
Administration of Hazardous drugs

INTRODUCCIÓN

Hazardous drugs (hereinafter HD) are those that present one or more of the following six characteristics in humans or animals:

1. Carcinogenicity.
2. Teratogenicity or other developmental toxicity.
3. Reproductive toxicity.
4. Evidence of severe organ toxicity or other low-dose toxicity in animal specimens or in treated patients.
5. Genotoxicity.
6. Structure and toxicity profiles of new drugs that have been determined to be dangerous according to the above criteria.

The National Institute for Occupational Safety and Health (NIOSH) classifies HD into:

• **Group 1:** antineoplastic drugs.

• **Group 2:** non-antineoplastic drugs that meet at least one of the above criteria.

• **Group 3:** drugs which present a risk to the reproductive process and which may affect men and women who are actively trying to conceive, and women who are pregnant or breastfeeding, but which do not pose a risk to other staff.

THIS SWS IS APPLICABLE FOR HD TYPES 1 AND 2.

Type 3 HD present a **risk** to the reproductive process, therefore **only for certain workers**, those who are actively trying to conceive, and women who are pregnant or breastfeeding (these people should contact their Prevention Supervisor), but not to other staff.

In September 2016, the **National Institute for Occupational Health and Safety** published the Technical Document: Hazardous drugs. Prevention measures for their preparation and administration. This document specifies recommendations on handling, associated preventive measures and individual protection equipment to be used **(information available at http://infomep.inssbt.es)**

The "Guidelines for action on the risk of exposure to hazardous drugs for health service workers in Castile-La Mancha" includes specific actions in this respect in our field.

PRECAUTIONS IN THE ADMINISTRATION OF HAZARDOUS DRUGS.

The administration of HD must be carried out by **qualified and properly trained healthcare personnel** who have sufficient experience in the handling of these drugs and who know the measures to be taken in the event of spillage, breakage or any other incident or accident.

HD administration procedures must guarantee the protection of the environment and the worker without altering patient safety.

Means of administration.

Any: oral, topical, parenteral (subcutaneous, intramuscular, intravenous, etc.), intrathecal, inhalation, intra-arterial and/or chemoembolisation, intracavitary.

General Measures.

The administration of the **HD** will be carried out following the recommendations of the technical specifications and always according to the protocols or guidelines of each centre:

• **Wash hands** before and after the procedure

• **Use the Personal Protective Equipment** (PPE) recommended in the following table.

• **Use of closed transfer systems** for Group 1 and Group 2 drugs.

• Apply the maximum **aseptic measures** in the area where the handling is carried out to minimise contamination.

• Do not eat, drink or chew gum and do not wear jewellery or make-up during administration.

• After the administration of HD, discard all material used and waste generated in the appropriate bin according to **SESCAM waste protocol.**

• Have suitable furniture to place the drug before it is used. Use non-slip tables and surfaces with ledges to prepare the technique and armchair or bed to place the patient. All furniture shall be made of waterproof materials, easy to clean and shall be cleaned after use and whenever necessary.

• Have a **spill kit** and know the procedure to be followed in the event of a spillage and the location of the Kit.

• Refer to the SESCAM HD Guidelines for the specific rules for each type of administration (oral, topical, parenteral, etc.).

HIGHLY SENSITIVE WORKERS

It is recommended that HD 1 and 2 not be handled by workers in the following groups:

• Women who are pregnant or breastfeeding.

• Allergic to cytostatic agents and/or with dermatological pathology.

• Women with a history of miscarriages at childbearing age.

• Personnel professionally exposed to ionising radiation (more than 15 mSv/year).

• Personnel who have previously received cytostatic or immunosuppressive treatments.

PERSONAL PROTECTIVE EQUIPMENT					
Pharmaceutical type	**Single glove**	**Double glove or specific for Group 1 HD**	**Eye protection**	**Respiratory protection FFP3**	**Waterproof protective gown**
Intact capsule/tablet	Yes	No	No[2]	No	No
Fractioned capsule/tablet	Yes	No[1]	No[2]	Yes	No
Oral solution/suspension	Yes	No[1]	No[2]	No[3]	No[2]
Local Methods	---	Yes	No[2]	No[3]	Yes
Parenteral forms (SC, IV, IM)	---	Yes	Yes	Yes	Yes
Solution for irrigation	---	Yes	Yes	Yes	Yes
Powder/Suspension for inhalation	--	Yes	No[2]	Yes	No[2]

1 Double glove or specific glove for Group 1 HD for frequent handling. **2** Required if there is risk of splattering. **3** Required if there is risk of inhalation.

• Staff with a previous history of neoplasia.

• Immunodeficiencies.

It is recommended that HD3 not be handled by workers at risk to the reproductive process (men and women who are actively trying to conceive), and women who are pregnant or breastfeeding; there is no risk to other staff.

DISPOSAL OF GENERATED WASTE

The following are considered type 1 HD waste:

• Remains of cytostatic drugs generated in the administration.

• The material used in the administration (needles, syringes, bottles, bags and infusion systems).

• Protective equipment for handlers (disposable protective clothing, gloves and masks).

• Material stemming from the treatment of accidental spills.

All these wastes fall within **class VI** as **Cytotoxic Waste** and will be disposed of according to the provisions of the Protocol for the management of sanitary waste generated in the SESCAM dependent centres **in specific BLUE containers.**

Sharp objects generated as a result of the administration of this type of medicine must be managed in the sharp objects bins specifically identified for this type of waste.

REGARDING HD2 AND HD3 WASTE:

• As a general rule, oral HD will be administered, whenever possible, in doses or presentations that avoid fragmentation and therefore the generation of HD residues.

• Waste containing traces of HD2 and HD3 (vials, systems, ampoules, vials, syringes, etc.) will be disposed of in **the blue container for hazardous drug waste**, selecting the smallest possible container in order to adjust its capacity to the volume of waste production. In many cases, the use of 3 or 10 litre containers will be appropriate.

• The PPE used for the administration of HD2 and HD3 will be disposed of as **urban waste**, except for evident contamination (splattering, spillage, etc.). The PPE used in preparation will be disposed of in the container for hazardous drug waste.

• The material used for cleaning spillages (absorbent material, PPE, etc.). will be disposed of in the blue container for hazardous drug waste.

HANDLING EXCRETA

Patients' excreta (basically urine and faeces) should be considered potentially dangerous **at least 48 hour**s after administration (although it may last up to a week for some drugs).

As a general rule and unless the information available in the drug datasheet makes a different practice advisable, the following precautions will be taken:

• Staff should be protected with gloves and gowns. In case of risk of splashes, face masks and goggles should also be worn.

• Dilution with plenty of water is recommended before disposal through the waste water system.

• The underwear of patients who have received cytotoxic medication in the last 7 days, and which is contaminated with urine, faeces, vomit, etc., should be placed inside a bag for washable material, and this bag, in turn, inside a properly marked waterproof bag.

• Attention will also be paid to the handling of biological fluids when carrying out analytical studies for these patients.

COMING FROM PATIENTS TREATED WITH HD1:

• Personnel who may come into contact with or handle the blood, vomit or excreta of patients who have received cytostatic medication in the past 48 hours should wear gloves (double pair) and a waterproof gown. In case of risk of

splashes, face masks and goggles should also be worn.

• They should wash their hands after removing gloves and after contact with excreta.

• Excreta and other biological fluids: disposal by sanitation system. Dilution with plenty of water is recommended (flushing the cistern several times).

• Excreta and other biological fluids during the first 48 hours from the administration of the medicine **when they are contained in devices without the possibility of emptying:** elimination as cytostatic waste.

• Disposable material contaminated with excreta and other biological fluids during the first 48 hours from the administration of the medicine (empty containers that have contained excreta, nappies, protector pads, etc.): disposed of as cytostatic waste.

• After 48 hours from the administration of the medicine, the waste will be disposed of as urban waste, except excreta and biological fluids contained in devices without the possibility of emptying that meet some criterion that determines its disposal as a specific biosanitary waste, according to the SESCAM waste protocol.

COMING FROM PATIENTS TREATED WITH HD2 AND HD3:

• Excreta and other biological fluids: disposal by sanitation system.

• Excreta and other biological fluids contained in devices without the possibility of emptying and contaminated disposable material: treated as urban waste, except when meeting some criterion that determines its disposal as a specific biosanitary waste, according to the SESCAM waste protocol.

PROCEDURE FOR SPILLAGE.

• Isolate and mark off the affected area identifying that it is a HD spillage.

• Open the spill kit and put on the personal protective equipment in the following order: shoe protectors, first pair of gloves, cap, waterproof gown, high filtration face mask, protective goggles, second pair of gloves on top of the gown.

• If there are pieces of glass, collect them with the tweezers or dustpan and brush, but never with your hands, and place

them inside the sharp objects container in the kit, which will then be disposed of in the cytostatic waste bin.

• In case of liquid spillage, cover it with absorbent cloths and let them soak it up. Also use pads or absorbent material to prevent the spillage from spreading.

• In the case of solid waste, damp cloths or pads should be used to help with collection.

• When cleaning floors and surfaces, proceed from the least polluted areas to the most polluted, always without extending the spillage.

• Wash with detergent solution and rinse 3 times (detergent - water - detergent - water - detergent - water).

• Remove the PPE in the following order: shoe protectors, outer gloves, gown (turning it inside out, the clean part must be on the outside), goggles, face mask, cap, discard in the bag as appropriate; if you are going to reuse the goggles, store in another bag marked as contaminated, and lastly remove the second pair of gloves.

• Wash hands, face and neck.

• All waste and material used must be treated as contaminated material for disposal purposes.

• Refill spill kit.

• Complete spillage data collection sheet.

PROCEDURE FOR ACCIDENTAL EXPOSURE.

Any professional who suffers accidental exposure as a result of a spill, accidental puncture or any other accident with HD must go to the corresponding Prevention of Occupational Risks Service (SPRL) for their department for assessment and monitoring. They shall also fill in and register the work accident/incident report, except in urgent cases, in which case the middle manager or Head of Service shall do so afterwards.

In the case of non-hospital personnel, they must go to the Emergency Department and inform their SPRL so that they can be monitored (as per the provisions of the Procedure for Coordination of Business Activities in preventive matters).

INHALATION EXPOSURE/INGESTION EXPOSURE:

• Monitor possible symptoms.

• Notify the immediate superior and the SPRL of any abnormal symptoms.

NON-CONTACT EXPOSURE TO SKIN OR MUCOUS MEMBRANES:

• Avoid exposure of skin and mucous membranes when the protective equipment is impregnated, removing them immediately, without exposing the skin to contaminated PPE and disposing of them in the corresponding container.

• Wash hands with soap and plenty of water for ten minutes.

EXPOSURE IN CONTACT WITH UNDAMAGED SKIN:

• Immediately remove contaminated PPE and/or clothing.

• Wash affected skin area immediately with mild, non-antiseptic soap and plenty of water for at least ten minutes. Shower if necessary.

• If the affected area is lacerated or irritated, it should be examined by a doctor, in any case medical monitoring of the affected area should be carried out.

• Dispose of contaminated PPE in the corresponding container and/or store clothes in a bag and dispose of them according to the Centre's Cleaning Protocol.

EXPOSURE IN CONTACT WITH EYES OR MUCOUS MEMBRANES:

• If the injured person wears contact lenses, remove them immediately.

• If substance has splashed in eyes, wash the conjunctiva with plenty of warm water for fifteen minutes and then apply 0.9% saline solution. Do not rub eyes.

• Seek immediate medical attention from the corresponding doctor and monitor the affected area.

CUTS OR PUNCTURES WITH CONTAMINATED NEEDLE OR GLASS:

• Immediately remove contaminated PPE and/or clothing.

• Rinse the area with plenty of warm water. Let the blood flow freely. Do not press on the wound area.
• Clean the area thoroughly with warm water and mild soap for at least ten minutes.

• If contact occurs by accidental inoculation (needle puncture): Do not remove the needle, remove only the syringe and with a new syringe aspirate the contents of the injected HD. If the needle has been moved, insert a new one at the point of injection and aspirate the medication.

• Seek immediate medical attention from the corresponding doctor and monitor the affected area.

• In the case of cuts or punctures with contaminated material, it must always be assessed whether the accident also involves exposure to biological material with blood or haemoderivative, in which case the centre will act according to its protocol.

Received by:

Name and surnames: .....

Date: .....

Signature:

For any queries or additional information please contact the Prevention Service or manager

Castilla-La Mancha

http://sescam.castillalamancha.es