GUIDE FOR MONITORING SURFACES

FOR

HAZARDOUS DRUG CONTAMINATION

Spanish Nursing Research Institute | 2021

Consejo General de Enfermería

Instituto Español de Investigación Enfermera

GUIDE FOR MONITORING SURFACES FOR HAZARDOUS DRUG CONTAMINATION

Edition: 2021
Coordination: Spanish Nursing Research Institute, a Spanish General Council of Nursing institution
ISBN: 978-84-09-36561-6
This guide should be cited as follows:
Domingo T, Fontán G, Enríquez M, Díaz A, Cobos JL, Fernández P, Ayuso D. Guía Monitorización de superficies de medicamentos peligrosos. 1.ª ed. Madrid: Instituto Español de Investigación Enfermera; Consejo General de Enfermería. 2021.

Collaborating experts

Ms Mª Amparo Benavent Benavent

Nurse specialist in Occupational Nursing. Regional Health Ministry. Valencia-La Fe Department Coordinator of the CECOVA Occupational Health Working Group. Member of the TASK FORCE on HAZARDOUS DRUGS of the International Commission on Occupational Health (ICOH). Member of the Working Group for the implementation of Good Practices in the Preparation and Handling of Drugs of the Valencian Regional Health Ministry

Ms Mª Amparo Ortuño Moreno

Nurse. Azucena Healthcare Centre. Hospital La Fe de Valencia Department. Occupational Risk Prevention Auditor. Member of the CECOVA Occupational Health Working Group. Member of the International Occupational Health Commission (ICOH). Member of the TASK FORCE on HAZARDOUS DRUGS of ICOH. Member of the Working Group on Hazardous Drugs of the Valencian Regional Health Ministry

Ms Mª Ángeles Sanchez de la Ventana

Nurse. University Master in Healthcare Research. Master's degree in Evidence-Based Nursing and Research. Thorax Surgery and Lung Transplant Unit. 12 de Octubre University Hospital, Madrid

Ms Juana Rueda Segura

Nurse specialist in Paediatrics. Paediatric onco-haematology. Torrecárdenas Maternity and Child University Hospital, Almería

Ms Monstserrat Guinovart Alemany

Nurse. General Nursing Supervisor, evening shift. Joan XXII University Hospital, Tarragona

Ms Mª Carmen Aragones Gisbert

Nurse specialist in Geriatric Nursing. Second-degree specialising in health science research methodology. Oncology Outpatient Clinic. Verge de la Cinta Tortosa Hospital, Tarragona

Ms Mª Carmen Gregorio Mayoral

Nurse. Onco-haematology Outpatient Clinic. San Jorge University Hospital, Huesca

Ms Olga Matas Palomares

Nurse. San Jorge University Hospital, Huesca

Ms Leticia Bravo Bizarro

Nurse, University Expert in Extra-hospital Emergencies. HDD Circuit Nurse, Campana Medical Hospital and Service. Barbastro Hospital. Huesca

Ms Mª Ángeles Alpin Demur

Nurse. Onco-haematology Outpatient Clinic. Barbastro Hospital. Huesca

Ms Mª Lourdes Martínez Panzano

Nurse. San Jorge University Hospital, Huesca

Ms Carolina Genoveva Diaz de Mera Aranda

Nurse specialist in Paediatrics. Supervisor of the Paediatric Hospitalisation Service. Gregorio Marañón General University Hospital, Madrid

Ms Esther María García Ruiz
Nurse specialist in Obstetrics and Gynaecology. Supervisor of the Maternity and High-Risk Pregnancy Emergency Nursing Unit. Gregorio Marañón General University Hospital, Madrid

Authors: Spanish Nursing Research Institute

Ms Tamara Domingo Pérez
Nurse specialist in Paediatrics. Spanish Nursing Research Institute
Ms Guadalupe Fontán Vinagre
Nurse. Spanish Nursing Research Institute
Dr María Enríquez Jimenez
Nurse. Spanish Nursing Research Institute
Ms Adriana Díaz Gautier
Spanish Nursing Research Institute
Dr José Luis Cobos Serrano
3rd Vicepresident. Spanish General Council of Nursing

Reviewers. Spanish General Council of Nursing

Dr Pilar Fernández Fernández
1st Vicepresident. Spanish General Council of Nursing
Dr Diego Ayuso
Secretary General of the Spanish General Council of Nursing

1. CONTENTS

Tables

INTRODUCTION

1. INTRODUCTION

So-called hazardous drugs (HDs) pose a significant risk to the health of healthcare professionals, and in particular of the nurses who come into contact with and handle these drugs on a regular basis. These are the main cause of adverse events in hospitals, not only due to their number, but also in terms of morbidity and mortality, with more than 20 million European workers exposed every year to hazardous drugs: carcinogens, mutagens, and reprotoxic chemicals(1,2). The 'Safer and Healthier Work for All'(3) document published by the European Commission states that in 2012 there were more than 106,500 deaths from cancer attributable to exposure to carcinogenic substances in the workplace, turning occupational cancer into the "leading cause of death among European workers" and, according to the International Labour Organisation (ILO), "in the world"(4).

It is estimated that there are more than 12.7 million healthcare professionals in Europe who are potentially exposed to carcinogenic, mutagenic, and reprotoxic hazardous drugs, 7.3 million of whom are nurses. Moreover, occupational exposure to these drugs has caused the death of 1,467 professionals (5).

According to these data, nursing staff are among the most exposed - 316,094 registered nurses and midwives in Spain (6) in 2019. It is no less true that other healthcare workers, such as storage and reception workers, janitors, pharmacists, physicians, cleaners, and nursing assistants, among others, are also exposed to hazardous drugs. According to the European Occupational Safety and Health Agency(7) (EU-OSHA) hazardous drugs are *the main chemical risk factor in healthcare*.

Although most occupational risks have been covered by European and national legislation, there are gaps regarding healthcare workers' exposure to hazardous drugs.

Exposure to hazardous drugs in the workplace and the ensuing risks to healthcare staff's health has been known and evidenced for more than four decades, even since it was first identified as a risk hazard in the USA in the 1970s, with the detection of harm to the staff in charge of preparing antitumoural drugs. Since the beginning of this century, the association between the use of antitumoural drugs and their potential negative effects on the health of those who handle them has extended to all types of drugs with hazardous characteristics. This is due to the fact that increasingly potent and effective drugs are being designed, manufactured, and administered, which improves efficacy for patients, while increasing the risk to occupationally exposed individuals, such as nursing staff.

The European Commission has acknowledged, in the case of antitumoural drugs, that the risk to healthcare workers' health is determined by the exposure level and frequency, the toxicity of the handled drugs, and the existence of unsuitable work practices, among others. The studies carried out, particularly with the nurses who prepare and administer them, have established an association between workplace exposure to antitumoural drugs and acute and/or chronic effects on health. In fact, an increase in genetic alterations in nursing staff has been proven, particularly among outpatient nurses, (8), who are the most vulnerable group (9) as they handle the largest amount of drugs during the administration process, due to their great load of care to haemato-oncologic or rheumatologic patients with antitumoural drugs, antineoplastic drugs, immunosuppressants, and other drugs. It is highly significant that the effects of this exposure can be subclinical, and not manifest for years or generations of permanent exposure. This is the case of occupational cancer, caused by occupational exposure, which often takes decades to appear. For example, a case of leukaemia diagnosed in a nurse today could be the result of repeated and frequent exposure in the workplace in the 1970s and 1980s. Unfortunately, in many cases a connection between work and disease has never been established, although many exposure risks are reported every day by professionals and workers' representatives(10,11).

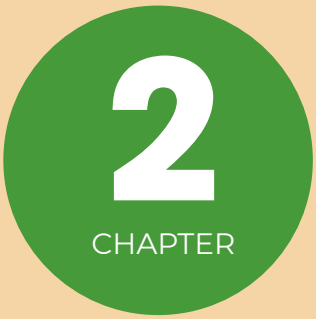
The risk of exposure to a hazardous drug depends on multiple factors, and staff protection must adapt to each activity, as the precautions to be taken are different in each case. Nurses must have the highest level of protection when handling hazardous drugs while ensuring adequate patient care. They must also be informed and trained on the risks associated with their activity and take the necessary measures to prevent risks to their health.

One of these protection measures would be the monitoring of surfaces to proactively detect hazardous drug contamination by means of two methods: quantitative and qualitative. High-performance liquid chromatography (HPLC), together with mass spectronometry (LC-MS/MS) is the current method used by commercial laboratories for the analysis of most hazardous drugs. This would be the costliest quantitative method, which requires the longest waiting time to obtain results, and does not provide on-site results that might help to take immediate measures. By contrast, lateral flow immunoanalysis (LFIA) would be the qualitative method to find immediately and take measures at once. This method allows for direct reading and field monitoring. They are portable, easy-to-use devices, which allow professionals to take immediate corrective measures as well as immediately retake samples to verify the effectiveness of those measures.

This document is meant to be an easy-to-read guide to monitor hazardous drugs in nursing

units and other areas where they are prepared, administered, or managed, as there is a specific guide for Hospital Pharmacy Services. This guide is based on that document, entitled "Monitoring of work surfaces for hazardous drugs in Pharmacy Services. Consensus document. Pharmaceutical practice guide of the Spanish Society of Hospital Pharmacy (SEFH)"(12).

JUSTIFICATION FOR THE NEED FOR HAZARDOUS DRUG MONITORING



2. JUSTIFICATION FOR THE NEED FOR HAZARDOUS DRUG MONITORING

Nurses face various risks to their health on an everyday basis. One of them is repeated exposure throughout our work life to environments where there is a clear risk of endangerment. Areas and surfaces where hazardous drugs are received, transported, prepared, administered, and discarded run the risk of being contaminated by those drugs with no routine exposure control.

Even though authorities are currently ramping up their efforts to decrease exposure risk, it is still difficult to avoid exposure to HDs. In the best-case scenario, the safety conditions in place hardly prevent the risk of coming into contact with the hazardous drugs. In some cases, they may give rise to contact through the skin, not only in preparation and administration, but also with drug residues in work surfaces or contaminated areas, handling of bodily fluids or bedding, decontamination and cleaning actions in thae preparation and residue management areas(8). Many surface contamination studies have been carried out throughout the world. Approximately 100 published studies proved the existence of surface contamination at different levels and locations by antineoplastic and hazardous drugs in healthcare environments (13).

The study by Kiffmeyer,T et al (14) published in 2012, on environmental monitoring of hazardous drugs at different intervals, with the involvement of 130 hospital pharmacies and 1,269 collected samples, shows that "the monitoring procedure is a reliable and affordable tool for routine analysis of workplace contamination by antineoplastic agents". During the study, a constant contamination level was achieved, while the percentage of contaminated patches remained more or less with no changes, at about 50%. This means that a zero level of exposure can hardly be achieved. However, some kind of threshold or activation value is required to assess individual results and decide whether countermeasures should be taken. The study proposes a technical guideline based on the analysis percentiles of 10 152 MEWIP. As a guideline separate from the substance, they suggest 0.1 ng cm −2 (1 µg m −2) based on the 90 percentile of the compound that is found in the highest MEWIP concentrations (fluorouracil at 0.117ng cm−2)(14).

Professional organisations and government bodies have developed guidelines, protocols, and standards for safe handling of hazardous drugs which include recommendations on the monitoring of surface contamination by hazardous drugs. These include the following:

I. International:

- International Society of Oncology Pharmacy Practitioners (ISOPP)(15)
- United States Pharmacopeia (USP)(16)

- American Society of Health-System Pharmacists (ASHP)(17)
- US Occupational Safety and Health Administration (OSHA)(18)
- Canadian National Association of Pharmacy Regulatory Authorities (NAPRA)(18)
- US National Institute of Occupational Safety and Health (NIOSH)(18)
- US Oncology Nursing Society (ONS)(19)

II. National:

- Instituto Nacional de Seguridad y Salud en el Trabajo (INSST)(16)
- Sociedad Española de Farmacia Hospitalaria (SEFH)(20)

Chapter <800> Hazardous Drugs-Handling in Healthcare Settings of The United States Pharmacopeia, as well as other similar documents, recommends the following:

"Environmental samples for hazardous drugs on surfaces must be taken on a routine basis (e.g. the first time as a reference and every 6 months or more frequently if necessary)"(21). This continued sample-taking frequency could fail to provide sufficient data to maintain the controlled risk or to identify deviations from safety good practice. Thus, it might be considered to expand the frequency of monitoring on the basis of risk assessment, the volume/type of hazardous drugs, and the existing safe handling practices in the healthcare centre or area.

There are no standards for acceptable levels of surface contamination by hazardous drugs in hospitals. The ALARA (As Low As Reasonably Achievable) concept must be applied to reduce exposure to hazardous drugs to the minimum possible (13). The information obtained from surface sample taking cannot be used as an indication of the worker's exposure, but as an indication of the environmental contamination in the workplace as a potential source of skin exposure(22).

A hazardous drug monitoring programme can determine whether contamination by this type of drug exists and makes it possible to assess the effectiveness of engineering and administrative controls, cleaning, deactivation, and decontamination methods.

Analytic monitoring techniques

Hazardous drugs have toxic properties, and thus can cause mutagenic, carcinogenic, and teratogenic effects. Thus the individuals who handle these drugs in the performance of their healthcare duties may face risks to their own health. For this reason, is it important to monitor occupational exposure to these drugs. A general description of the exposure monitoring methods is given below, and their importance is described. For occupational health services and occupational risk prevention services, it is important to have sensitive

and specific methods to monitor exposure to cytostatic drugs, among others.
The analytic methods used to detect hazardous drugs are the following:

- Gas chromatography (GC), e.g. that used in determining cyclophosphamide levels in urine.
- High-performance liquid chromatography (HPLC).
- Ultra-performance liquid chromatography (UPLC).

All in combination with mass spectronometry (MS) or tandem mass spectronometry (MS/MS)(23).

High-performance liquid chromatography (HPLC), together with mass spectronometry (LC-MS/MS) is the current method used by commercial laboratories for the analysis of most hazardous drugs. This would be the costliest quantitative method, which requires the longest time and does not provide immediate results that might help to take immediate measures. Analytic techniques to calculate surface contamination by antineoplastic drugs through LC-MS/MS are sensitive, specific, and precise. The initial cost is high and trained professionals are required to handle the devices, which may entail a high amount and a potential inability to use them frequently. In most cases, the results obtained through this analytic method take a long time, which might result in continued exposure to contamination until decontamination or attenuation actions are launched. "For this reason, these methods cannot usually provide immediate observations for the development and launch of occupational practices required to decrease exposure, due to the time gap between sample taking and the analytic results"(23).

The National Institute for Occupational Safety and Health (NIOSH) (24) has developed a new technology that employs a lateral flow immunoanalysis (LFIA) to detect surface contamination by hazardous drugs. This would be the qualitative method to obtain results immediately and take measures at once. Lateral flow analyses are used in many consumer products, e.g. pregnancy tests, and are being used in many analyses for clinical use (25). Lateral flow analysis cassettes usually have two lines: a test line the intensity of which varies depending on the analyte concentration, and a control line that is relatively constant for all samples and has been mainly used to check that the cassette works correctly(26). Lateral flow tests have a number of advantages such as quick results, suitability for on-site analysis, high specificity, validation, no laboratory equipment requirements, no hazardous materials, and ease of use.

This method makes direct reading and field monitoring possible to measure the hazardous drugs selected on surfaces. These devices are portable, sensitive, easy to use, and also provide results practically in real time. By offering results in real time, in less than 10 minutes,

they enable professionals to take immediate corrective measures as well as immediately retake samples to verify the effectiveness of those measures.

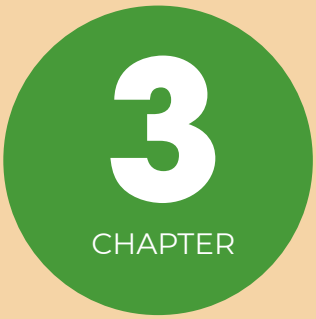
The drawback of lateral flow immunoanalysis (LFIA) is that the current commercial meters available offer qualitative results, whereas the LC-MS provides quantitative results. The combination of LFIA for routine monitoring and to take immediate corrective actions, and of LC-MS/MS for periodic quantitative measurements could be useful.

Another environment to consider is the container or means of transport in which hazardous drugs are received, prepared, administered, and discarded, as it runs the risk of being contaminated by those drugs. This in turn might place professionals, as well as relatives and patients, at risk of exposure.

The Spanish Society of Hospital Pharmacy (SEFH) has recently published the document "Monitoring hazardous drug work surfaces in Pharmacy Services. Consensus document. Pharmaceutical practice guide of the Spanish Society of Hospital Pharmacy (SEFH)"(12). Such document, which has been approved by the Spanish General Council of Nursing, provides the recommendations for the identification and monitoring of hazardous drugs in Pharmacy services.

This document is intended to supplement the SEFH document and serve as a guide for the identification and monitoring of hazardous drugs where they are the object of quantitative monitoring during the preparation process outside Hospital Pharmacy, transport, administration, and discarding in the different areas of all types of healthcare centres (acute patient centres, outpatient clinics, general practices, and social healthcare centres), as well as in the home if necessary. This document is intended to explain the qualitative procedure for the monitoring of hazardous drug surfaces.

CONTEXTUAL FRAMEWORK OF HAZARDOUS DRUGS (HDS)



3. CONTEXTUAL FRAMEWORK OF HAZARDOUS DRUGS (HDS)

The various aspects pertaining to the monitoring of hazardous drug surfaces are described below.

3.1. Definitions

The term "Hazardous Drug" was first introduced by the American Society Hospital Pharmacy (ASHP) in 1990 and later adopted by the Occupational Safety and Health Administration (OSHA)(27). It was first used by the National Institute for Occupational Safety and Health (NIOSH)(7) in its alert published in 2004 for those drugs that have one or more of the following hazardous characteristics for humans:

- Carcinogenicity
- Teratogenicity or other developmental toxicity
- Reproductive toxicity
- Low-dose organ toxicity
- Genotoxicity
- New drugs with similar structure and toxicity profiles as existing drugs that were determined to be hazardous according to the previous criteria are also included.

3.2. Classification

NIOSH(28) distinguishes between the risk of these drugs in its document, establishing three main groups:

- Group 1: Antineoplastic drugs.
- Group 2: Non-antineoplastic drugs that meet at least one condition to be regarded as hazardous drugs.
- Group 3: Drugs that pose a risk to the reproduction of men and women who are trying to conceive, pregnant or lactating women, but which do not pose risks to the rest of the staff.

NIOSH Note(28) of 12 May 2020

The manufacturers of trabectedin (Yondelis®), inotuzumab ozogamicin (Besponsa TM), polatuzumab vedotin (Polivy TM), enfortumab vedotin (Padcev TM) and trastuzumab deruxtecan (Enhertu®), and sacituzumab govitecan (Trodelvy TM) recommend that they be handled as hazardous drugs. Thus, NIOSH considers that these drugs are included in Table 1 of the NIOSH hazardous drug list.

NIOSH published a list of hazardous drugs in 2004, which was updated in 2010, 2012, 2014,

and 2016. The list, updated in 2016, is available here: https://www.cdc.gov/niosh/docs/2016-161/default.html

3.3. Hazardous drug handling stages

In addition to the reception and storage of hazardous drugs, these drugs are handled in other areas that do not belong to the Hospital Pharmacy Services. Four distinct stages can be established(29):

1. **Preparation stage**: includes the time between the opening of the vial containing the hazardous drug and the time when the mix is ready for release to the healthcare service.
2. **Transport stage:** the period of time from departure from the place of preparation to the healthcare service where it is administered.
3. **Administration stage:** the period of time from the connection of the drug for infusion to the patient to start to the time when the patient infusion system is disconnected.

   Administration of the hazardous drug must be restricted to the healthcare staff who are informed of its toxic effects, have sufficient experience in the administration of these drugs, and know the action measures in the event of spillage, breakage, or any other incident. The number of people handling HDs must be reduced to the minimum possible, through organisational measures and the use of preparations that require the least handling possible, as established in Section 15 of Law 31/ 95 on Occupational Risk Prevention, regarding the principles of preventive action.

   Two closed HD infusion systems can be available in a healthcare environment: the tree-type system and the valve system, which has one single infusion line. The former type of system (tree type) is more advantageous in terms of safety in the administration process, as there are no disconnections that increase the risk of exposure to the HD(30). However, they have the drawback of the risk of accidental spillage if the secondary system is not clamped shut.

4. **Removal stage:** the time between the patient's disconnection to discarding by the hospital.

3.4. Risk determination

Not all cytostatic drugs have the same effects, and their dangerousness varies depending on the type of drug. In the case of antitumoural drugs, the risk to healthcare workers' health may be influenced by the exposure level and frequency, the toxicity of the handled drugs, and the existence of unsuitable work practices, among others.

• Chemical risk

  - Ignorance of the dangerousness of the substances.

- Unidentified substances.
- Inadequate, prolonged storage.
- Ignorance of work methods and procedures.
- Environmental contamination from the formation of aerosols generated during preparation, when withdrawing the needle from a vial, opening a blister, expelling air from a syringe, or disabling used needles.
- Incorrect handling.

• Splatters.
- Spills, punctures.

• Cuts
- Vial breakage.

Another significant consideration is that, as patients receive concentrated doses of a limited number of cytotoxic drugs for a specific period of time, the healthcare staff may be exposed to small doses from a wide range of cytotoxic drugs every working day, year after year(31). In particular, nurses, together with other healthcare professionals such as physicians and pharmacists, are at the highest risk of exposure(31)(32)(33)(9)(22)(34).

The scientific data have confirmed that sporadic exposure affects nurses more than pharmacists (35). However, it should be borne in mind that, because pharmacists handle pure drugs during the preparation stage, they are exposed to much more concentrated drugs.

Workers may be exposed to hazardous drugs through the inhalation of contaminated air or skin contact with surfaces, contaminated clothes and medical equipment(7)(34)(36)(37) throughout the life cycle of the drug (e.g. from manufacturing for transport and distribution, unpacking and storage, during the preparation of perfusions, internal transport, inadequately packaged perfusion syringes, administration of cytotoxic drugs in the rooms, cleaning activities, residue removal, etc.)(26).

The following table shows some of the most frequently used hazardous drugs classified by therapeutic group.

Table 1 Commonly used hazardous drugs

ANTIFUNGALS	**VORICONAZOL, FLUCONAZOL**
ANTIRETROVIRALS	**ABACAVIR, EFAVIRENZ, ZIDOVUDINE, NEVIPARINE**
ANTIVIRALS	**ENTECAVIR, GANCICLOVIR, VALGANCICLOVIR, RIBAVIRIN, CIDOFOVIR**
ANTIEPILEPTICS	**VALPROIC ACID, CARBAMAZEPINE, PHENYTOIN, TOPIRAMATE, CLONAZEPAM, OXCARBAZEPINE, ESLICARBAZEPINE**
ANTIDEPRESSANTS	**PAROXETINE**
ANTIPARKINSONIANS	**RASAGILINE**
ANTIPSYCHOTICS	**RISPERIDONE, PALIPERIDONE, ZIPRASIDONE**
ANTICOAGULANTS	**ACENOCUMAROL, WARFARIN**
ANTIGOUT	**COLCHICINE**
ORAL CYTOSTATICS	**AFATINIB, AXITINIB, CAPECITABINE, DASATINIB, IMATINIB**
IMMUNOSUPPRESSANTS	**AZATHIOPRINE, CICLOSPORIN, MYCOPHENOLATE, TACROLIMUS, SIROLIMUS, METOTREXATE**
HORMONES	**OXITOCIN, PROGESTERONE, ESTROGENS**
OTHER	**ZOLEDRONIC ACID, APOMORPHNE, MACITENTAN, METIMAZOL, MISOPROSTOL, RIOCIGUAT**

Source: Instituto Sindical de Trabajo, Ambiente y Salud (ISTAS)(38).

3.5. Preventive measures

To prevent exposure to hazardous drugs, the prevention measure hierarchy(8) should be articulated as follows:

I. Replacing the hazardous drug by a non-hazardous drug, if possible.
II. Isolating the preparation procedure: Collective protection. Preparation in biological safety cabins/robots/insulators, with closed drug transfer systems (internationally known as CSTDs).
III. Placing identification labels on all HDs.
IV. Developing safe work protocols in all facilities where HDs are handled. Improving work

techniques.

V. Making specific locations suitable for storage.

VI. Using personal protection equipment: gloves, lab coats, face masks, goggles, boots, caps, etc.

VII. Signalling the work areas where hazardous drugs (HDs) are being handled.

VIII. Placing and using specific containers for HD residues: blue

IX. Using special equipment for the administration of hazardous drugs: tree-type systems

The advantage of tree-type systems is the safety of their administration process, as there are no disconnections that increase the risk of exposure to HDs as in valve systems. However, they have as a drawback the risk of accidental spillage if the secondary system is not clamped shut. Those that use systems designed to minimise chemical contamination in preparation are more likely to reach the administration area with a lower contamination level(30).

Valve systems are simpler and more intuitive, but few studies assess their safety. These systems are not designed to contain chemical contamination in the critical disconnection points. There are also membrane-type systems that combine port and injector with no needles to create a closed system with linked integrated connections that prevent contamination(30).

X. Providing adequate information and training to all individuals involved in preparation, administration, and handling. Access to the drug safety data files and the lists of hazardous drugs.

XI. Having spillage kits and a procedure for action in a location known to all.

XII. Performing adequate monitoring of the specific health of the professionals handling hazardous drugs.

The precautions to be taken are different in each case, as the risk of exposure to a hazardous drug is multi-causal. Staff precautions should be adapted to each task.

3.6. Legislation in force

A hazardous drug is understood as an agent that contains an active principle whose inherent toxicity poses a risk to the health of the healthcare staff who will handle it. The dangerousness of these drugs is understood according to their chemical risk, connected to the carcinogenic, teratogenic, genotoxic, and toxic activity on the reproductive process or on a specific organ at a low dose, or because it is a new drug similar to others with this type of risk(39). In this regard, hazardous drugs fall under the scope of the workers' protection standards pertaining to exposure to chemicals (*RD 374/2001*), carcinogens (*RD 665/1997*), and their later modification RD 349/2003) and to workers' protection against risks related

to exposure to carcinogens or mutagens during work (Directive 2004/37/EC).

Royal Decree 773/1997, on minimum health and safety provisions regarding the use by workers of personal protection equipment.

Royal Decree 298/2009 modifying Royal Decree 39/1997 of 17 January, approving the Regulation of Prevention Services regarding the application of measures to promote the improvement of health and safety in the workplace for pregnant workers, workers who have recently given birth, and lactating workers.

In 2003 INSHT published the technical prevention note *(NTP) 740 Occupational exposure to cytostatic substances in healthcare settings*, which includes recommendations for the reception, storage, preparation and reconstitution, transport, administration, and protection equipment. In 2016, the document *Hazardous drugs. Prevention measures for their preparation and administration* was published. There are also other standards such as *NTP 1051, replaced by NTP 1134, Occupational exposure to cytostatic compounds: safe systems for their preparation*, *NTP 233 Biological safety cabins, and NPT 1135 Hazardous drugs: administration and available equipment.*

Moreover, in section 15 of *Law 31/1995 on the Prevention of Occupational Risks (LPRL)* regarding the principles of preventive action, the implementation of collective protection measures, both technical and organisational, should be prioritised over individual protection.

3.7. Potentially exposed healthcare and non-healthcare professionals

The categories of staff potentially exposed to hazardous drugs are listed below(31):

- Nurses.
- Midwives.
- Nursing assistants.
- Physicians.
- Pharmacists.
- Janitors.
- Carers of elderly patients in nursing homes, where there are nurses and nurse assistants and/or carers specialised in gerontology.
- Home care staff, as drugs are administered in patients' homes, often with a high degree of ignorance of the inherent risks and a complete lack of preventive measures. For example, chemotherapy treatment in the home.
- Transport, storage, and reception staff.

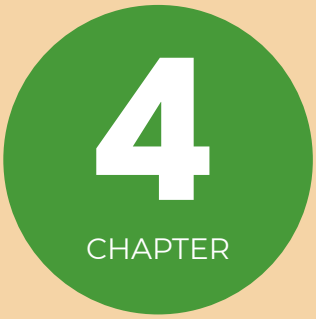
- Cleaning staff.
- Laundry staff.
- Residue management and processing staff.

3.8. Forms of exposure

The main forms of exposure to hazardous drugs (8) are:

- **Dermal exposure**, through contact with contaminated surfaces. In dermal exposure, the substance or product comes into contact with the skin or mucous membranes. This is one of the most common forms of exposure to hazardous drugs.
- **Ophthalmic exposure**, through eyes splashes (including the cornea).
- **Inhalation exposure**, through gases, vapours, and aerosols (liquids or particles). Exposure takes place through the inhalation of dust, aerosols, or vapours in the air of the locations where the drugs are prepared or administered. E.g. when reconstituting powdered or lyophilised drugs, when diluting drugs in fluid bags, or when crushing pills to dissolve and administer them.
- **Oral exposure**, by eating, drinking, or smoking in contaminated areas, or else, having handling hazardous drugs, by not having properly washed hands or through oral splashing.
- **Parenteral exposure**, through accidental punctures or cuts from blisters.

OBJECTIVES



4. OBJECTIVES

4.1. Main objective

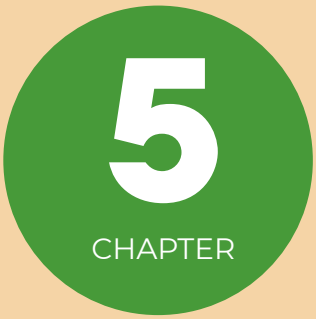
To improve the safety conditions of nurses who prepare, handle, administer, and discard hazardous drugs.

4.2. Specific objectives

SO1.- To identify the hazardous drugs to monitor, as well as to describe monitoring zones and frequency.

SO2.- To develop and implement a procedure to quantitatively monitor contamination levels.

PHASES



5. PHASES

This project will take place in two phases, briefly described below:

5.1. Phase 1.

In this phase, an expert group will be assembled to reach a consensus on the hazardous drugs to be monitored, confirm administration areas, validate, and approve the risk defined according to frequency in sample taking.

5.1.1. Specific objectives Phase 1

- SO1. - To identify the most frequent hazardous drugs to be monitored.
- SO2.- To confirm risk areas in the administration of hazardous drugs.
- SO3.- To approve classification in the monitoring of hazardous drugs according to the risk level allocated to the area during the risk assessment.
- SO4.- To reach an agreement of the assessment of the risk, classified by likelihood, seriousness, and contamination prevention into low, medium, and high.
- SO5. - To validate the risk level defined according to the sample taking frequency.
- SO6.- To reach an agreement on the suitable time for the taking of samples in work surfaces.

5.1.2. Methodology Phase 1

This study was carried out on the basis of expert assessment or expert judgement validity(40), in two stages.

In the first stage, the measurement instrument, which had only been used for Pharmacy areas, was adapted. This was the one published in the document "Monitoring work surfaces for hazardous drugs in Pharmacy Services. Consensus document. Pharmaceutical practice guide of the Spanish Society of Hospital Pharmacy (SEFH)"(12).

In the second stage, the instrument "Assessment of the risk of surface contamination by hazardous drugs" was validated and standardised through validation by an expert panel to assess content validity.

A highly competent expert panel reached an agreement on the aspects defined in the specific objectives, which as a whole made it possible to carry out risk assessment. All the work carried out is specified in appendix 3. **For this reason, a group of 13 professionals in this field determined the hazardous drugs to be monitored, confirmed administration areas, validated the risk level defined according to the frequency of sample taking, and reached an agreement on risk assessment classified by likelihood, seriousness, and contamination prevention into low, medium, and high.**

The process was carried out by invitation, with a confidentiality agreement and a declaration of interests signed by the experts. A total time of 7-10 days was determined for experts to conduct their observation. The assessment had 2 phases, validation, and standardisation: the first phase was carried out on the basis of the risk assessment model that assesses each item separately. Thus, the experts would identify whether the item was connected to the subscale being measured. Answers were given on a Likert-type scale in an assessment/aspect table ranging from "Completely disagree", through "Somewhat disagree", "Agree", and "Quite agree", to "Completely agree", to which we assigned a numerical number from 1 to 5 in the same order. If these aspects had not been previously determined, we were able to use the experts' experience and knowledge to establish the aspects to be assessed, leaving a table for comments.

Finally, each expert was able to correct the text of any items which they believed to be confusing to maintain consistency with the definition assessed through observation.

Professionals targeted

Expert nurses whose profile includes an educated view based on experience in this matter, recognised by others as qualified experts, who are able to provide information, evidence, views, and assessments to be included in the validation. They should have at least 5 years' experience and work in an oncology hospital service, outpatient hospital, internal medicine hospital service, or special services where hazardous drugs are administered.

5.1.3. Results Phase 1

5.1.3.1. Drugs to be monitored

Not all the hazardous drugs used in the centre can be monitored, so "target drugs" should be established to assess contamination by hazardous drugs. Each healthcare centre should assess the target drugs used and select the target drug to be used to monitor surfaces. The areas where hazardous drugs are prepared and/or administered, the number of preparations per drug, and how they are administered should be considered.

The target drugs usually employed include the following:

- Cyclophosphamide: a hazardous drug that is commonly used and is the one most frequently studied and characteristic of surface contamination. It can be used in monotherapy or in combination with other chemotherapeutical drugs, depending on indication. This drug is highly toxic, resistant, and has high skin permeability; moreover, it has been proven that healthcare staff absorb this drug. It has an oral and an intravenous formulation, so it is an ideal replacement in acute, non-acute, and primary care settings. Individuals in charge of preparing it should wear protective gloves. Eye splashes should be avoided. The material should not be

handled by pregnant or lactating women.

Cyclophosphamide is the most widely monitored drug. The fact that it is a carcinogenic recognised by the International Agency for Research on Cancer (IARC) (group 1)(27) and that its capacity for transdermal absorption (main form of occupational exposure) has been proven turn it into an ideal candidate for the purpose sought. Moreover, it is a drug that requires reconstitution prior to dilution in a vehicle for administration, increasing the number of manipulations to be performed by the preparing staff. It is also an active principle that is handled in large amounts on a very regular basis, and has validated analytic methods for its determination and quantification.

- Methotrexate: indicated for the treatment of some types of cancer such as gestational trophoblastic neoplasia (choriocarcinoma), which is the development of a tumour directly associated with pregnancy. It is a widely used hazardous drug that is usually employed in oncology and non-oncology treatment in the following areas: primary care for rheumatoid arthritis, emergency services for ectopic pregnancies, and paediatrics.

- Doxorubicin: indicated in various neoplastic diseases, frequently in chemotherapy combined with other cytotoxic drugs. It is a hazardous drug that is usually administered intravenously. The risk of exposure and contamination varies depending on the form of administration. Thus it is important to select the target drugs that include all preparation and administration forms or procedures.

- 5-Fluorouracil (5-FU): indicated for the treatment of various malignant neoplasias. It is a hazardous drug that is usually administered as a continuous infusion (home treatment), so preparation and administration might differ from other drugs and increase the risk of surface contamination.

According to experts, the drugs most frequently selected as contamination markers are cyclophosphamide, 5-fluorouracil, methotrexate, and doxorubicin. Moreover, they highlight the importance of monitoring ganciclovir, tacrolimus, mycophenolate, Bacillus Calmette Guerin (BCG), epirubicin, pegylated doxorubicin, paclitaxel, azacitidine, ciclosporin, phenytoin.

Table 2 Final recommendation

RECOMMENDATION
It is recommended to monitor at least cyclophosphamide as a subrogated marker for control of surface contamination in administration areas. If all the hazardous drugs employed in each nursing service cannot be monitored, at least the following should be monitored: doxorubicin, 5-fluorouracil, methotrexate; as well as ganciclovir, tacrolimus, mycophenolate, Bacillus Calmette Guerin (BCG), epirubicin, pegylated doxorubicin, paclitaxel, azacitidine, ciclosporin, phenytoin.

Source: Own work

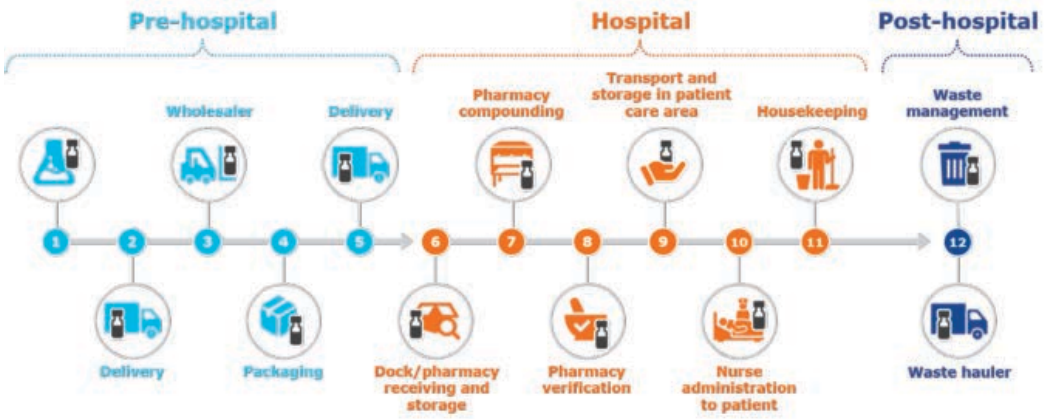
5.1.3.2. Locations to monitor

Even though several surface contamination studies have confirmed that there is greater exposure to hazardous drugs during their preparation(26)(41), concentrations of hazardous drugs can also be detected in administration areas(42).

Thus, the risk of exposure arises both in the preparation and in the administration phases, and thus procedures should be established to ensure the least exposure possible in either phase, both regarding the collective measures (the facilities used during preparation) and the individual protection measures (the personal protection equipment and the close systems for the preparation and administration of hazardous drugs)(43).

To this end, it is crucial to implement a suitable work system in which preparation is carried out in such a way that the mix is ready for administration without requiring later handling and ensuring, in addition to its composition and stability, the safety of the staff preparing it and who later administer it, as well as the prevention of environmental contamination(39). The route of a hazardous drug, from manufacturing to the hospital and later removal, is represented in the image below.

Image 1 Traceability of a hazardous drug



Source: BD

The areas, zones, or services in which hazardous drug contamination can arise, and which thus should be monitored, are the following:

- **Reception area:** areas where HDs are received in healthcare or social and health centres. These areas may include the main reception area of a centre (e.g., in hospitals, the hospital pharmacy loading areas where drugs are usually received) or the drug reception areas in each unit or service near the preparation and/or administration areas.

- **Hazardous drug preparation areas:** areas where hazardous drugs are stored, prepared, and/or packaged for administration.
  - Potential contamination areas in the HD preparation areas:
  - Floor in the nursing room for the preparation of medication
  - Counters
  - Intravenous therapy equipment
  - Cupboards with storage drawers
  - Drug vials
  - Doorknobs, handles, other areas that are touched on a mass scale
  - Keyboard and computer mouse

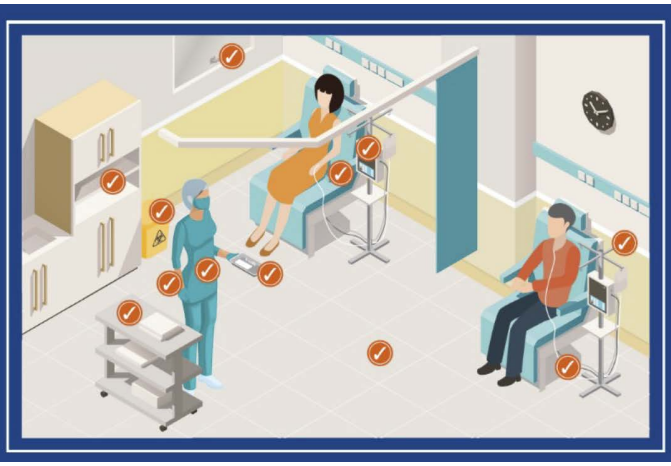
- **Hazardous drug verification areas:** areas where hazardous drugs are precisely verified (e.g., dosage, correct drug) before transport for administration.

- **Hazardous drug transport for administration:** the transport equipment, including the containers used for the delivery of hazardous drugs from the preparation area to the administration area.

- **Hazardous drug administration areas:** areas where patients are provided with hazardous drugs. These could also include non-oncology areas in the centre.
  - Oncology hospital nursing rooms
  - Outpatient hospital
  - Haemato-oncologic hospital nursing rooms
  - Intake areas or emergency rooms
  - Consultation rooms
  - Operating theatres
  - Respiratory therapy areas
  - Primary care centres, nursing homes, and patients' homes

Image 2 Administration area

Administration areas
Contamination may occur in 1,2,5:
- preparation areas
- storage areas
- administrative areas
- healthcare professionals themselves, whether they are directly responsible for patient care or not
- floor
- containers

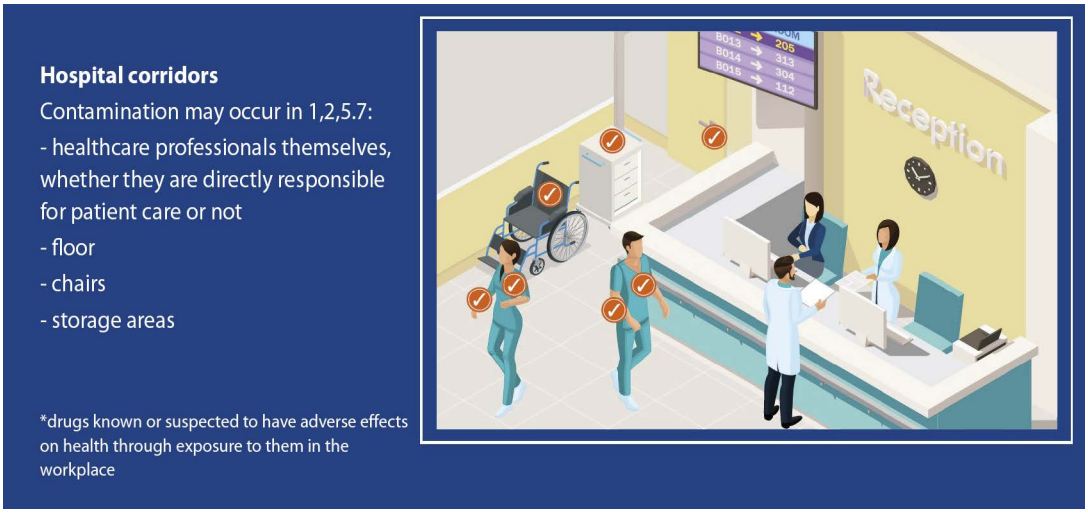


Source: BD

Potential contamination areas:
- Nursing workstations or rooms
- Medication rooms
- Areas where fluid/drug IV bags are stored
- Counters and medication trolleys
- Keyboard and computer mouse
- Floor in patient care areas

- Bathrooms
- Intravenous infusion pumps and drip stands
- Chairs
- Intravenous therapy equipment
- Transit areas and patient reception areas

Image 3 Transit areas and corridors



Source: BD

- **Hazardous drug removal areas:** areas where hazardous drugs are placed in the centre's waste flow. These include all those areas in which hazardous drugs are administered.
- **Home administration areas:** areas in the home of patients who require treatment with these drugs. Depending on the area of the home where the patient is when receiving treatment, they could include:
  - Floor in patient care areas
  - Intravenous infusion pumps
  - Intravenous therapy equipment
  - Chairs
  - Table where the medication is prepared
  - Bathroom floors

Table 3 Final recommendation

RECOMMENDATION
The locations to be sampled will be defined on the basis of the manipulation circuit and the location of administration of the hazardous drug. It is recommended to monitor at least the following locations:

- Nursing workstations or rooms
- Medication rooms
- Areas where fluid/drug IV bags are stored
- Counters and medication trolleys
- Keyboard and computer mouse
- Floor in patient care areas
- Bathroom floors
- Intravenous infusion pumps
- Chairs
- Intravenous therapy equipment
- Other areas or materials to be considered by experts would be: patient's nightstand, PPE used in administration, the patient's table, telephone, location where residue containers already used are stored, doorknobs and handles, knob of the door to the medication room, container for transport of the hazardous drug.

Source: Own work

5.1.3.3. Risk determination and sampling plan. Monitoring frequency

When designing a surface contamination monitoring plan, it is necessary to determine the risk (Appendix 4) of contamination in the various administration and discarding areas to efficiently design the plan in terms of sampling locations and frequency. Risk should be determined at least on a yearly basis and could be determined more frequently depending on the changes in monitoring procedures or results.

A significant finding of the 2013 MEWIP (Monitoring-Effect Study of Wipe Sampling in Pharmacies) study(14) was the constant decrease in the surface contamination observed by the group that took regular work surface samples. There was a 13% reduction in contaminated samples between the first and fifth cycle in comparison to no changes between samples 1 and 2 in the control group.

Surfaces could be identified as being at *high*, *medium*, or *low* risk of contamination by hazardous drugs.

The experts agree or strongly agree with the likelihood classification for low and medium risk and quite agree or strongly agree with the classification of likelihood and seriousness as high. The experts agree or strongly agree with the prevention classification for low risk and quite agree or strongly agree with the classification as medium or high.

Thus, the following risk assessments are given:

Table 4 Risk assessment (1): Contamination likelihood

Classification	Contamination likelihood
Low(1)	Low level of handling of hazardous drugs, none or very occasional manipulation and administration (e.g., orally administered drugs) **More than once a month**
Medium(2)	Medium level of handling of hazardous drugs, with some manipulation or administration by means of safe practices. **2 or 3 times a month**
High(3)	High level of hazardous drugs with frequent manipulation or administration with less safe practices (e.g., intravenous infusion bags) **1 or more times a week**

Source: Adapted from Risk Assessment Pharmacy Report

Table 5 Risk assessment (2): Contamination seriousness

Classification	Contamination seriousness
Low(1)	Restricted and highly limited access (e.g., trained staff)
Medium(2)	Semi-controlled access (e.g., staff only)
High(3)	Open access (e.g., public areas)

Source: Adapted from Risk Assessment Pharmacy Report

Table 6 Risk assessment (3): Contamination prevention

Classification	Contamination prevention
Low(1)	Engineering controls[1], administrative controls,[2] and PPE[3]
Medium(2)	Administrative controls and PPE
High(3)	PPE only

Source: Adapted from Risk Assessment Pharmacy Report

[1] Class II biological safety cabins / aseptic containment insulators to prepare the medication, robotic systems, ventilation, closed-system transfer devices, and closed intravenous systems.

[2] Implementation of work practices, administrative policies, and qualification programmes to reduce workers' risks.

[3] Standards for the use of Personal Protection Equipment (PPE) and compliance with these standards and use of PPE by employees Availability of the adequate PPE such as double gloves tested for use with hazardous drugs [ASTM 2005], waterproof coats, respiratory protection [NIOSH 2009] and eye and face covers.

5.1.3.4. Risk level and sampling frequency

Sampling frequency is defined by the risk level assigned to the area during the risk assessment, in accordance with the table below.

Table 7 Risk level and sampling frequency

Risk level of the area	Sampling frequency
High	Weekly
Medium	Monthly
Low	Quarterly

Source: Own work

So far, there are regulations or standards on surface contamination by hazardous drugs, but there are no acceptable occupational exposure levels.

The Ministry of Labour's document "Prevention measures for their preparation and administration Occupational Health and Safety Institute (Instituto Seguridad e Higiene en el trabajo, INSHT)"(44), describes the regulations and documents of interest connected to workers' protection against Hazardous Drugs, namely the following:

1. Law 31/1995 of 8 November on the prevention of Occupational Risks.
2. Royal Decree 374/2001 of 6 April on the protection of workers' health and safety against risks connected to occupational agents in the workplace.
3. Royal Decree 665/1997 of 12 May on workers' protection against the risks associated with exposure to carcinogens in the workplace.
4. Directive 2004/37/EC of the European Parliament and of the Council of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens or mutagens at work.
5. Specific directive under Article 16(1) of Council Directive 89/391/EEC.
6. Royal Decree 298/ 2009 of 6 March, modifying Royal Decree 39/1997 of 17 January, approving the Regulation of Prevention Services regarding the application of measures to promote the improvement of health and safety in the workplace for pregnant workers, workers who have recently given birth, and lactating workers.

7. Royal Decree 773/1997 of 30 May, on minimum health and safety provisions regarding the use of personal protection equipment by workers.

According to the Labour Ministry website: "it should be borne in mind that current scientific knowledge does not make it possible to identify exposure levels below which there is no risk that mutagens and most carcinogens have their characteristic effects on health".

According to the bibliography, surface contamination higher than 1.00 ng/cm^2 has been correlated to exposed workers' urine absorption(45). There are no data and no studies have been published on the potential risk to health associated with environmental contamination of surfaces by hazardous drugs(13)(13). It would be reasonable to use the lowest levels reasonably possible, as is already done in radiologic safety.

Table 8 Final recommendation

RECOMMENDATION Sampling frequency should be established on the basis of the risk level assigned to the area during the risk assessment, in accordance with the table below.

Source: Own work

5.1.3.5. Sampling time

Samples should be taken from surfaces in normal work conditions, without having previously cleaned them, to make it possible to obtain relevant data that are representative of the work processes. It is recommended that samples be taken at the end of the working date, before any cleaning, deactivation, and decontamination, in order to find the staff's highest possible exposure.

It is recommended to take extraordinary samples if there is a spillage or incident in the handling of the hazardous drugs or a substantial change in their handling procedures to verify their impact on contamination levels.

If the purpose of the sampling is to verify the effectiveness of new contamination containment measures, new handling protocols, or new cleaning and/or decontamination agents, it should be carried out before and after the change is implemented.

Table 9 Final recommendation

RECOMMENDATION
It is recommended to take the samples at the end of the working day, before the usual cleaning protocols and/or decontamination are carried out and after them.

Source: Own work

5.2. Phase 2.

5.2.1. Specific objectives Phase 2

- SO1.- To develop and implement a procedure to monitor contamination levels.

5.2.2. Methodology Phase 2

It was carried out by monitoring hazardous drug surfaces.

Scope Phase 2

This guide will serve all healthcare and social and health centres (spaces, areas, and rooms) where hazardous drugs are transported, received, prepared, administered, and discarded, outside the Hospital Pharmacy area, to develop and maintain a routine hazardous drug monitoring programme.

Professionals targeted

This guide is aimed at nurses who are involved in the preparation, administration, and discarding of hazardous drugs, outside the Hospital Pharmacy, during their work in healthcare and social and health centres.

Key aspects

The staff involved in the sampling must be trained and prove sufficient competence in the procedures. The following factors should be considered when implementing a procedure to monitor hazardous drug surfaces:

- Selection of analytic methods for analysis and monitoring.
- Sampling areas.
- Risk determination.
- Sampling frequency.
- Indicator of hazardous drugs to be sampled.
- Sampling time.

5.2.3. Results Phase 2

5.2.3.1. Immediate qualitative monitoring of Hazardous Drugs in surfaces

A portable meter with an independent battery, with a camera similar to that of a mobile phone for fast, immediate reading of the results, would be required to monitor hazardous drugs on surfaces. Other requirements would be a buffer to collect drugs from different types of surfaces, being able to move the sample along the cartridge, validation of the system for different surfaces such as stainless steel, polyethylene, resin, epoxy, formica, vinyl, linoleum, etc. As well as cartridges for the various hazardous drugs, a stencil for the surface of the area to be analysed, and a sampling kit.

To monitor hazardous surfaces, the following procedures, which are also given in appendix 2 to this document, should be carried out:

1. Use of the various types of personal protection equipment (PPE) in accordance with the protocol in the centre that guarantees all risk prevention measures.

2. For each area or location to be sampled, prepare a sampling kit, comprising a sampling tube, cartridges for the various drugs, an analyser, and a stencil to delimit the area to be analysed.

3. Select and stabilise the area to be tested. Then place the stencil, if used. Open the sampling kit and carefully take out the sampling device.

4. Firmly and slowly pass the sampling device, which will be wet, across the entire area to be sampled.

5. Insert the sampling device in the transfer vial, firmly close it, and completely turn the vial vertically five times.

6. Leave the sampling device inside the vial, remove the yellow vial lid and place 4 drops in each cartridge.

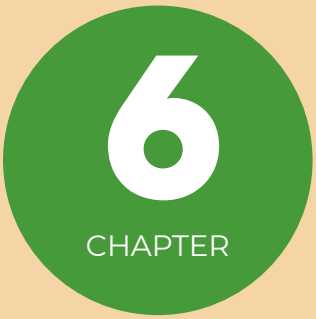
7. Wait 5 minutes after adding the sample.

8. Turn the analyser on and insert the first cartridge when the message appears on the screen.

9. The analyser will process the cartridge and the result will be displayed on the screen.

10. Record the result.

CONCLUSIONS



6. CONCLUSIONS

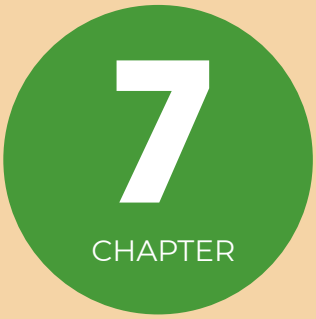
The risk to health posed by handling these drugs has been studied and well argued in the scientific literature, and is a matter of particular concern for occupational health. It is necessary to act and take preventive measures for safe handling of these hazardous drugs in healthcare settings throughout the entire chain, from intake at the healthcare centre, through their preparation and administration, to residue management.

For safe handling of hazardous drugs it is necessary to have not only the main technical measures for primary prevention, such as the facilities (biological safety cabins [BSCs] and white rooms) and closer drug transfer systems, but also secondary prevention measures such as personal protection equipment, PPE. However, to prevent the potential harmful effects of inadequate handling of hazardous drugs, it is crucial to implement organisational measures for collective primary prevention that should include, at a minimum, the implementation of an appropriate work system, the validation of specific manipulation techniques, the establishment of standardised procedures or protocols that comprise all phases of manipulation of hazardous drugs, and the measures for action against any exceptional risk situation or potential complications or incidents.

It is recommended that all medical care settings where antineoplastic and other hazardous drugs consider monitoring work surfaces through rubbing as part of an integral programme for the "safe handling" of hazardous drugs. Even though there are no standards for acceptable or permissible surface concentrations for these drugs in medical care settings, surface monitoring can be used as a method to characterise the potential risk of occupational dermal exposure and to assess the effectiveness of the controls implemented and the safety programme for a service or area. An integral programme for safe manipulation of antineoplastic drugs can use the monitoring of work surfaces as a detection tool to assess environmental contamination and reduce contamination levels as much as possible, using the industrial hygiene control hierarchy. Work surface monitoring can be used as an immediate qualitative method to characterise the potential risk of occupational skin exposure and to assess the effectiveness of the controls implemented and the general safety programme. An integral programme for safe manipulation of antineoplastic drugs can use the sampling of work surfaces as a detection tool to assess environmental contamination and reduce contamination levels as much as possible, using the industrial hygiene control hierarchy. Work surface sampling can be used as a method to characterise the potential risk of occupational skin exposure and to assess the effectiveness of the controls implemented and the general safety programme. An integral programme for safe manipulation of antineoplastic drugs can use the sampling of work surfaces as a detection tool to assess environmental contamination and reduce contamination levels as much as possible, using the industrial hygiene control hierarchy.

After having completed the surface sampling, all results should be reviewed by the individuals proposed by the centre for adequate assessment and action plan design.

GLOSSARY

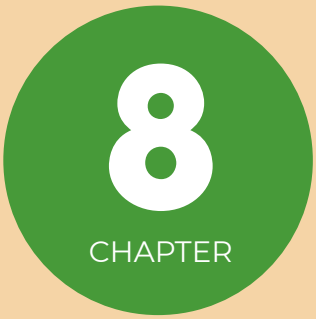


7. GLOSSARY

Hazardous drug (HD): an agent that contains an active principle whose inherent toxicity poses a risk to the health of the healthcare staff who will handle it. The dangerousness of these drugs is understood according to their chemical risk, connected to the carcinogenic, teratogenic, genotoxic, and toxic activity on the reproductive process or on a specific organ at a low dose, or because it is a new drug similar to others with this type of risk. HDs fall under the scope of the workers' protection standards pertaining to exposure to chemicals (RD 374/2001), carcinogens (RD 665/1997), and their later modification (RD 349/2003) and to workers' protection against risks related to exposure to carcinogens or mutagens during work (Directive 2004/37/EC). This category also includes the raw materials used in magistral formulas whose active principle is included in the list of hazardous drugs, as well as magistral formulas prepared with HDs and the medical products that contain substances classified as HDs (e.g., paclitaxel-impregnated stents).

Handling cytostatic drugs: the set of operations performed when preparing a dose from a commercial presentation, its administration to the patient, the collection of waste derived from professional action, the removal of the excreta and biological fluids of patients in treatment with cytostatic drugs, and any other action that involves potential contact with the medication.

BIBLIOGRAPHY



8. BIBLIOGRAPHY

1. European Parliament and of the Council. Directive (2004/37/EC) of the European Parliament and of the Council of 29 April 2004 on the Protection of Workers from the Risks Related to Exposure to Carcinogenic or Mutagens at Work. Off J Eur Union [Internet]. 2004 [cited 2019 Sep 2];(229):23. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52017SC0007&from=EN

2. Proposición de Ley reguladora del derecho a la gestación por subrogación. CONGRESO DE LOS DIPUTADOS XII LEGISLATURA BOLETÍN OFICIAL DE LAS CORTES GENERALES. In: Presentada por el Grupo Parlamentario Ciudadanos [Internet]. 2017 [cited 2019 Sep 2]. p. 12. Available from: http://www.congreso.es/public_oficiales/L12/CONG/BOCG/D/BOCG-12-D-479.PDF

3. European Commission. Safer and Healthier Work for All - Modernisation of the EU Occupational Safety and Health Legislation and Policy. Brussels; 2017. Report No.: {SWD(2017) 9 final}, {SWD(2017) 10 final}.

4. Organizacion Internacional del Trabajo. Surgen nuevos problemas de seguridad y salud a medida que el trabajo cambia [Internet]. OIT. 2019 [cited 2020 Dec 7]. p. 5. Available from: http://www.ilo.org/global/about-the-ilo/newsroom/news/WCMS_686761/lang—es/index.htm

5. Redacción Médica. ¿Cuántas enfermeras están expuestas a fármacos peligrosos? web page [Internet]. 2020 Dec 6 [cited 2020 Dec 6];1–3. Available from: https://www.redaccionmedica.com/secciones/enfermeria/medicamentos-peligrosos-enfermeria-millones-de-enfermeras-expuestas-europa-1713

6. INE. Enfermeros colegiados por tipo de especialidad, año y sexo [Internet]. INEbase. Estadística de profesionales sanitarios colegiados. 2019 [cited 2020 Dec 14]. p. 1. Available from: https://www.ine.es/jaxi/Datos.htm?path=/t15/p416/serie/l0/&file=s08001.px#!tabs-tabla

7. National Institute for Occupational Safety and Health. NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings [Internet]. web page. 2004 [cited 2020 Dec 13]. p. 1–2. Available from: http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf.

8. Benavent A, Ortuño A, Pavía Á, Forcada JA. GUÍA BREVE DE MEDICAMENTOS PELIGROSOS PARA PROFESIONALES DE ENFERMERÍA [Internet]. Consejo de Enfermería de la Comunidad Valenciana. Valencia: Consejo de Enfermería de la Comunidad Valenciana; 2018 [cited 2020 Dec 7]. p. 22. Available from: http://portalcecova.es/output/files/guia_medicamentos_peligrosos_enfermeria.pdf

9. Rioufol C, Ranchon F, Schwiertz V, Vantard N, Joue E, Gourc C, et al. Administration of anticancer drugs: exposure in hospital nurses. Clin Ther. 2014 Mar;36(3):401–7.

10. Diario Enfermero. Profesionales, pacientes y sindicatos piden a Europa que incluya en su directiva de medicamentos peligrosos ciertos fármacos cancerígenos y mutagénicos - Noticias de enfermería y salud. CGE [Internet]. 2020 Oct 15 [cited 2020 Dec 7];1. Available from: https://diarioenfermero.es/profesionales-pacientes-y-sindicatos-piden-a-europa-que-incluya-en-su-directiva-de-medicamentos-peligrosos-ciertos-farmacos-cancerigenos-y-mutagenicos/

11. Prensa SATSE. Más de 200 medicamentos peligrosos ponen en riesgo la salud de las enfermeras y enfermeros. SATSE [Internet]. 2020 [cited 2020 Dec 7];1. Available from: http://euskadi.satse.es/comunicacion/noticias/mas-de-200-medicamentos-peligrosos-ponen-en-riesgo-la-salud-de-las-enfermeras-y-enfermeros

12. Valero-García S, González-Haba E, Gorgas-Torner M, Alonso-Herreros J, Cercós-Lletí A, Poveda-Andrés, JL et al. Monitorización de las superficies de trabajo de medicamentos peligrosos en los Servicios de Farmacia. Documento de consenso. Guía de práctica farmacéutica de la Sociedad Española de Farmacia Hospitalaria (SEFH). Farm Hosp [Internet]. 2021;45(2):96–107. Available from: https://www.sefh.es/fh/208_10consenso0111655esp.pdf

13. Connor TH, Zock MD, Snow AH. Surface wipe sampling for antineoplastic (chemotherapy) and other hazardous drug residue in healthcare settings: Methodology and recommendations. J Occup Environ Hyg. 2016 Sep;13(9):658–67.

14. Kiffmeyer TK, Tuerk J, Hahn M, Stuetzer H, Hadtstein C, Heinemann A, et al. Application and assessment of a regular environmental monitoring of the antineoplastic drug contamination level in pharmacies - the MEWIP project. Ann Occup Hyg [Internet]. 2013 May [cited 2021 Jul 16];57(4):444–55. Available from: https://pubmed.ncbi.nlm.nih.gov/23125441/

15. ISOPP standards of practice. Safe handling of cytotoxics. J Oncol Pharm Pract Off Publ Int Soc Oncol Pharm Pract. 2007;13 Suppl:1–81.

16. United States Pharmacopeial Convention. <800> Hazardous Drugs-Handling in Healthcare Settings. United States Pharmacopeia 42–National Formulary 37 [Internet]. Rockville, MD; 2019 [cited 2020 Dec 7]. Available from: https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

17. Power LA, Coyne JW. ASHP Guidelines on Handling Hazardous Drugs. Am J Heal Pharm [Internet]. 2018 Dec 15;75(24):1996–2031. Available from: https://doi.org/10.2146/ajhp180564

18. Occupational Safety and Health Administration (OSHA). Controlling occupational exposure to hazardous drugs. In: U.S. Occupational Safety and Health Administration (OSHA)., editor. OSHA Technical Manual [Internet]. 2016 [cited 2020 Dec 14]. Available from: https://www.osha.gov/hazardous-drugs

19. Polovich M, Olsen MM. Manejo seguro de medicamentos peligrosos (tercera edición) | ONS [Internet]. 3ed ed. Pittsburgh, PA: Oncology Nursing Society; 2018 [cited 2020 Dec 14]. 112 p. Available from: https://www.ons.org/books/safe-handling-hazardous-drugs-third-edition

20. Sociedad Española de Farmacia Hospitalaria. Consultas de Medicamentos Peligrosos [Internet]. 2017 [cited 2020 Dec 17]. p. 4. Available from: https://gruposdetrabajo.sefh.es/gps/index.php/consultas-med-peligrosos

21. United States Pharmacopeial Convention. <800> Hazardous Drugs-Handling in Healthcare Settings. United States Pharmacopeia 42–National Formulary 37. Rockville, MD; 2019.

22. Connor TH, Massoomi F. Environmental monitoring and medical surveillance of health care workers who handle hazardous drugs (HDs). In: Improving Safe Handling Practices for Hazardous Drugs. Mansur J.,. Oak Brook, IL: Joint Commission Resources; 2016. p. 140–9.

23. Turci R, Sottani C, Spagnoli G, Minoia C. Biological and environmental monitoring of hospital personnel exposed to antineoplastic agents: a review of analytical methods. J Chromatogr B, Anal Technol Biomed life Sci. 2003 Jun;789(2):169–209.

24. Departamento de Salud y Servicios Humanos, Centros para la Prevención y el Control de las Enfermedades, Instituto Nacional para la Salud y Seguridad Ocupacional. Vigilancia médica para los trabajadores de la salud expuestos a medicamentos

peligrosos [Internet]. NIOSH. 2013 [cited 2020 Dec 9]. p. 4. Available from: https://www.cdc.gov/spanish/niosh/docs/wp-solutions/2007-117_sp/default.html

25. Marketsandmarkets. Análisis de flujo lateral Mercado por aplicación (Pruebas clínicas (embarazo, enfermedades infecciosas (mosquitos, influenza, ITS, hepatitis, TB), prueba de lípidos de marcadores cardíacos) veterinaria, seguridad alimentaria), producto, técnica, usuario f [Internet]. 2018 [cited 2020 Dec 9]. Available from: https://www.marketsandmarkets.com/Market-Reports/lateral-flow-assay-market-167205133.html

26. European Commission Directorate-General for Employment SA. Occupational health and safety risks in the Healthcare sector - Guide to prevention and good practice. 2011; Available from: http://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=6108&type=2&furtherPubs=yes

27. EU-OSHA. REACH: Reglamento de registro, evaluación, autorización y restricción de sustancias químicas - Salud y seguridad en el trabajo - EU-OSHA [Internet]. web page. [cited 2020 Dec 4]. p. 1–2. Available from: https://osha.europa.eu/es/themes/dangerous-substances/reach

28. NIOSH. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. (Supersedes 2014-138). Fed Regist [Internet]. 2016 Sep 1 [cited 2020 Dec 11];83(31):Publication Number 2016-161 (Supersedes 2014-138). Available from: https://www.cdc.gov/niosh/docs/2016-161/

29. Garate L, Gutiérrez A, López-Argumedo M, Asua J, Larrinaga U, Cidoncha MA, et al. Sistemas cerrados versus abiertos para la preparación y administración de fármacos citostáticos y biopeligrosos (Grupo 1 NIOSH): análisis de la evidencia científica, costes y requisitos organizativos TT - Closed vs open systems for the preparation and ad [Internet]. itoria-Gasteiz; 2019. Available from: https://www.euskadi.eus/web01-a2aznscp/es/k75aWebPublicacionesWar/k75aObtenerPublicacionDigitalServlet?R01HNoPortal=true&N_LIBR=052485&N_EDIC=0001&C_IDIOM=es&FORMATO=.pdf

30. González-Haba Peña E, Gaspar Carreño M, Guardino Solá X. Medicamentos peligrosos : administración y equipos disponibles [Internet]. Instituto Nacional de Seguridad y Salud en el Trabajo (INSST). España; 2018. Available from: https://www.insst.es/documents/94886/564690/ntp-1.135w.pdf/93006224-6ced-4fff-b898-1e59229fbc41

31. European Parliament and of the Council. Preventing occupational exposure to cytotoxic and other hazardous drugs. European Policy Recommendations. 2016. p. 28.

32. Centers for Disease Control and Prevention. Occupational exposure to antineoplastic agents. Available from: http://www.cdc.gov/niosh/

33. Connor TH, McDiarmid MA. Preventing occupational exposures to antineoplastic drugs in health care settings. CA Cancer J Clin [Internet]. 2006 Sep 1 [cited 2021 Jul 16];56(6):354–65. Available from: https://www.cdc.gov/niosh/docs/2004-165/

34. Fransman W, Vermeulen R, Kromhout H. Dermal exposure to cyclophosphamide in hospitals during preparation, nursing and cleaning activities. Int Arch Occup Env Heal [Internet]. 2005;78(40):3e12. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15887018.

35. Hon C-Y, Teschke K, Chua P, Venners S, Nakashima L. Occupational Exposure to Antineoplastic Drugs: Identification of Job Categories Potentially Exposed throughout the Hospital Medication System. Saf Health Work [Internet]. 2011 Sep;2(3):273–81. Available from: http://www.researchgate.net/publication/230805767_Occupational_Exposure_to_Antineoplastic_Drugs_Identification_of_Job_Categories_Potentially_Exposed_throughout_the_Hospital_Medication_System

36. Connor TH, DeBord DG, Pretty JR, Oliver MS, Roth TS, Lees PSJ, et al. Evaluation of antineoplastic drug exposure of health care workers at three university-based US cancer centers. J Occup Environ Med. 2010 Oct;52(10):1019–27.

37. Hedmer M, Georgiadi A, Bremberg ER, Jönsson BAG, Eksborg S. Surface contamination of cyclophosphamide packaging and surface contamination with antineoplastic drugs in a hospital pharmacy in Sweden. Ann Occup Hyg. 2005 Oct;49(7):629–37.

38. INSHT. Medicamentos peligrosos: Medidas de prevención para su preparación y administración [Internet]. Documentos técnicos. 2016 [cited 2020 Dec 18]. Available from: http://www.insht.es/%0AInshtWeb/Contenidos/Documentacion/FICHAS DE PUBLICACIONES/EN %0ACATALOGO/Higiene/2016 medicamentos peligrosos/Medicamentos peligrosos.%0Apdf

39. Sociedad Española de Farmacia Hospitalaria. SISTEMAS CERRADOS PARA EL MANEJO

DE LOS MEDICAMENTOS Y PRODUCTOS PELIGROSOS. SEFH [Internet]. 2017 [cited 2020 Dec 10];1–10. Available from: https://www.sefh.es/sefhpdfs/SistemasCerrados_2017_Rcn.pdf

40. Escobar-Pérez J, Cuervo-Martínez Á. Validez De Contenido Y Juicio De Expertos: Una Aproximación a Su Utilización. Av en Medición. 2008;6:27–36.

41. Spivey S, Connor TH. Determining sources of workplace contamination with antineoplastic drugs and comparing conventional IV drug preparation with a closed system. Hosp Pharm [Internet]. 2003 Feb 20 [cited 2020 Dec 14];38(2):135–9. Available from: http://journals.sagepub.com/doi/10.1177/001857870303800213

42. Bruce RH, Peters BG, Bing M. Comparison of surface contamination with cyclophosphamide and fluorouracil using a closed-system drug transfer device versus standard preparation techniques. Am J Heal Syst Pharm. 2006;63(18):1736–44.

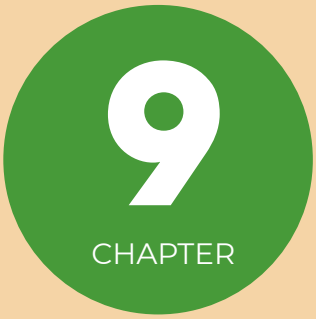
43. Siderov J, Kirsa S, McLauchlan R. Reducing workplace cytotoxic surface contamination using a closed-system drug transfer device. J Oncol Pharm Pract Off Publ Int Soc Oncol Pharm Pract. 2010 Mar;16(1):19–25.

44. Delgado O, Guardino X, Moreno E, Cercós AC, Alonso JM, Gaspar M, et al. Medicamentos peligrosos. Medidas de prevención para su preparación y administración [Internet]. Instituto Nacional de Seguridad e Higiene en el Trabajo. 2016 [cited 2020 Dec 18]. p. 85. Available from: http://www.insht.es/%0AInshtWeb/Contenidos/Documentacion/FICHAS DE PUBLICACIONES/EN %0ACATALOGO/Higiene/2016 medicamentos peligrosos/Medicamentos peligrosos.%0Apdf

45. United States Pharmacopeial Convention. <800> Hazardous Drugs-Handling in Healthcare Settings [Internet]. United States Pharmacopeia 42–National Formulary 37. 2019 [cited 2020 Dec 11]. Available from: https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

46. Instituto Nacional de Seguridad e Higiene en el trabajo. Real Decreto 374 de 06 de abril de 2001 Proteccion de la Salud y Seguridad de los Trabajadores contra los Riesgos Relacionados con los Agentes Químicos Durante el Trabajo [Internet]. Boletín Oficial del Estado 2001 p. 1–14. Available from: https://www.boe.es/buscar/act.php?id=BOE-A-2001-8436&tn=1&p=20150704

APPENDICES



9. APPENDICES

Appendix 1. Template for the assessment of the risk of surface contamination by hazardous drugs

Administration areas	Likelihood	Seriousness	Prevention	Risk
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	2	High
Counter in the patient's room	1	3	2	Medium
Counter in the nursing staff's room	1	2	3	Medium
Graph room outside the room	1	2	3	Medium
Nightstand	1	3	2	Medium
Medication trolley	2	2	3	High
Intravenous pump	2	2	2	High
Floor under the intravenous pump	3	3	2	High
Keyboard in the patient's room	1	2	3	Medium
Patient's bathroom	2	3	2	High
Chair armrest	2	3	2	High
Floor under the chair	2	3	2	High
Drug residue container	3	2	3	High
Floor in front of the hazardous drug residue container	3	2	3	High

Low
Medium
High

Appendix 2. Template for the sampling of surface contamination by hazardous drugs

Procedure activities:

1. Use of the various types of personal protection equipment (PPE) in accordance with the protocol in the centre that guarantees all risk prevention measures.

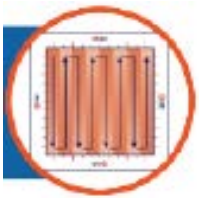
2. For each area or location to be sampled, prepare a sampling kit, comprising a sampling tube, cartridges for the various drugs, an analyser, and a stencil to delimit the area to be analysed.

Image 4 Sampling kit.

Source: BD image

3. Select and stabilise the area to be tested. Then place the stencil, if used. Open the sampling kit and carefully take out the sampling device.

Image 5 Area to be tested.



Source: BD image

4. Firmly and slowly pass the sampling device, which will be wet, across the entire area to be sampled.

5. Insert the sampling device in the transfer vial, firmly close it, and completely turn the vial vertically five times.

6. Leaving the sampling device inside the vial, remove the yellow vial lid and place 4 drops in each cartridge.

Image 6 Sampling kit.

Source: BD image

7. Wait 5 minutes after adding the sample.

8. Turn the analyser on and insert the first cartridge when the message appears on the screen.

9. The analyser will process the cartridge and the result will be displayed on the screen.

Image 7 Portable analyser.

Source: BD image

10. Record the outcome.

Appendix 3. Procedure to establish standards and expert consensus for the Guide for monitoring surfaces for hazardous drug contamination

Appendix 3 Contents

Tables

Expert assessment

I. Introduction

So-called hazardous drugs (HDs) constitute a significant risk factor for the health of the nurses who come into contact with and handle these drugs on a regular basis. These are the main basis for adverse events in hospitals, not only in number, but also in terms of morbidity and mortality, exceeding more than 20 million European workers who are exposed every year to hazardous drugs: carcinogens, mutagens, and reprotoxic chemicals(1,2).

When defining a surface contamination monitoring plan, it is necessary to determine the risk of contamination in the various administration and discarding areas, to efficiently design the plan in terms of sampling locations and frequency.

II. Basis

Nurses face various risks to health on an everyday basis. One of them is repeated exposure throughout our work life to environments where there is a clear risk of endangerment. Areas and surfaces where hazardous drugs are received, transported, prepared, administered, and discarded run the risk of being contaminated by those drugs with no routine exposure control.

A guide is being developed for the routine control of hazardous drug surface monitoring, which will serve all healthcare and health and social centres (spaces, areas, and rooms) where hazardous drugs are transported, received, prepared, administered, and discarded.
So far, there are regulations or standards on surface contamination by hazardous drugs, but there are no acceptable occupational exposure levels.

The Ministry of Labour's document "Prevention measures for their preparation and administration Occupational Health and Safety Institute (Instituto Seguridad e Higiene en el trabajo, INSHT)", describes the regulations and documents of interest connected to workers' protection against Hazardous Drugs, namely the following:

1. Law 31/1995 of 8 November on the prevention of Occupational Risks.
2. Royal Decree 374/2001 of 6 April on the protection of workers' health and safety against risks connected to occupational agents in the workplace.
3. Royal Decree 665/1997 of 12 May on workers' protection against the risks associated with exposure to carcinogens in the workplace.
4. Directive 2004/37/EC of the European Parliament and of the Council of 29 April 2004 on the protection of workers from the risks related to exposure to

carcinogens or mutagens at work.

5. Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work.
6. Royal Decree 298/ 2009 of 6 March, modifying Royal Decree 39/1997 of 17 January, approving the Regulation of Prevention Services regarding the application of measures to promote the improvement of health and safety in the workplace for pregnant workers, workers who have recently given birth, and lactating workers.
7. Royal Decree 773/1997 of 30 May, on minimum health and safety provisions regarding the use by workers of personal protection equipment.

According to the bibliography, surface contamination higher than 1.00 ng/cm^2 has been correlated to exposed workers' urine absorption(3). There are no data and no studies have been published on the potential risk to health associated with environmental contamination of surfaces by hazardous drugs(4). It would be reasonable to use the lowest levels reasonably possible, as is already done in radiologic safety.

III. Objectives

III.1. General objective

GO. - To create an expert group that will reach a consensus on the hazardous drugs to be monitored, confirm administration areas, validate, and approve the risk defined according to frequency in sample taking.

III.2. Specific objectives

SO1. - To identify the most frequent hazardous drugs to be monitored.
SO2.- To confirm risk areas in the administration of hazardous drugs.
SO3.- To approve classification in the monitoring of hazardous drugs according to the risk level allocated to the area during the risk assessment.
SO4.- To reach an agreement on the assessment of the risk, classified by likelihood, seriousness, and contamination prevention into low, medium, and high.
SO5. - To validate the risk level defined according to the sample taking frequency.
SO6.- To reach an agreement on the suitable time for the taking of samples in work surfaces.
SO7. - To validate the content of the various measurement tools as quality criteria.

IV. Method

This study will be carried out on the basis of expert assessment or expert judgement validity(5), in two stages:

In the first stage, the measurement instrument, which had only been used for Pharmacy areas, was adapted. This was the one published in the document "Monitoring work surfaces for hazardous drugs in Pharmacy Services" by the Spanish Society of Hospital Pharmacy (Sociedad Española de Farmacia Hospitalaria (SEFH)) (6).

In the second stage, the instrument "Assessment of the risk of surface contamination by hazardous drugs" was validated and standardised through validation by an expert panel to assess content validity.

A highly competent expert panel must reach an agreement on the aspects defined in the specific objectives as a whole to enable the risk assessment. **For this reason, a group of 13 professionals in this field determined the hazardous drugs to be monitored, confirmed administration areas, validated the risk level defined according to the frequency of sample taking, and reached an agreement on risk assessment classified by likelihood, seriousness, and contamination prevention into low, medium, and high.**

Phase 1. Definition.

On the basis of the research problem defined, the objective of the consultation is formulated and the dimensions to be explored are identified, specifying potential sources of information.

Phase 2. Expert participation

The experts must be professionals whose profile includes an educated view based on experience in this matter, recognised by others as qualified experts, who are able to provide information, evidence, views, and assessments to be included in the validation. They should have a least 5 years' experience and work in an oncology hospital service, outpatient hospital, internal medicine hospital service, or special services where hazardous drugs are administered, making the selected group heterogeneous.

In a second phase, contact is made with experts, who are asked to participate in a panel by means of a letter of invitation (appendix 1) and a declaration of interests.

Phase 3. Consultation rounds

A questionnaire is provided to panel members, requesting them to give their opinion on the different tables. The answers are analysed, and the areas of agreement and disagreement

are identified. 2 consultation rounds were held.

Phase 4. Results

A summarised analysis of all answers was sent to the panel members, who were asked to answer again the questionnaire questions that received the worst ratings, with 1 "strongly disagree" and 2 "disagree", from two or more experts. A "Comments" field w given for the experts to explain and justify their views when they differ from those presented.

The process is repeated until answers are stabilised in a maximum of 2 rounds.

The process starts by sending an invitation and a confidentiality agreement to be accepted by the experts, as well as a letter of invitation specifying the participant's professional profile: title, hospital, service, and current position, education, fields of work and research experience, and career. Instructions are given in a previous meeting in which the procedure to be followed is established. A total of 20 days is given for the experts to return their remarks for each consultation round. The assessment had 2 phases, validation, and standardisation: the first phase was carried out on the basis of the risk assessment model that assesses each item separately. Thus, the experts would identify whether the item was connected to the subscale being measured. Answers were given on a Likert-type scale in an assessment/aspect table ranging from "Completely disagree", through "Somewhat disagree", "Agree", and "Quite agree", to "Completely agree", to which we assigned a numerical number from 1 to 5 in the same order. If these aspects had not been previously determined, we were able to use the experts' experience and knowledge to establish the aspects to be assessed, leaving a table for comments.

Finally, each expert is able to correct the text of any items which they believed to be confusing to maintain consistency with the definition assessed through observation.

Phase 5. Data analysis

A total of 13 expert professionals was taken as the sample in the first phase (n=13). 11 professionals took part in the second phase, as all the documents were sent again to all the experts, but only 11 of them replied. Descriptive and frequency statistical analyses were conducted. For internal consistency (reliability) purposes, a reliability analysis was carried out by means of the Cronbach alpha coefficient.

The program used for the statistical analysis was the Statistical Package for Social Sciences (SPSS), version 28.0.

V. Aspects to be assessed by the experts

Section 7. of the Appendices provides the "Expert View Templates" for assessment.
The aspects to be assessed by the expert panel are described below. These are 6 appendices to be assessed by the professionals, namely:

- the most common hazardous drugs to be monitored (Appendix 2A. Hazardous Drugs)
- the most common hazardous drugs to be monitored that should be assessed in addition to those stated in the first review (Appendix 2B. Hazardous Drugs (II)
- the most frequent locations in the administration of medication to be monitored (Appendix 3. Locations to monitor)
- risk assessment model (Appendix 4A. Risk assessment model)
- risk assessment model specifying the various hazardous drug administration areas and contamination risk assessment provided in the first review (Appendix 4B. Risk assessment model (II))
- the risk assessment based on contamination likelihood, seriousness, and prevention (Appendix 5. Risk determination and sampling plan Monitoring frequency)
- risk level and sampling frequency (Appendix 6. Risk level and sampling frequency)
- a table providing the indicators and criteria for the validity of the contents of the measurement instruments (Appendix 7. Final assessment)

VI. Results

Once the expert assessment has been completed, their contributions are considered to make the relevant modifications, as their suggestions endorse the correspondence between the design of the methodological instrument being validated, its effectiveness regarding the purpose for which it was created, and the construct.

VI.1. Drugs

Not all the hazardous drugs used in the centre can be monitored, so "target drugs" should be established to assess contamination by hazardous drugs. Appendix 2 describes those drugs that might be monitored.

The results of the first review by the expert group agree or strongly agree on monitoring the following hazardous drugs, with a 4.31 mean for Cyclophosphamide and Methotrexate and 4.23 for Doxorubicin and 5-Fluorouracil (5-FU), with a standard deviation of 1.37 and 1.36 respectively.

Other very important drugs in nursing services were also mentioned that should be

monitored.

According to experts, the drugs most frequently selected as contamination markers are: cyclophosphamide, 5-fluorouracil, methotrexate, ifosfamide, gemcitabine, cytarabine, platinum derivatives, paclitaxel, doxorubicin, and etoposide phosphate.

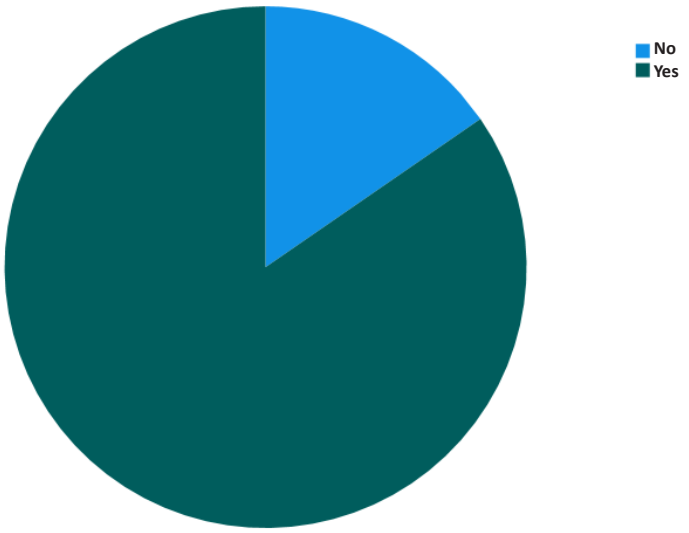
Table 1 Medication Results

Descriptive statistics

	N	Minimum	Maximum	Average	Standard deviation	Variance	Asymmetry		Kurtosis	
	Statistical	Statistical	Statistical	Statistical	Statistical	Statistical	Statistical	Standard error	Statistical	Standard error
Cyclophosphamide	13	1	5	4,31	1,377	1,897	-1,786	,616	1,943	1,191
Methotrexate	13	1	5	4,31	1,377	1,897	-1,786	,616	1,943	1,191
Doxorubicin	13	1	5	4,23	1,363	1,859	-1,655	,616	1,625	1,191
5-Fluorouracil (5-FU)	13	1	5	4,23	1,363	1,859	-1,655	,616	1,625	1,191
N valid (from list)	13									

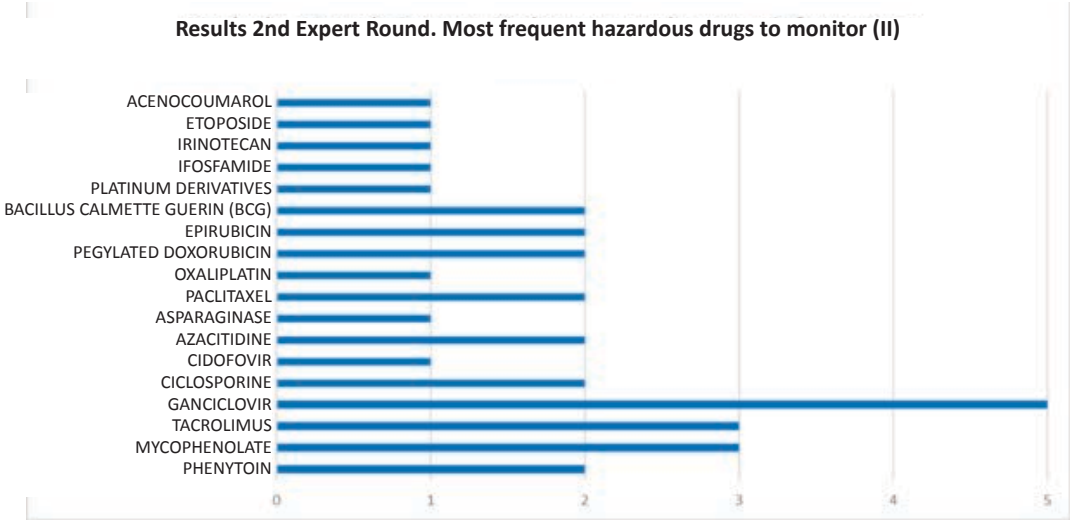
Regarding the recommendation provided to monitor hazardous drugs determined by the experts in the various nursing services, 84.6% of experts recommend monitoring at least cyclophosphamide as opposed to 15.4%. This percentage finds it insufficient to monitor one or 4 drugs, so in the second round a qualitative question was made so that the experts could specify those drugs that, in their experience, could be equally important and hazardous for nurses.

Do you agree that it should be recommended to monitor at least cyclophosphamide as a subrogated market for control of surface contamination in administration areas?



In the second round, 5 experts pointed out the importance of monitoring ganciclovir and 4 experts agreed on also monitoring tacrolimus, mycophenolate. 2 experts agreed on also monitoring Bacillus Calmette Guerin (BCG), epirubicin, pegylated doxorubicin, paclitaxel, azacitidine, ciclosporin, and phenytoin.

Table 2 Most frequent hazardous drugs to monitor (II)



As for Cronbach's alpha, it has a value of 0.997, an acceptable margin for reliability coefficients which falls between 0.7 and 0.9(7,8), so, the closer it is to its maximum value, 1, the greater the reliability of the scale to find which drugs are suitable for monitoring.

Table 3 Cronbach's alpha for Drugs

Reliability statistics

Cronbach's alpha	N of elements
,997	4

VI.2. Locations to monitor

Even though several surface contamination studies have confirmed that there is greater exposure to hazardous drugs during their preparation (24)(40), concentrations of hazardous drugs can also be detected in administration areas(41).

The areas, zones, or services in which hazardous drug contamination can arise, and which thus should be monitored and assessed by the experts, are the following:

Hazardous drug preparation areas: areas where hazardous drugs are stored, prepared, and/or packaged for administration.

Potential contamination areas in the HD preparation areas:

- Floor in the nursing room for the preparation of medication.
- Counters.
- Intravenous therapy equipment.
- Cupboards with storage drawers.
- Drug vials.
- Doorknobs, handles, other areas that are touched on a mass scale.
- Keyboard and computer mouse.

Hazardous drug administration areas: areas where patients are provided with hazardous drugs. These could also include non-oncology areas in the centre.

- Oncology hospital nursing rooms.
- Outpatient hospital
- Haemato-oncologic hospital nursing rooms.
- Intake areas or emergency rooms.
- Consultation rooms.
- Operating theatres.
- Respiratory therapy areas.
- Primary care centres, nursing homes, and patients' homes

Potential contamination areas:

- Nursing workstations or rooms.
- Medication rooms.
- Areas where fluid/drug IV bags are stored.
- Counters and medication trolleys.
- Keyboard and computer mouse.
- Floor in patient care areas.

- Bathroom floors.
- Intravenous infusion pumps.
- Chairs.
- Intravenous therapy equipment.
- Transit areas and patient reception areas.

Home administration areas: areas in the home of patients who require treatment with these drugs. Depending on the area of the home where the patient is when receiving treatment, they could include:

- Floor in patient care areas.
- Intravenous infusion pumps.
- Intravenous therapy equipment.
- Chairs.
- Table where the medication is prepared.
- Bathroom floors.

The locations to be sampled is defined on the basis of the manipulation circuit and the location of administration of the hazardous drug. Experts state that they quite agree on monitoring at least the following locations with 92.3% nursing workstations or rooms, medication rooms, medication counters and trolleys, and intravenous infusion pumps.

Table 4 Risk areas

Statistics

		Positions	Rooms	Areas	Counters	Keyboards	Floor	Bathroom floor	Pumps	Chairs	IV equipment
N	Valid	13	13	13	13	13	13	13	13	13	13
	Lost	0	0	0	0	0	0	0	0	0	0
Mean		4,92	4,77	4,54	4,85	4,15	4,46	4,00	4,85	4,08	4,38
Median		5,00	5,00	5,00	5,00	5,00	5,00	4,00	5,00	5,00	5,00
Dev. Deviation		,277	,832	,877	,555	1,144	,967	1,000	,555	1,256	1,193
Variance		,077	,692	,769	,308	1,308	,936	1,000	,308	1,577	1,423
Asymmetry		-3,606	-3,606	-2,327	-3,606	-1,139	-1,831	,000	-3,606	-,765	-1,592
Standard asymmetry error		,616	,616	,616	,616	,616	,616	,616	,616	,616	,616
Kurtosis		13,000	13,000	5,902	13,000	-,025	2,704	-2,273	13,000	-1,318	,824
Standard kurtosis error		1,191	1,191	1,191	1,191	1,191	1,191	1,191	1,191	1,191	1,191
Percentiles	25	5,00	5,00	4,00	5,00	3,50	4,00	3,00	5,00	3,00	4,00
	50	5,00	5,00	5,00	5,00	5,00	5,00	4,00	5,00	5,00	5,00
	75	5,00	5,00	5,00	5,00	5,00	5,00	5,00	5,00	5,00	5,00

A negative asymmetry indicates that most of the experts' answers concentrate in values 4 and 5, quite agreeing and strongly agreeing with the locations to monitor. A typical deviation of less than 1.5 indicates that there is little dispersion. Most observations concentrate in a few values (and more specifically in the higher scores in the scale). So they agree on assessing the following areas.

Table 5 Frequency of nursing workstations or rooms

Nursing workstations or rooms

		Frequency	Percentage	Valid percentage	Total percentage
Valid	4	1	7.7	7.7	7.7
	5	12	92.3	92.3	100.0
	Total	13	100.0	100.0	

Table 6 Drug room frequency

Medication rooms

		Frequency	Percentage	Valid percentage	Total percentage
Valid	2	1	7.7	7.7	7.7
	5	12	92.3	92.3	100.0
	Total	13	100.0	100.0	

Table 7 Frequency areas where fluid/drug IV bags are stored

Areas where fluid/drug IV bags are stored

		Frequency	Percentage	Valid percentage	Total percentage
Valid	2	1	7.7	7.7	7.7
	4	3	23.1	23.1	30.8
	5	9	69.2	69.2	100.0
	Total	13	100.0	100.0	

Table 8 Counter and medication trolley frequency

Counters and medication trolleys

		Frequency	Percentage	Valid percentage	Total percentage
Valid	3	1	7.7	7.7	7.7
	5	12	92.3	92.3	100.0
	Total	13	100.0	100.0	

Table 9 Frequency keyboard and computer mouse

Keyboard and computer mouse

		Frequency	Percentage	Valid percentage	Total percentage
Valid	2	2	15.4	15.4	15.4
	3	1	7.7	7.7	23.1
	4	3	23.1	23.1	46.2
	5	7	53.8	53.8	100.0
	Total	13	100.0	100.0	

Diagram 1 Boxplot: computer keyboard

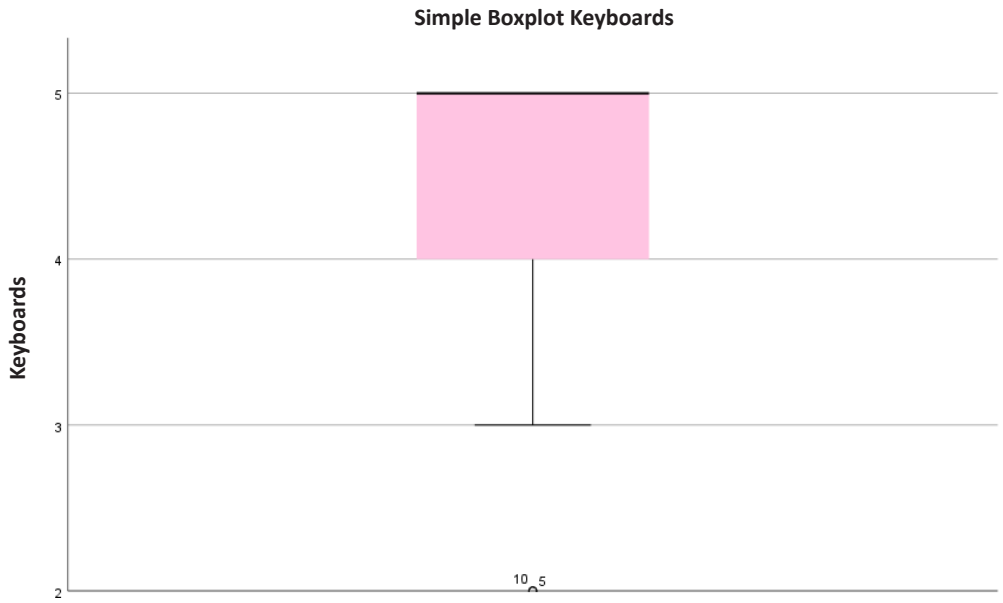


Table 10 Frequency care areas

Floor in patient care areas

		Frequency	Percentage	Valid percentage	Total percentage
Valid	2	1	7.7	7.7	7.7
	3	1	7.7	7.7	15.4
	4	2	15.4	15.4	30.8
	5	9	69.2	69.2	100.0
	Total	13	100.0	100.0	

Table 11 Frequency bathroom floor

Bathroom floor

		Frequency	Percentage	Valid percentage	Total percentage
Valid	3	6	46.2	46.2	46.2
	4	1	7.7	7.7	53.8
	5	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

Diagram 2 Boxplot: floor in patient care areas

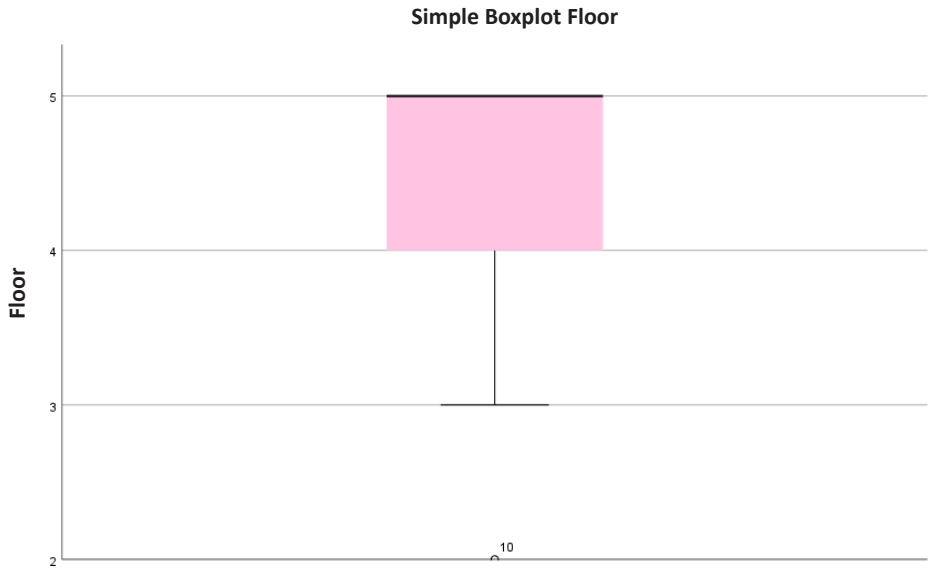


Table 12 Frequency IV infusion pump

Intravenous infusion pumps

		Frequency	Percentage	Valid percentage	Total percentage
Valid	3	1	7.7	7.7	7.7
	5	12	92.3	92.3	100.0
	Total	13	100.0	100.0	

Table 13 Chair location frequency

Chairs

		Frequency	Percentage	Valid percentage	Total percentage
Valid	2	2	15.4	15.4	15.4
	3	3	23.1	23.1	38.5
	5	8	61.5	61.5	100.0
	Total	13	100.0	100.0	

Diagram 3 Boxplot: chairs

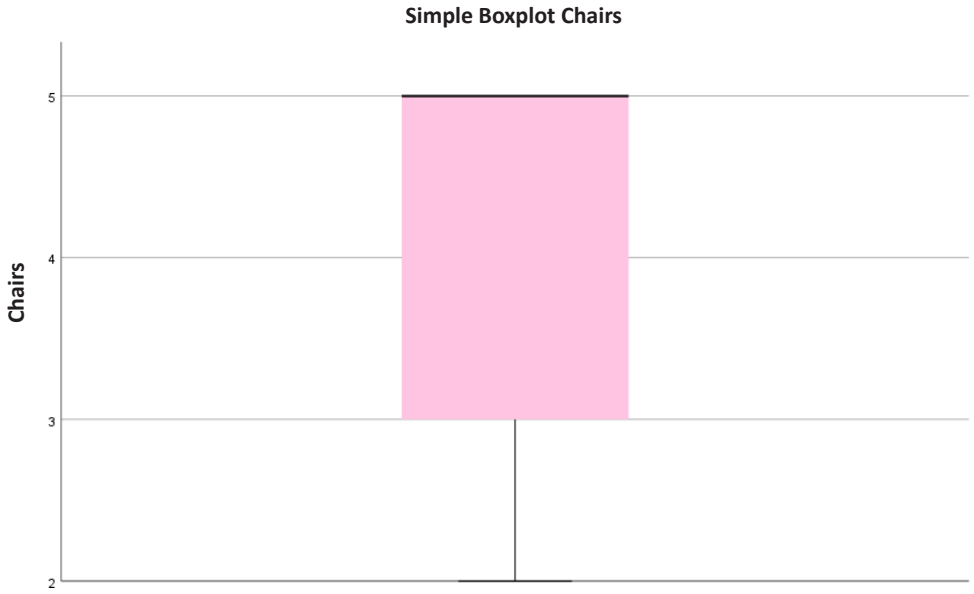


Table 14 Frequency IV therapy equipment

Intravenous therapy equipment (IV)

		Frequency	Percentage	Valid percentage	Total percentage
Valid	2	2	15.4	15.4	15.4
	3	1	7.7	7.7	23.1
	5	10	76.9	76.9	100.0
	Total	13	100.0	100.0	

Other areas or materials to be considered by experts would be: patient's nightstand, PPE used in administration, the patient's bed, telephone, location where residue containers already used are stored, doorknobs and handles, knob of the door to the medication room, container for transport of the hazardous drug.

In this case, Cronbach's alpha is 0.886, very close to 1, so it can be stated that the results are remarkably reliable.

Reliability statistics

Cronbach's alpha	N of elements
,886	10

VI.3 Contamination risk assessment model

VI.3.1. First consultation round with experts

The experts state that they quite or strongly agree with the classification of the containers in the medication room/areas, the refrigerator in the medication room/area, the medication room/area trolley, the counter in the patient's room, the floor under the intravenous pump, the patient's bathroom, the chair armrest, the floor under the chair, the hazardous drug residue container, the floor in front of the hazardous drug residue container.

Table 15 Assessment model results

Statistics

		Do you agree with the classification of the counter in the medication room/area?	Do you agree with the classification of containers in the medication room/area?	Do you agree with classification of the refrigerator in the medication room/area?	Do you agree with classification of the trolley in the mediation room/area?	Do you agree with the classification of the floor in the room/medication room?	Do you agree with the classification of the counter in the patient's room?	Do you agree with classification of the counter in the nursing staff's room?	Do you agree with classification of the graph room outside the room?	Do you agree with the classification of the night stand?
N	Valid	13	13	13	13	13	13	13	13	13
	Lost	0	0	0	0	0	0	0	0	0
Mean		3,54	4,46	4,46	4,46	3,77	4,00	3,62	3,62	3,15
Median		4,00	5,00	5,00	5,00	4,00	4,00	4,00	4,00	3,00
Dev. Deviation		1,266	,967	,967	,967	1,423	1,000	1,121	1,121	1,281
Variance		1,603	,936	,936	,936	2,026	1,000	1,256	1,256	1,641
Asymmetry		-,102	-1,831	-1,831	-1,831	-,752	-,591	-,340	-,340	-,053
Standard asymmetry error		,616	,616	,616	,616	,616	,616	,616	,616	,616
Kurtosis		-1,728	2,704	2,704	2,704	-,806	-,618	-1,145	-1,145	-1,168
Standard kurtosis error		1,191	1,191	1,191	1,191	1,191	1,191	1,191	1,191	1,191
Percentiles	25	2,00	4,00	4,00	4,00	2,50	3,00	2,50	2,50	2,00
	50	4,00	5,00	5,00	5,00	4,00	4,00	4,00	4,00	3,00
	75	5,00	5,00	5,00	5,00	5,00	5,00	4,50	4,50	4,00

In the case of the medication trolley, this is a standard deviation of 1.561, which means that the values in the dataset are farther from the mean, on average and with a variance of 2.436. This means that it is one of the questions with the highest level of result dispersion. The questions asked again in a second round to reach a consensus are: Do you agree with classification of the counter in the medication room/area? Do you agree with the classification of the floor in the room/medication room? Do you agree with the classification of the counter in the nursing staff's room? Do you agree with the classification of the graph room outside the room? Do you agree with the classification of the nightstand? Do you agree with the classification of the medication trolley? Do you agree with the classification of the intravenous pump? Do you agree with the classification of the keyboard in the patient's room?

Statistics

		Do you agree with the classification of the medication trolley?	Do you agree with the classification of the intravenous pump?	Do you agree with classification of the floor under the intravenous pump?	Do you agree with the classification of the counter in the patient's room?	Do you agree with the classification of the patient's bathroom?	Do you agree with classification of chair armrest?	Do you agree with classification of floor under the chair?	Do you agree with the classification of drug residue container?	Do you agree with the classification of the floor in front of the hazardous drug residue container?
N	Valid	13	13	13	12	13	13	13	13	13
	Lost	0	0	0	1	0	0	0	0	0
Mean		3,54	3,08	4,31	3,83	4,46	4,38	4,23	4,62	4,62
Median		4,00	3,00	5,00	4,00	5,00	5,00	5,00	5,00	5,00
Dev. Deviation		1,561	1,320	,855	1,193	,776	,768	1,013	,768	,768
Variance		2,436	1,744	,731	1,424	,603	,590	1,026	,590	,590
Asymmetry		-,317	,349	-,705	-,392	-1,114	-,849	-1,107	-1,760	-1,760
Standard asymmetry error		,616	,616	,616	,637	,616	,616	,616	,616	,616
Kurtosis		-1,803	-,946	-1,240	-1,446	-,155	-,580	,242	1,615	1,615
Standard kurtosis error		1,191	1,191	1,191	1,232	1,191	1,191	1,191	1,191	1,191
Percentiles	25	2,00	2,00	3,50	3,00	4,00	4,00	3,50	4,50	4,50
	50	4,00	3,00	5,00	4,00	5,00	5,00	5,00	5,00	5,00
	75	5,00	4,50	5,00	5,00	5,00	5,00	5,00	5,00	5,00

Table 16 Do you agree with the classification of the counter in the medication room/area?

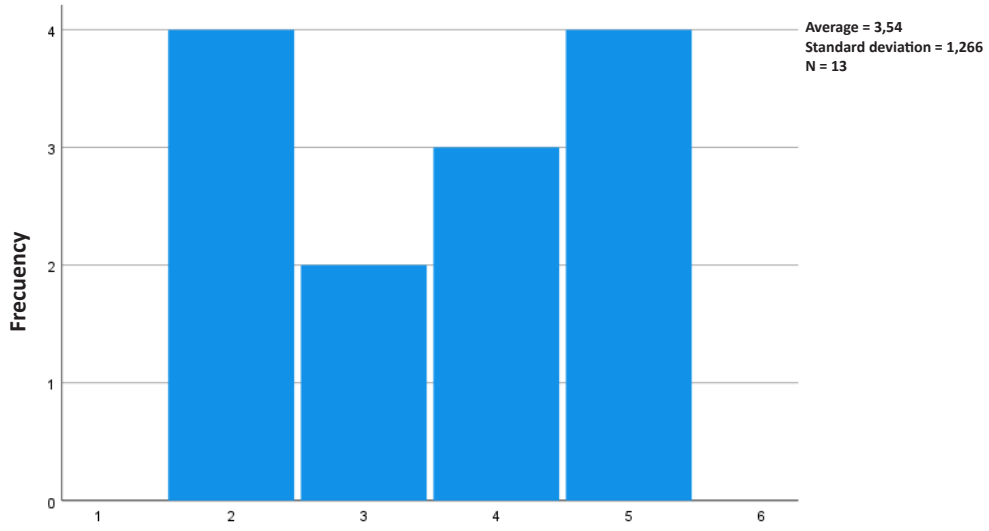


Table 17 Do you agree with the classification of the floor in the room/medication room?

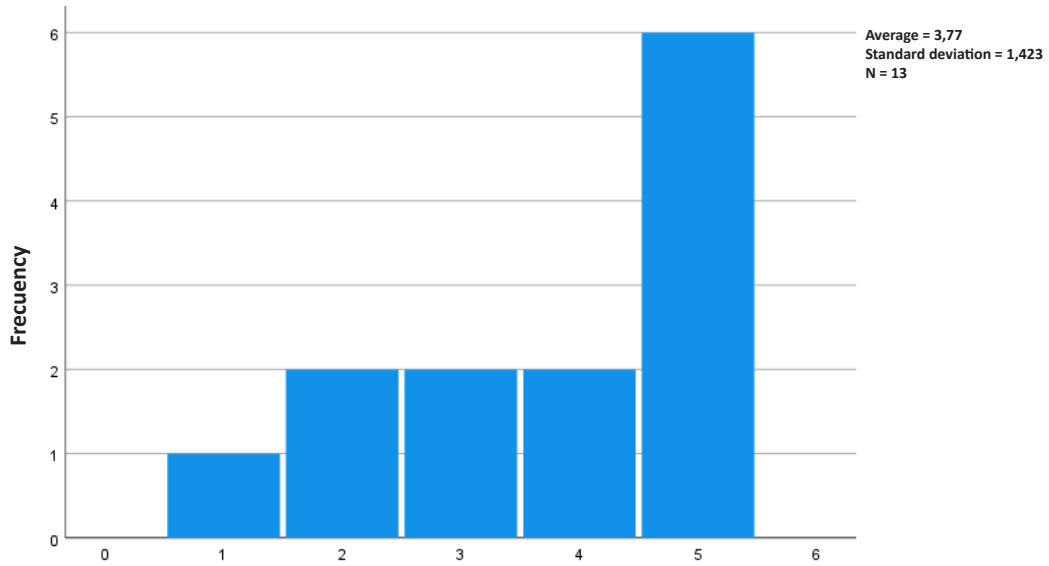


Table 18 Do you agree with classification of the counter in the nursing staff's

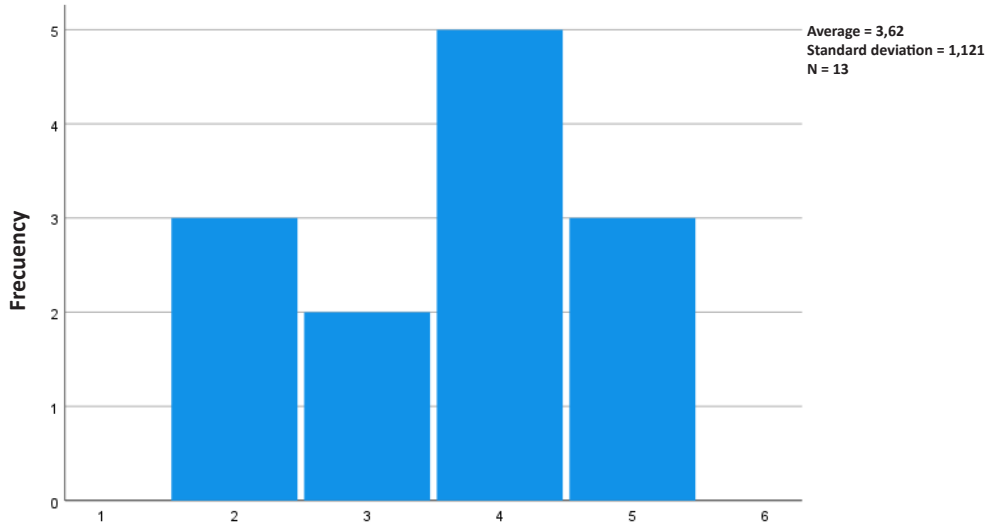


Table 19 Do you agree with the classification of the graph room outside the room?

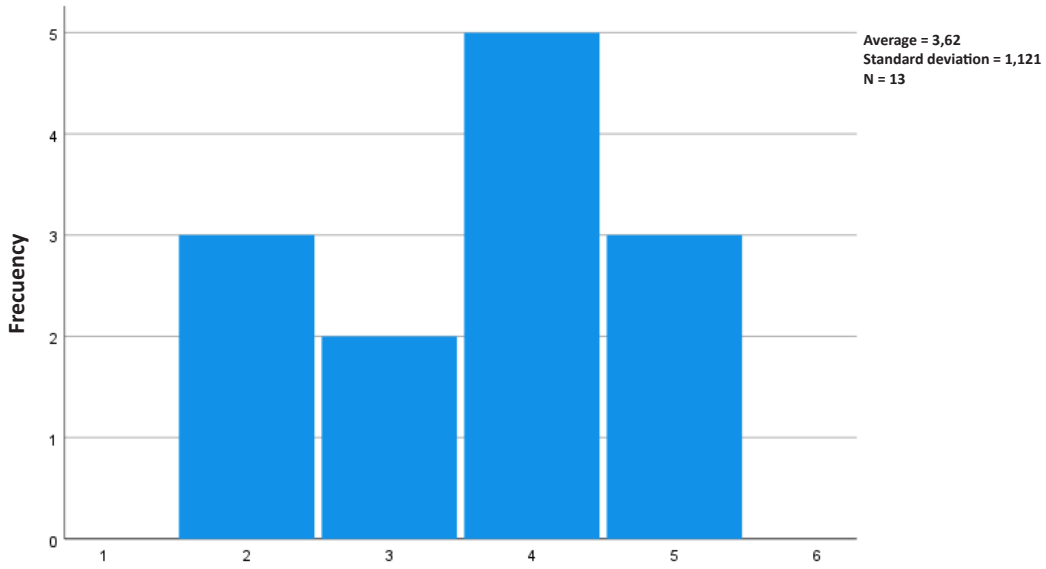


Table 20 Do you agree with the classification of the nightstand?

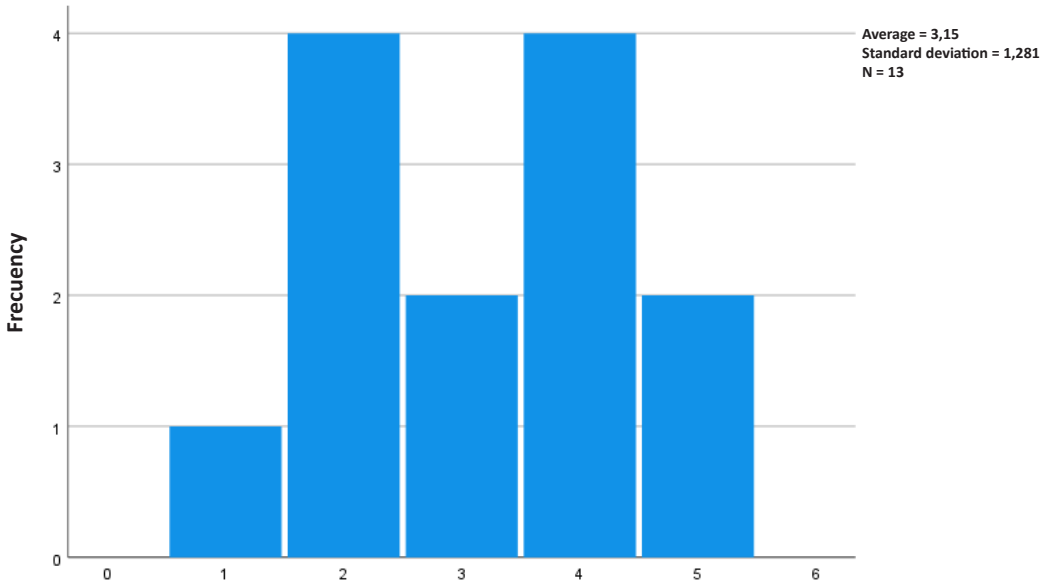


Table 21 Do you agree with the classification of the medication trolley?

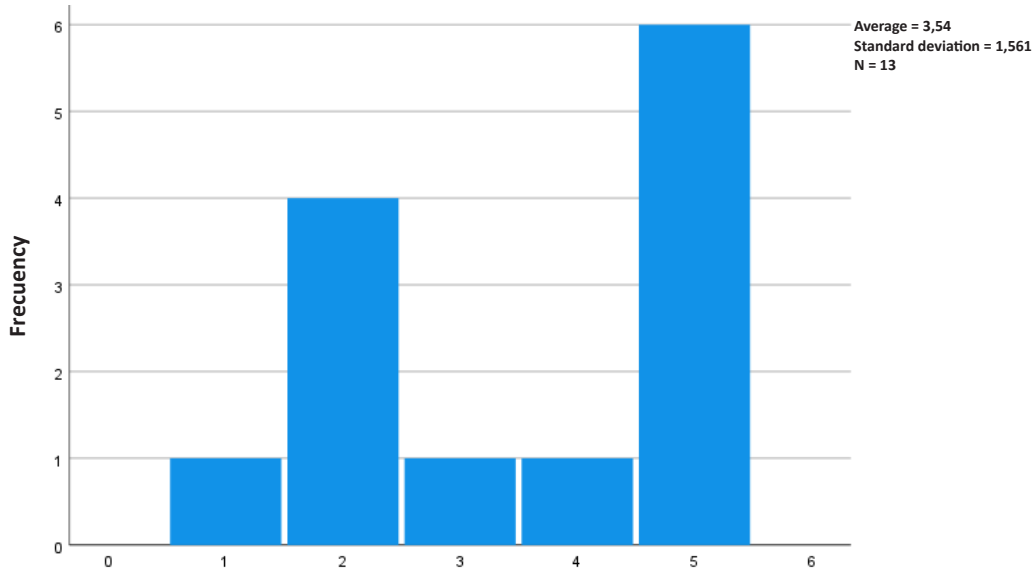


Table 22 Do you agree with the classification of the intravenous pump?

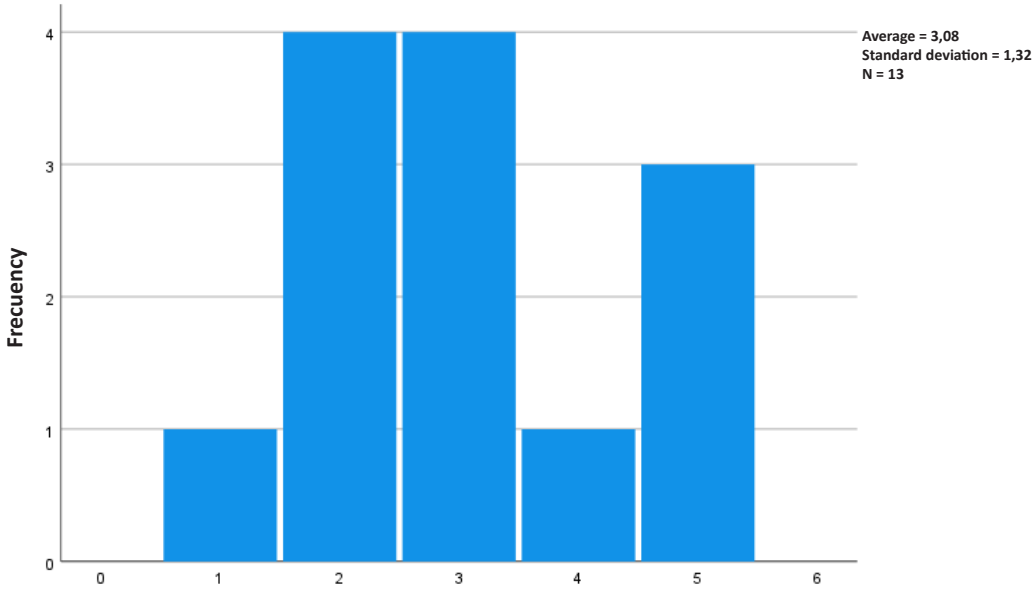
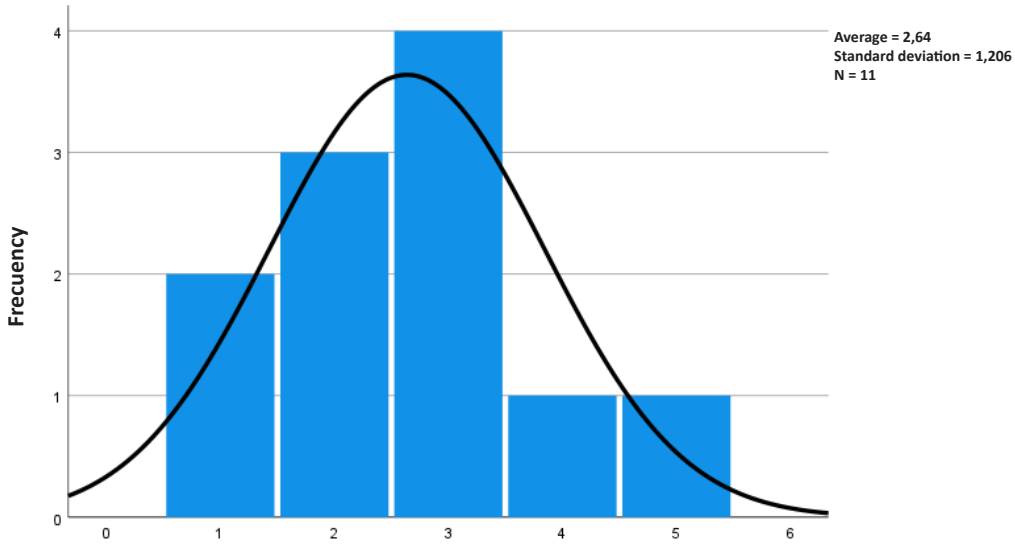


Table 23 Do you agree with the classification of the keyboard in the patient's room?



The table below details the assessment model established by consensus in the first round of expert consultations, where the areas marked in grey are those where a consensus was reached in the second round.

Table 24 Assessment model (1st expert round)

Administration areas	Likelihood	Seriousness	Prevention	Risk
Room counter/medication room				
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room				
Counter in the patient's room	1	3	2	Medium
Counter in the nursing staff's room				
Graph room outside the room				
Nightstand Medication trolley				
Intravenous pump				
Floor under the intravenous pump	3	3	2	High
Keyboard in the patient's room				
Patient's bathroom	2	3	2	High
Chair armrest	2	3	2	High
Floor under the chair	2	3	2	High
Drug residue container	3	2	3	High
Floor in front of the hazardous drug residue container	3	2	3	High

As for Cronbach's alpha, it has a value of 0.915 , so, the closer it is to its maximum value, 1, the greater the reliability of the scale to find the assessment model in accordance with the risk assigned.

Table 26 Cronbach's alpha for assessment model

Reliability statistics

Cronbach's alpha	N of elements
,915	18

VI.3.2. Second consultation round with experts

The results of the second round of consultation with the experts for the contamination risk assessment are that they completely disagree or disagree with a mean of about 2.20 and 3.18, and a greater typical deviation of about 1.483 for the observation of the intravenous pump, where more observations are more scattered than in other administration areas. Other areas where there was little consensus among experts is the classification of the room counter/medication room ($\sigma^2$1.433), nightstand (σ^2 1,446).

Table 27 Results 2nd expert round. Risk assessment model

Descriptive statistics

	N	Minimum	Maximum	Average	Standard deviation
Do you agree with the classification of the counter in the medication room/area?	11	1	5	2,64	1,433
Do you agree with the classification of the floor in the room/medication room?	11	1	5	2,82	1,401
Do you agree with classification of the counter in the nursing staff's room?	11	1	5	3,18	1,168
Do you agree with classification of the graph room outside the room?	11	1	5	3,00	1,265
Do you agree with the classification of the night stand?	11	1	5	2,91	1,446
Do you agree with the classification of the medication trolley?	10	1	3	2,20	,789
Do you agree with the classification of the intravenous pump?	11	1	5	3,00	1,483
Do you agree with the classification of the counter in the patient's room?	11	1	5	2,64	1,206
N valid (from list)	10				

Table 28 Simple boxplot for Do you agree with the classification of the counter in the medication room/area?

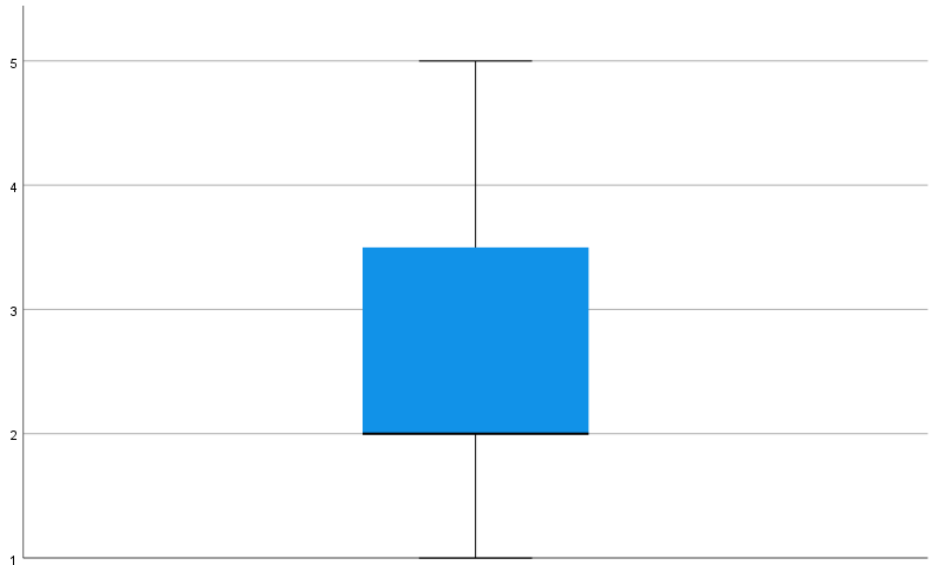
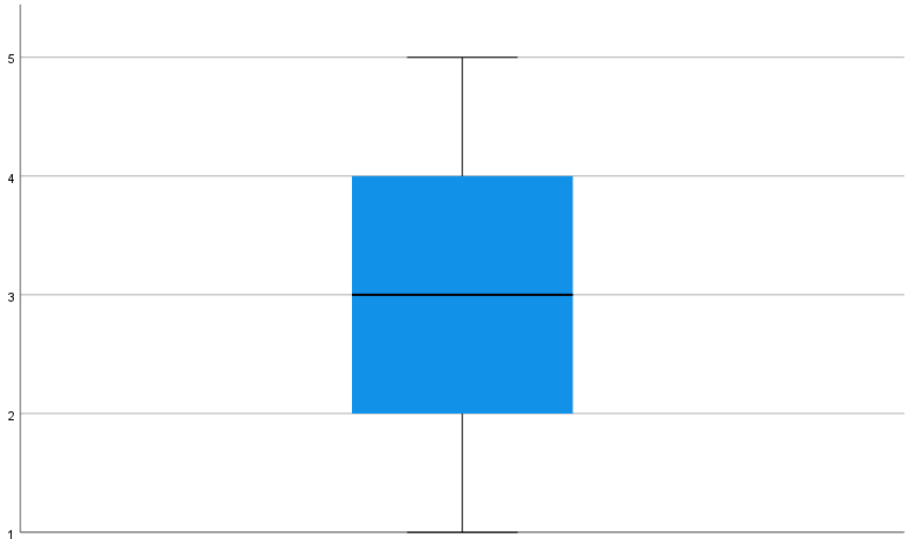


Table 29 Simple boxplot for Do you agree with the classification of the nightstand?



For the second round of consultation with the experts, the majority of the administration areas were established as having a medium or high risk.

The assessment of the risk of surface contamination by hazardous drugs in the second round is described in the table below.

Table 30 Assessment model (2nd expert round)

Administration areas	Likelihood	Seriousness	Prevention	Risk
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	3	High
Room counter/medication room	2	2	2	High
Counter in the patient's room	1	3	2	Medium
Counter in the nursing staff's room	1	2	3	Medium
Graph room outside the room	1	2	3	Medium
Nightstand	1	3	2	Medium
Medication trolley	2	2	3	High
Intravenous pump	2	2	2	High
Floor under the intravenous pump	3	3	2	High
Keyboard in the patient's room	1	2	3	Medium
Patient's bathroom	2	3	2	High
Chair armrest	2	3	2	High
Floor under the chair	2	3	2	High
Drug residue container	3	2	3	High
Floor in front of the hazardous drug residue container	3	2	3	High

VI.4. Risk determination and sampling plan Monitoring frequency

Risk should be determined at least on a yearly basis and could be determined more frequently depending on the changes in monitoring procedures or results.

A significant finding of the 2013 MEWIP (Monitoring-Effect Study of Wipe Sampling in Pharmacies) study(9) was the constant decrease in the surface contamination observed by the group that took regular work surface samples. There was a 13% reduction in contaminated samples between the first and fifth cycle in comparison to no changes between samples 1 and 2 in the control group.

The risk for each area can be determined by completing a risk assessment (Appendix 4). It is used to identify areas where there can be environmental contamination from hazardous drugs. In the table in appendix 4 the hazardous drug administration areas are identified in accordance with the risk assessment classification in terms of the likelihood of contamination, seriousness, and contamination prevention. These tables are taken from the document "Monitoring hazardous drug working surfaces in Pharmacy Services" of the Spanish Society for Hospital Pharmacy (Sociedad Española de Farmacia Hospitalaria, SEFH)(6), and they are those that were submitted to the experts' judgement for their assessment. They specify the areas identified with the corresponding classification and the risk level assigned to the area.

Surfaces could be identified as being at *high*, *medium*, or *low* risk of contamination by hazardous drugs.

a) Likelihood

The experts agree or strongly agree with the likelihood classification for low and medium risk and quite agree or strongly agree with the classification of likelihood and seriousness as high as shown in the boxplots below.

Table 31 Boxplot Low Risk

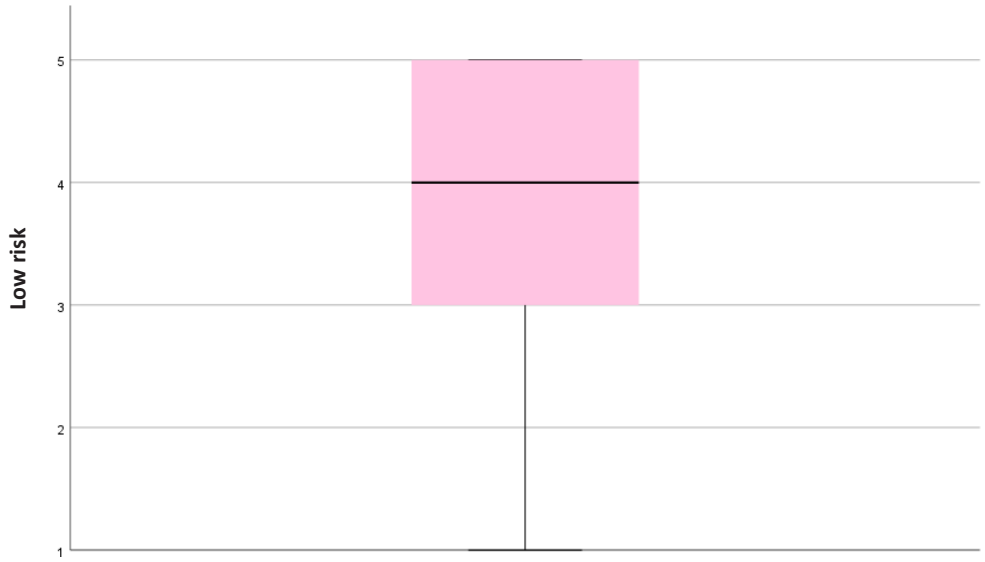


Table 32 Boxplot Medium Risk

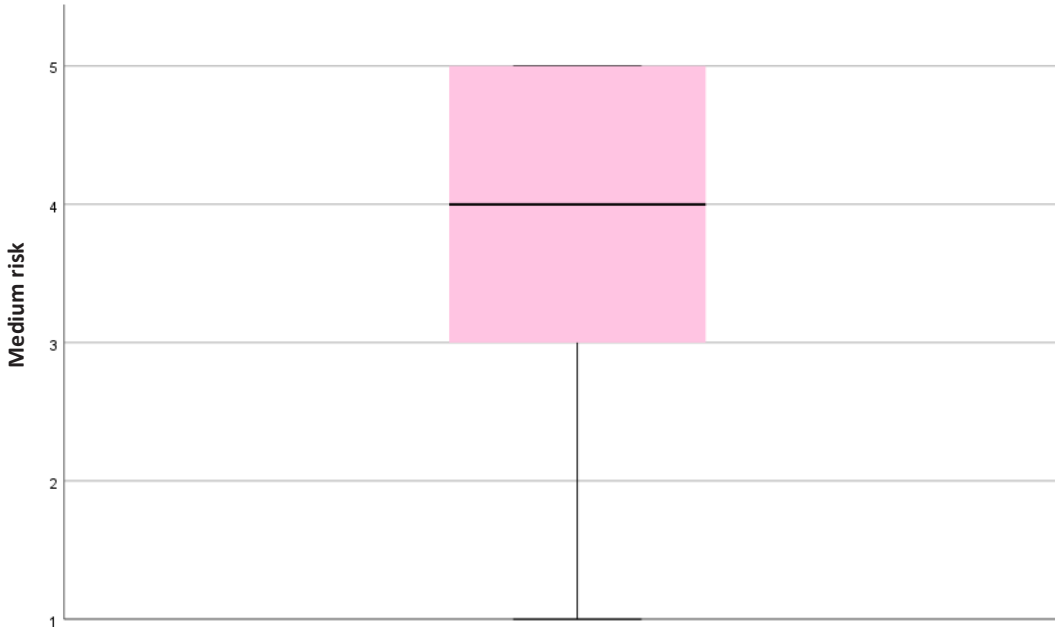


Table 33 Boxplot High Risk

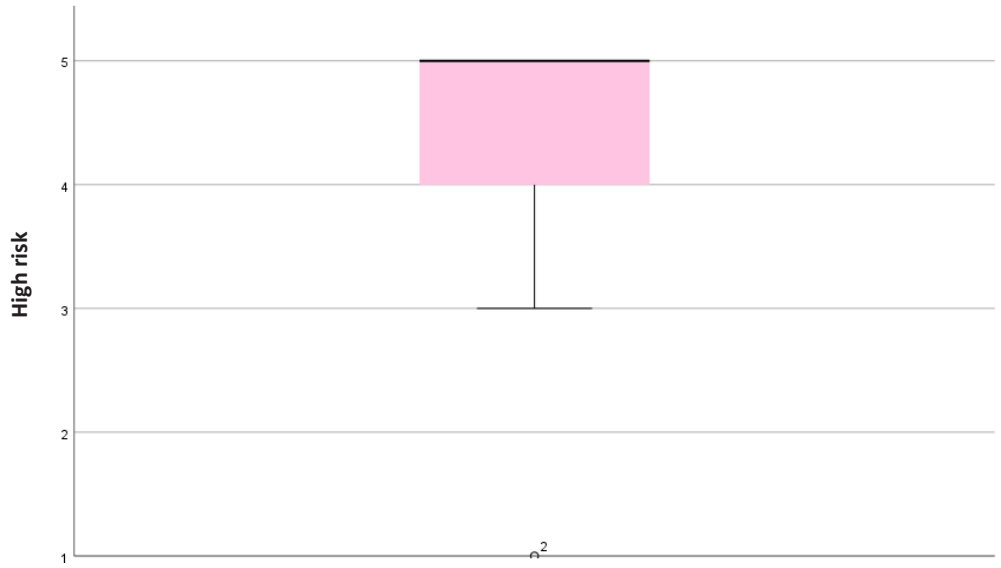


Table 34 Risk assessment (1): Contamination likelihood

Classification	Contamination likelihood
Low(1)	Low level of handling of hazardous drugs, none or very occasional manipulation and administration (e.g. orally administered drugs) **More than once a month**
Medium(2)	Medium level of handling of hazardous drugs, with some manipulation or administration by means of safe practices. **2 or 3 times a month**
High(3)	High level of hazardous drugs with frequent manipulation or administration with less safe practices (e.g., intravenous infusion bags) **1 or more times a week**

Source: Adapted from Risk Assessment Pharmacy Report

b) Seriousness

The experts agree or strongly agree with the seriousness classification for low and medium risk and quite agree or strongly agree with the classification of likelihood and seriousness as high as shown in the boxplots below.

Table 35 Simple Boxplot Low Risk

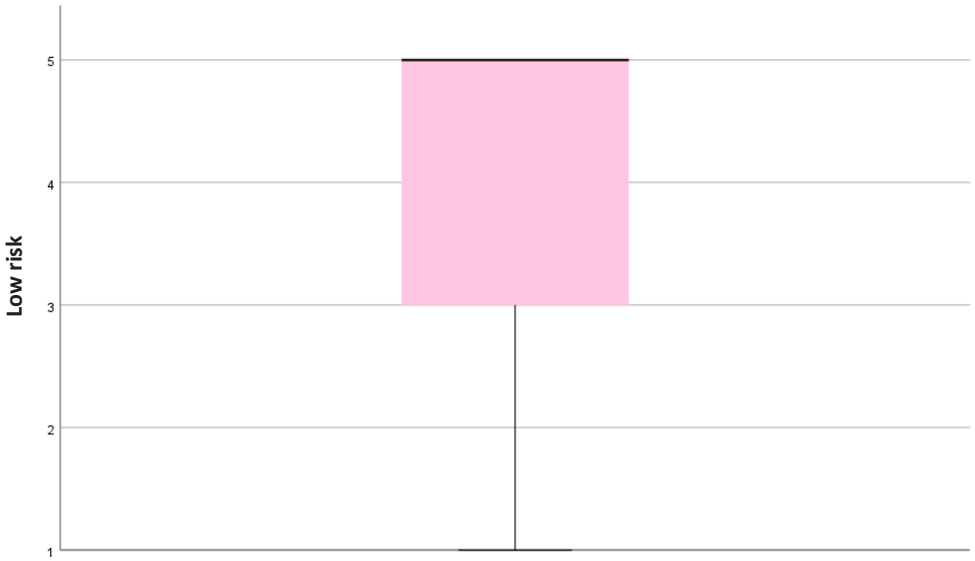


Table 36 Simple Boxplot Medium Risk

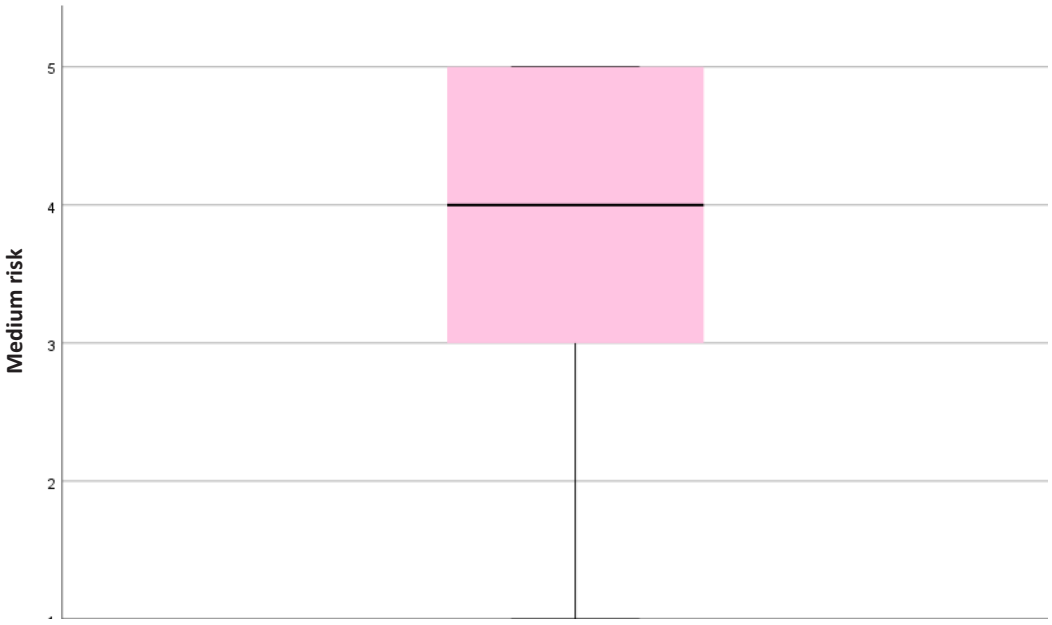


Table 37 Simple Boxplot High Risk

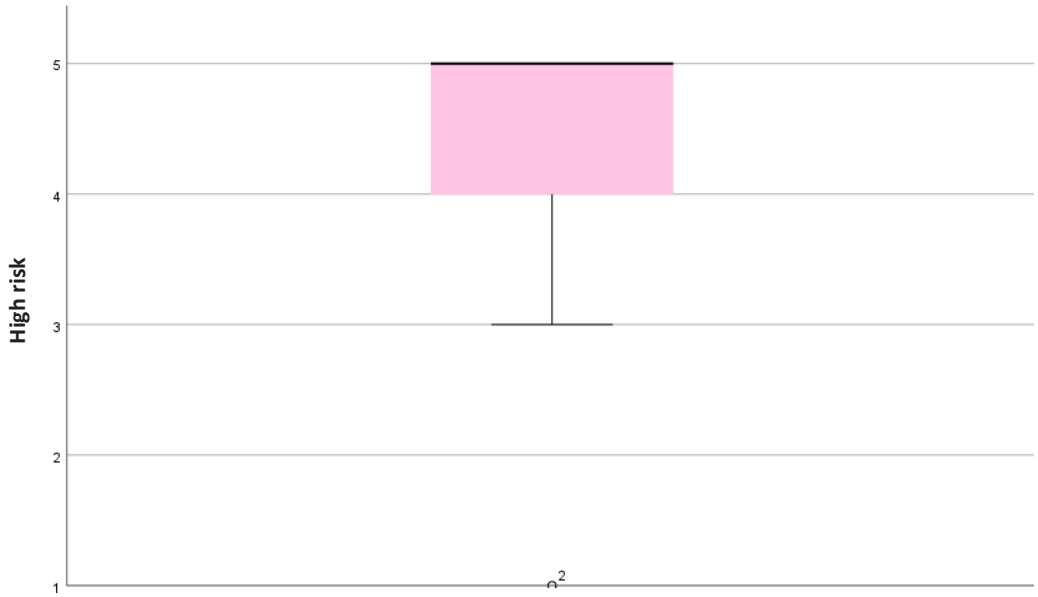


Table 38 Risk assessment (2): Contamination seriousness

Classification	Contamination seriousness
Low(1)	Restricted and highly limited access (e.g. trained staff)
Medium(2)	Semi-controlled access (e.g. staff only)
High(3)	Open access (e.g., public areas)

Source: Adapted from Risk Assessment Pharmacy Report

c) Prevention

The experts agree or strongly agree with the prevention classification for low and medium risk and quite agree or strongly agree with the classification of likelihood and seriousness as high as shown in the boxplots below.

Table 39 Simple Boxplot Low Risk

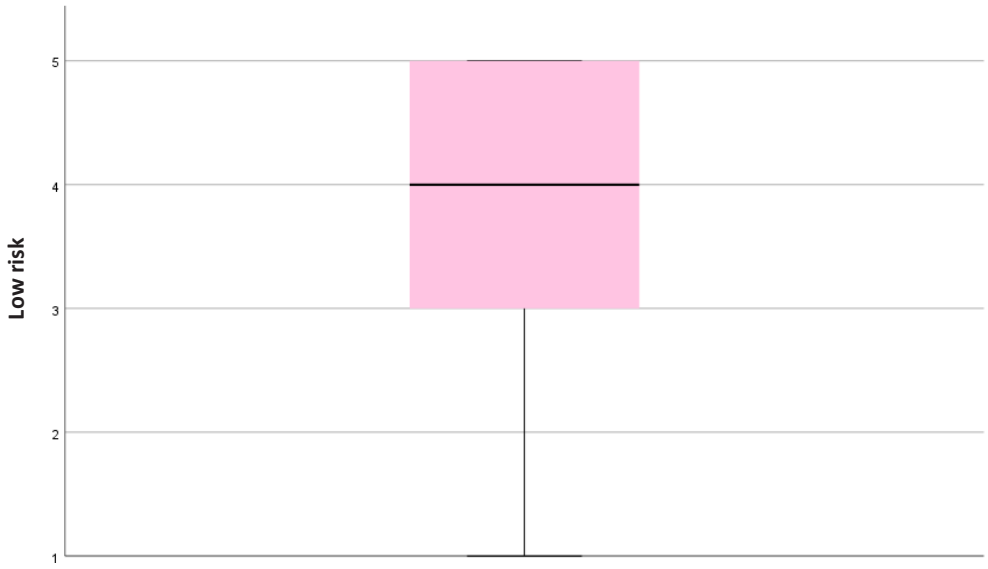


Table 40 Simple Boxplot Medium Risk

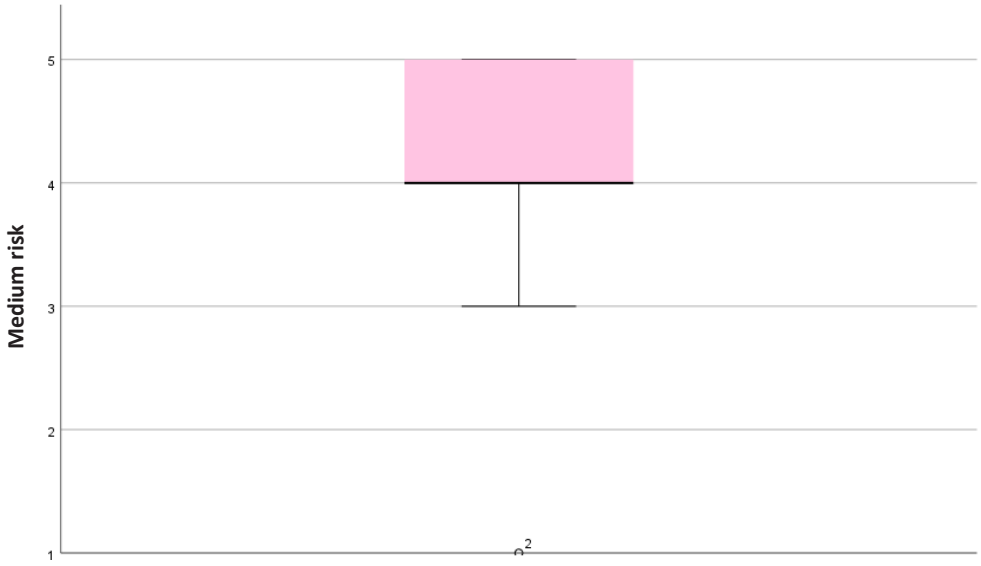


Table 41 Simple Boxplot High Risk

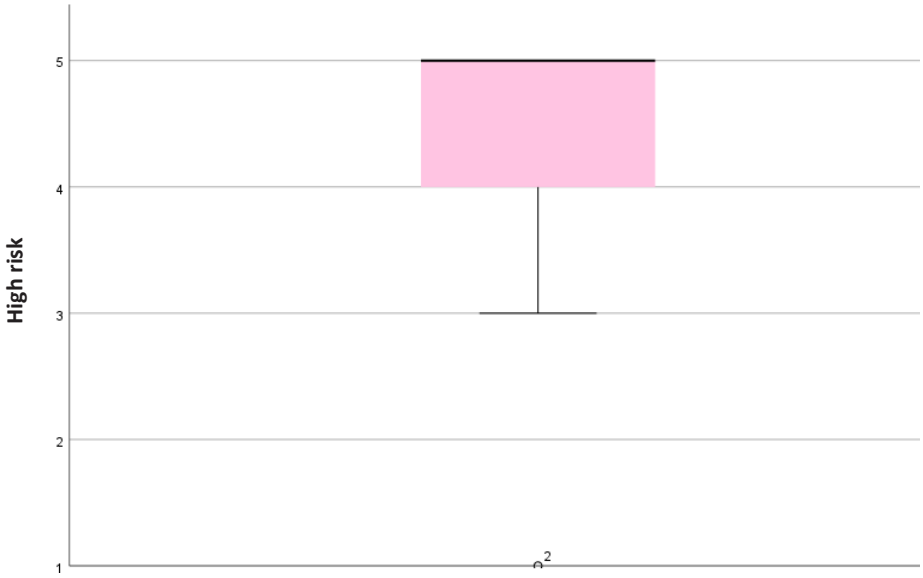


Table 42 Risk assessment (3): Contamination prevention

Classification	Contamination prevention
Low(1)	Engineering controls[4], administrative controls,[5] and PPE[6]
Medium(2)	Administrative controls and PPE
High(3)	PPE only

Source: Adapted from Risk Assessment Pharmacy Report

[4]Class II biological safety cabins / aseptic containment insulators to prepare the medication, robotic systems, ventilation, closed-system transfer devices, and closed intravenous systems

[5]Implementation of work practices, administrative policies, and qualification programmes to reduce workers' risks

[6]Standards for the use of Personal Protection Equipment (PPE) and compliance with these standards and use of PPE by employees. Availability of the adequate PPE such as double gloves tested for use with hazardous drugs [ASTM 2005], waterproof coats, respiratory protection [NIOSH 2009] and eye and face covers.

VI.5. Risk level and sampling frequency

The expert consensus on the risk level by area and its correspondence with the sampling frequency are shown below. According to Fisher's asymmetry coefficient, which assesses data proximity to their mean, the distribution has negative asymmetry, and extends to lower values than the mean as shown in the table below. The mean of the results is 4.08 for the weekly sampling frequency, the risk being high, so experts quite agree. For the monthly sampling frequency in the medium risk level and quarterly frequency for low risk, with a mean of 3.85, on which experts agree.

It should also be pointed out that two experts have given low scores, completely or strongly disagreeing, for the quarterly sampling frequency and low risk level. They state in their comments that they find the measure insufficient, and the frequency should be fortnightly for the medium level, and monthly for the low level. Another expert states that the weekly item should be 2-3 days per week, the monthly item at least every 15 days, and the quarterly items several times every month.

Descriptive statistics

	N	Minimum	Maximum	Average	Standard deviation	Variance	Asymmetry		Curtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Standard error	Statistic	Standard error
Weekly	13	2	5	4,08	1,038	1,077	-,704	,616	-,718	1,191
Monthly	13	2	5	3,85	1,281	1,641	-,509	,616	-1,546	1,191
Quarterly	13	2	5	3,85	1,281	1,641	-,509	,616	-1,546	1,191
N valid (from list)	13									

Thus, the recommendation for sampling frequency is that it should be established on the basis of the risk level assigned to the area during the risk assessment, in accordance with the table below.

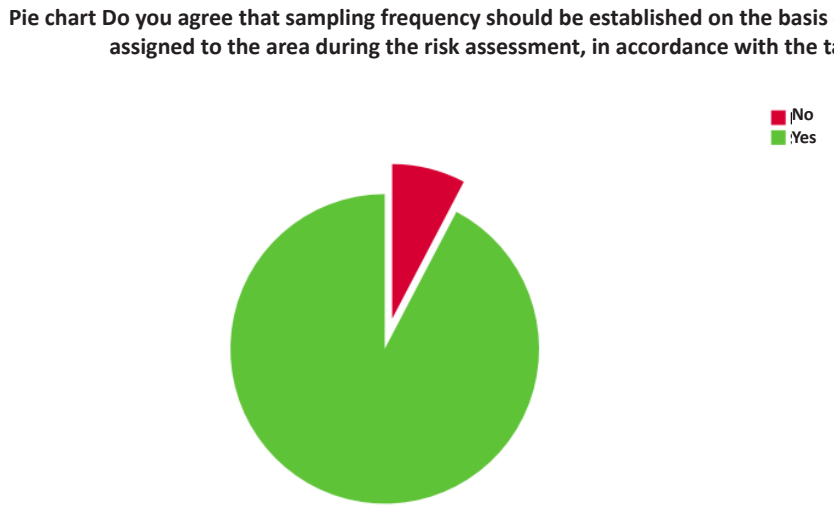
Table 43 Risk level and sampling frequency

Risk level of the area	Sampling frequency
High	Weekly
Medium	Monthly
Low	Quarterly

Source: Own work

Another aspect to be assessed by the experts was whether they agreed with the following recommendation: *"Sampling frequency should be established on the basis of the risk level assigned to the area during the risk assessment, in accordance with the table above".* 92.3% agree with this recommendation, as opposed to 7.7%.

Figure 4 Recommendation on risk level assigned to area



It should be pointed out that experts state that the risk level depends also on the toxicity of the drug, its formula, the workplace, the handling procedures, and the forms of exposure.

VI.6 Sampling time

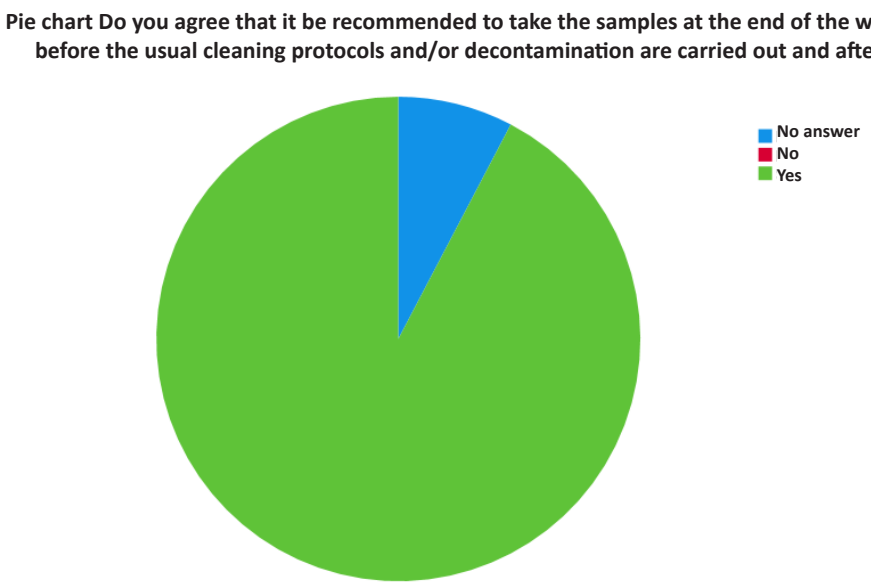
Samples should be taken from surfaces in normal work conditions, without having previously cleaned them, to make it possible to obtain relevant data that are representative of the work processes. It is recommended that samples be taken at the end of the working day, before any cleaning, deactivation, and decontamination, in order to find the staff's highest possible exposure.

It is recommended to take extraordinary samples if there is a spillage or incident in the handling of the hazardous drugs or a substantial change in their handling procedures to verify their impact on contamination levels.

If the purpose of the sampling is to verify the effectiveness of new contamination containment measures, new handling protocols, or new cleaning and/or decontamination agents, it should be carried out before and after the change is implemented.

92.3% of experts agreed with the following recommendation, as opposed to 7.7% who did not answer: *"It is recommended to take the samples at the end of the working day, before the usual cleaning protocols and/or decontamination are carried out and after them."*

Figure 5 Recommendation on sampling time



VI.7. To validate the content of the various measurement tools as quality criteria

The quality of the methodology used is necessary to ensure that the results obtained in the study can be adequately interpreted and used in clinical practice.

The two key metric characteristics to assess the precision of the instrument are reliability and validity. Reliability pertains to the constant measurement of a variable and validity to the fact that the instrument measures what is to be measured. Not every reliable instrument is valid. An instrument can be reliable because it constantly measures a variable, but invalid if it does not measure the phenomenon to be measured. Sensitivity and feasibility are other metric characteristics that also measure the validity of an instrument.

The instruments intended to obtain factual information related to the actions carried out by the subjects will require that the validity of the contents be verified by experts. However, quantitative measurement instruments, which assess the importance of a variable, will require verifying the validity of the contents by analysing the concept expressed by the variable in question. In our study, content validity was established by means of a survey. Its results are the following.

The asymmetry of the final assessments is negative, so most results concentrate around 4-5, which means that the experts quite or strongly agree with such aspects clarity, objectivity, organisation, sufficiency, consistency, coherence, and methodology. The highest negative asymmetry of the results is currently -1.099, coinciding with a higher mean, 4.00.

Table 44 Results of the Final Assessment

Descriptive statistics

	N	Minimum	Maximum	Average	Standard deviation	Variance	Asymmetry		Curtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Standard error	Statistic	Standard error
Clarity	13	1	5	3,62	1,387	1,923	-,503	,616	-,972	1,191
Objectivity	13	1	5	3,92	1,382	1,910	-,959	,616	-,214	1,191
Topicality	13	1	5	4,00	1,291	1,667	-1,099	,616	,639	1,191
Organisation	13	1	5	3,62	1,387	1,923	-,503	,616	-,972	1,191
Sufficient	13	1	5	3,54	1,506	2,269	-,606	,616	-,934	1,191
Consistency	12	1	5	3,67	1,557	2,424	-,719	,637	-,792	1,232
Coherence	13	1	5	3,62	1,502	2,256	-,611	,616	-,776	1,191
Methodology	13	1	5	3,77	1,363	1,859	-,676	,616	-,585	1,191
N valid (from list)	12									

Figure 6 Clarity graph

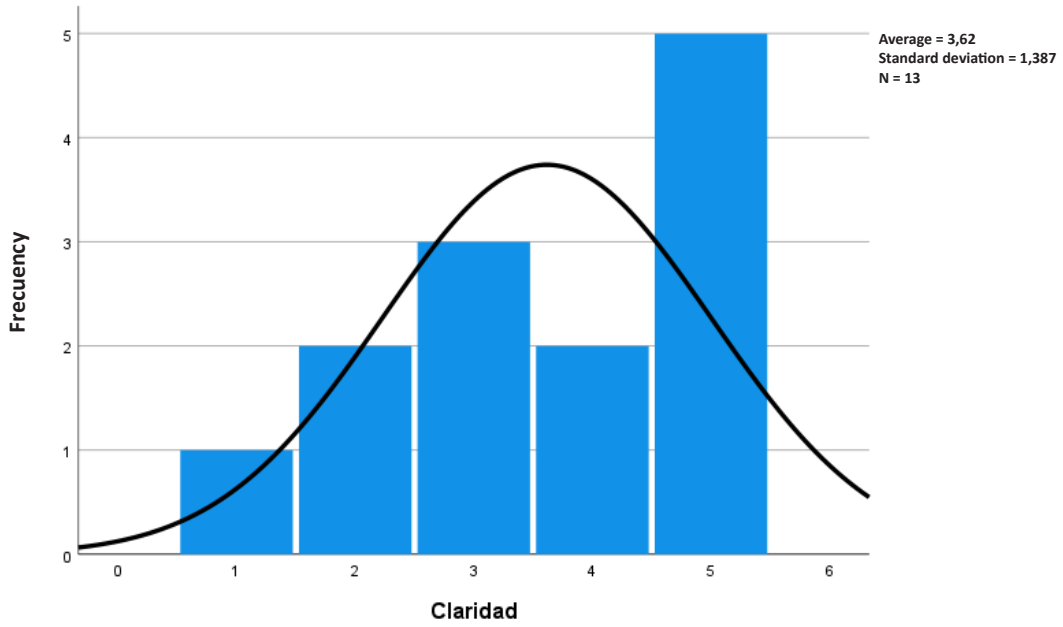


Figure 7 Objectivity graph

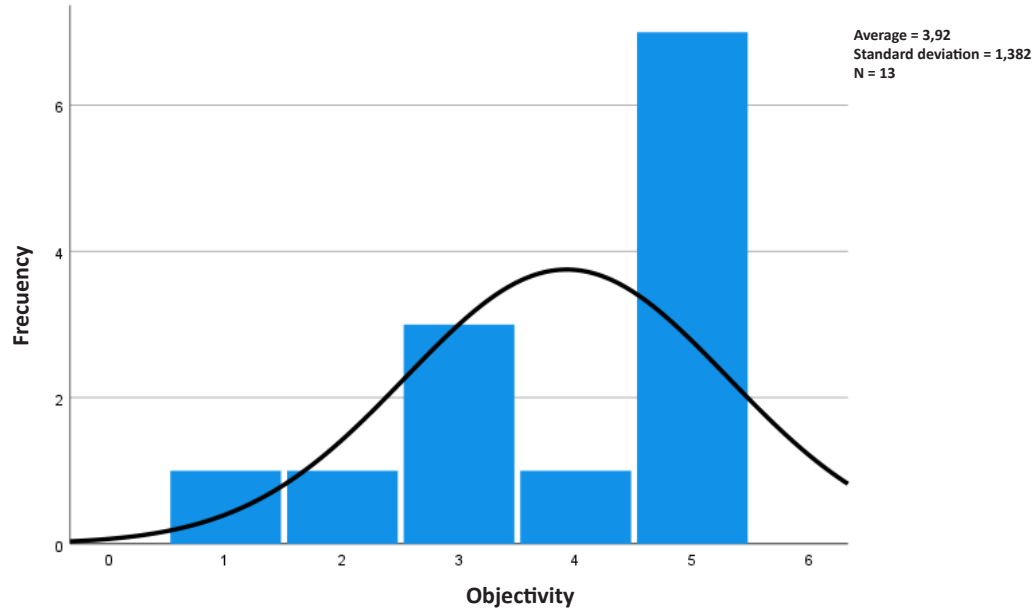


Figure 8 Topicality graph

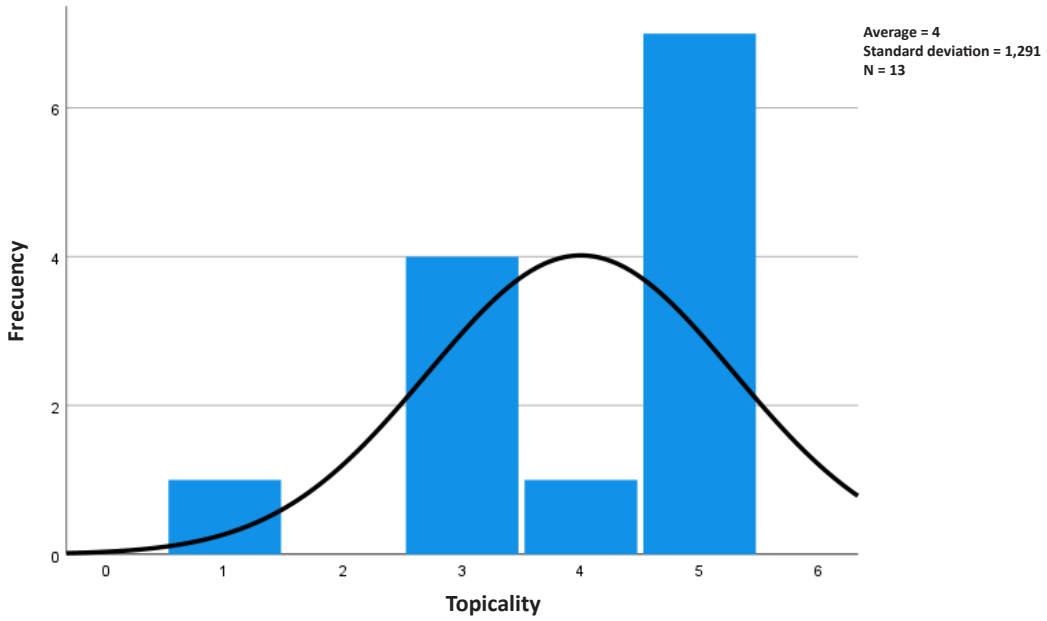


Figure 9 Organisation graph

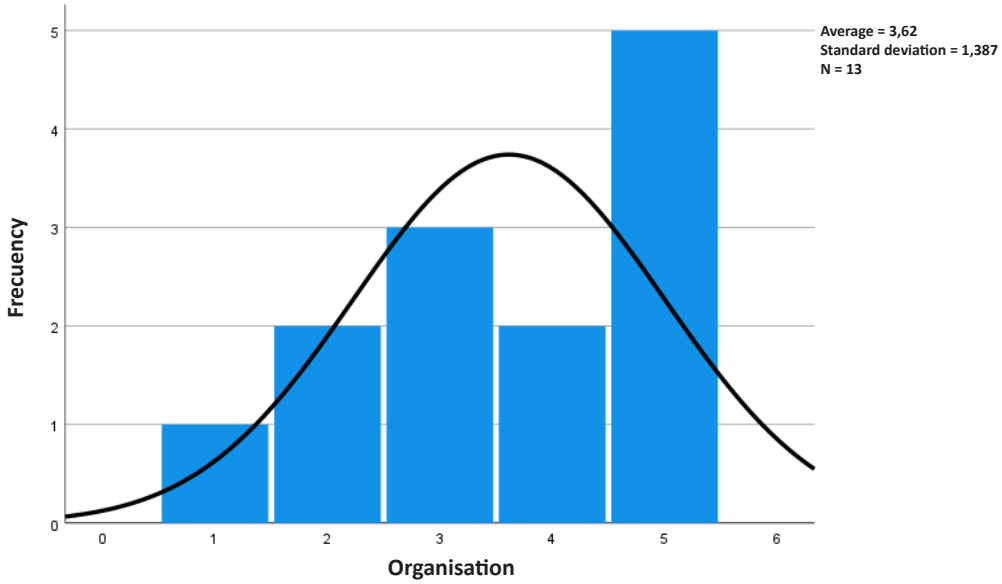


Figure 10 Sufficient graph

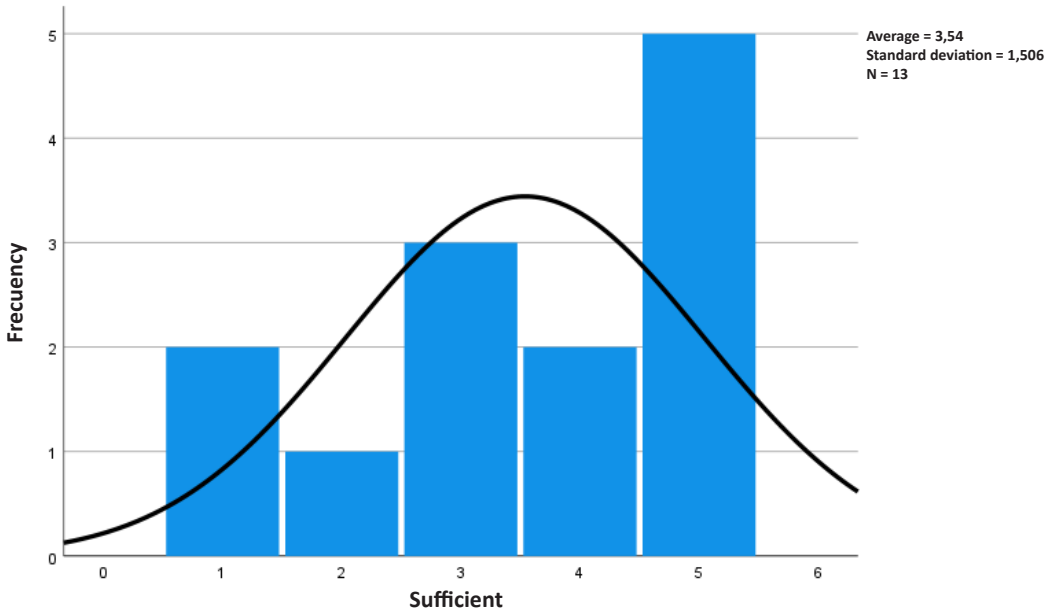


Figure 11 Consistency graph

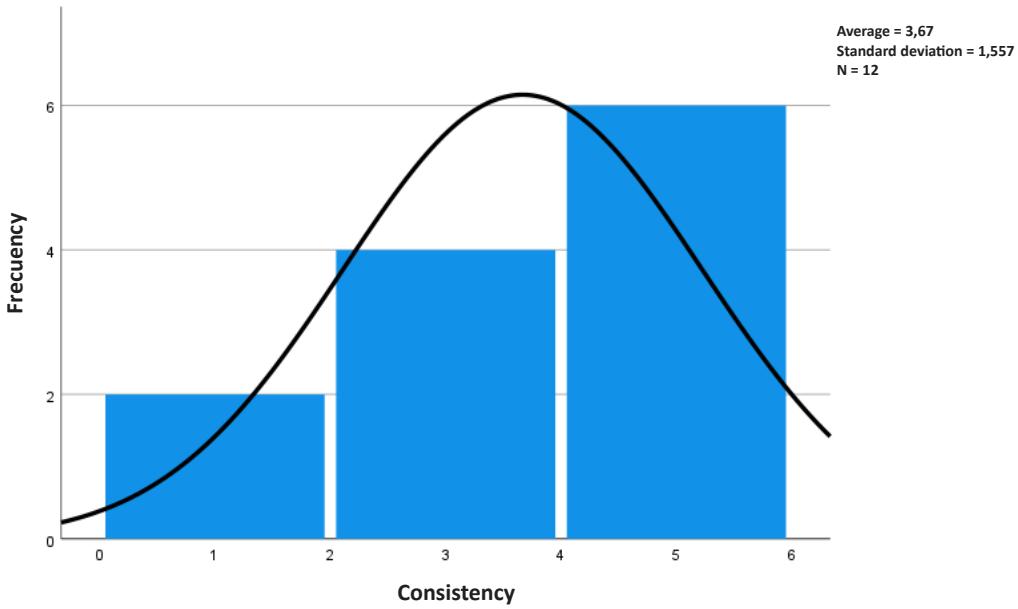


Figure 12 Coherence graph

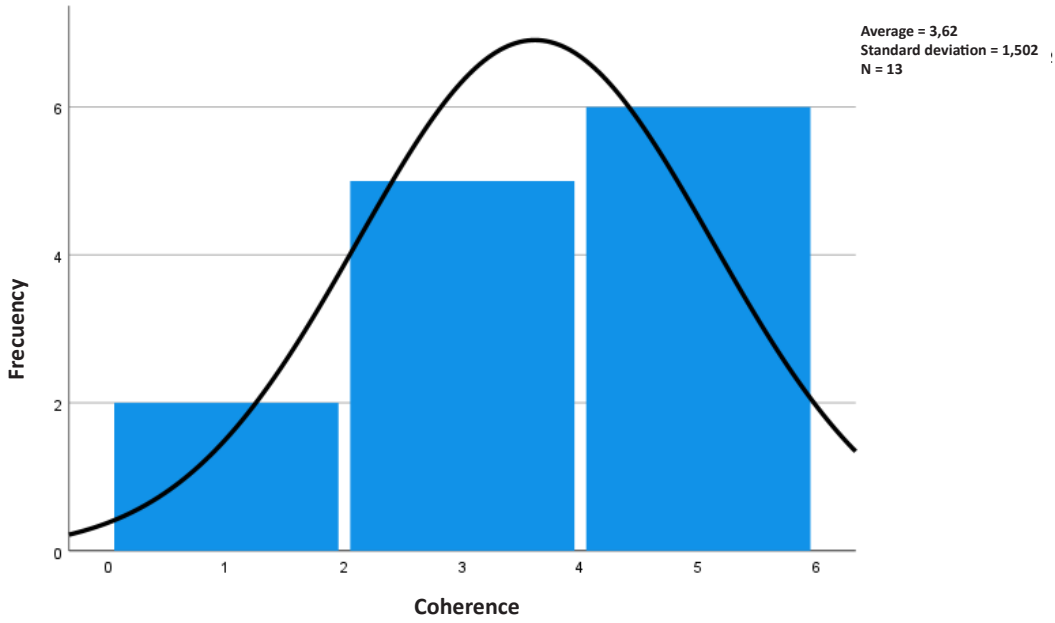


Figure 13 Methodology graph

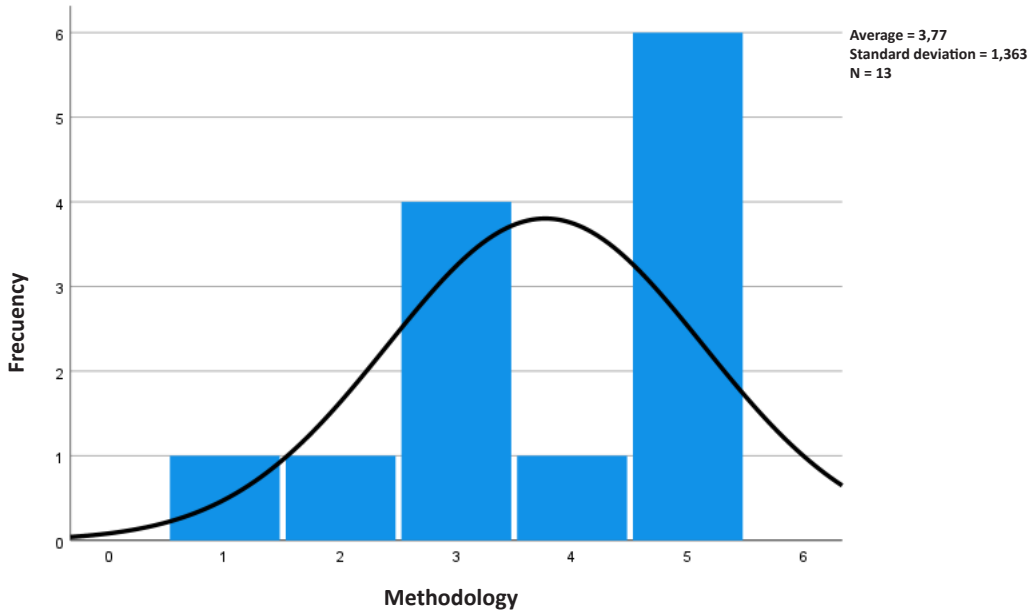


Table 45 Summary cases Final assessment

Case processing summary

		N	%
Cases	Valid	12	92,3
	Excluded [a]	1	7,7
	Total	13	100,0

a. Removal from the list is based on all the procedure variables

Table 46 Cronbach's alpha for Final assessment

Reliability statistics

Cronbach's alpha	Cronbach's alpha based on standardised elements	N of elements
,989	,989	8

As for Cronbach's alpha, it is 0.989, when the acceptable margin for reliability coefficients ranged between 0.7 and 0.9. (7,8). Thus a high reliability coefficient is clearly desirable when differences among experts are legitimate and expected.

VII. Limitations

It should be pointed out that some limitations were found in the search for experts, which extended the duration of the process. Indeed, the assessment of the various appendices did not require only the collaboration of judges with a specific education and experience profile, but they also had to be available to send the results in due time and form in the midst of the current global pandemic. The process for the validation of the contents of the research instruments through the judgment of experts is more efficient when what is expected of them is specified, but also when their timing is considered given their workloads.

As the number of judges was small, the degree of agreement among them was assessed by contrasting their answers and taking as a reference low scores under 2 points, with the disagreement of at least two judges. After the assessment, their remarks were considered, methodological decisions were made, and changes and reformulations were carried out to adjust the content of the second consultation round.

In this project, a typical five-level Likert scale has been used. For this reason, there could be a central-trend bias which might have been avoided with a scale with an even number of points, where the intermediate "neither agree nor disagree" option is not available. This is sometimes called a "forced choice" method, as the neutral option is removed.

VIII. Discussion and future research lines

Future research lines should be aimed at designing and validating monitoring scales for hazardous drugs used in the various fields of nursing. Although not all hazardous drugs can be monitored, at least those most frequently used can, as well as other frequent areas of use, other than the pharmacy, oncology, and outpatient services.

The OSHA risk communication standard [29 CFR 1910.1200] requires that health services establish a risk communication programme adequate for the exclusive workplace conditions. A key part of the programme is the identification of all the toxic drugs that professionals may come across in the facilities. Compliance with the OSHA risk communication standard involves (1) assessing whether these drugs meet one or more of the conditions to be defined as toxic drugs, and (2) placing a list of the drugs in a visible location to ensure safety(10). Institutions may wish to compare their lists with a NIOSH list of examples. Thus, the list of drugs to be monitored should be an open list, and should be adjusted to new scientific evidence, and updated on a regular basis.

A short list of hazardous drugs may not correspond to nurses' actual exposure, as the 4 main hazardous drugs mentioned in the document are used in very specific areas, such as the outpatient, pharmacy, and oncology services. There are many other hazardous drugs that are handled outside the pharmacy and oncology services, such as home hospitalisation units, general practices, outpatient urology services, and operating theatres where intraperitoneal chemotherapy is administered. It would be important to conduct new research studies on the handling of other hazardous drugs, what drugs are used, how they are used, where they are used, how frequently, their circuit, etc.

Healthcare workers who handle, prepare, or administer hazardous drugs may face risks to their own health, such as skin rashes, cancer, and reproductive disorders. The various international organisations, such as NIOSH, recommend that health services establish a medical surveillance programme to help to protect the staff who handle hazardous drugs

at work. Routine monitoring of healthcare professionals who are exposed to hazardous drugs should be guaranteed as part of a medical surveillance programme(11,12). Workers who directly handle hazardous drugs, such as nurses, should be included in this monitoring.

The elements of a medical surveillance programme for hazardous drugs should include (at least)(13):

- General and reproductive health questionnaires that should be completed when recruiting healthcare staff and later given on a regular basis.
- Laboratory analyses including full blood and urine tests to be carried out when recruiting healthcare staff and later on a regular basis. Additional tests, such as liver function and transaminase tests, may also be considered.
- A physical examination upon recruitment and later as required, if abnormal results are detected in the healthcare staff's health questionnaires or in their blood tests.
- Monitoring of healthcare workers who have experienced health changes or who are significantly exposed (significant skin contact, cleaning an extensive spill [bag rupture, intravenous catheter leak], etc.)

Healthcare questionnaires and laboratory analysis results should be monitored on a regular basis to detect any trends that might indicate health changes due to exposure to hazardous drugs. If changes are detected in the worker's health, the employer should take the following measures:

- Assessing the protection measures in place:

    1. Engineering controls (biological safety cabins / insulators, ventilation, closed system transfer devices and closed systems with biosafety level IV).
        - Comparing the controls to the recommended standards.
        - Taking environmental samples if analytic methods are available.

    2. Establishing standards for the use of Personal Protection Equipment (PPE) and compliance with these standards and use of PPE by employees
    3. Availability of adequate PPE such as double gloves, waterproof lab coats, and respiratory protection.

- **Designing an action plan to prevent more employee exposure, such as hazardous drug surface monitoring guides.**

- Guaranteeing confidential notification to exposed workers of any adverse effect on their health and offering them an alternative task or a temporary relocation.
- Providing continuous medical surveillance to all workers at risk in order to determine the effectiveness of the new plan.

IX. Bibliography

1. European Parliament and of the Council. Directive (2004/37/EC) of the European Parliament and of the Council of 29 April 2004 on the Protection of Workers from the Risks Related to Exposure to Carcinogenic or Mutagens at Work. Off J Eur Union [Internet]. 2004 [cited 2019 Sep 2];(229):23. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52017SC0007&from=EN

2. Proposición de Ley reguladora del derecho a la gestación por subrogación. CONGRESO DE LOS DIPUTADOS XII LEGISLATURA BOLETÍN OFICIAL DE LAS CORTES GENERALES. In: Presentada por el Grupo Parlamentario Ciudadanos [Internet]. 2017 [cited 2019 Sep 2]. p. 12. Available from: http://www.congreso.es/public_oficiales/L12/CONG/BOCG/D/BOCG-12-D-479.PDF

3. United States Pharmacopeial Convention. <800> Hazardous Drugs-Handling in Healthcare Settings [Internet]. United States Pharmacopeia 42–National Formulary 37. 2019 [cited 2020 Dec 11]. Available from: https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

4. Connor TH, Zock MD, Snow AH. Surface wipe sampling for antineoplastic (chemotherapy) and other hazardous drug residue in healthcare settings: Methodology and recommendations. J Occup Environ Hyg. 2016 Sep;13(9):658–67.

5. Escobar-Pérez J, Cuervo-Martínez Á. Validez De Contenido Y Juicio De Expertos: Una Aproximación a Su Utilización. Av en Medición. 2008;6:27–36.

6. Valero-García S, González-Haba E, Gorgas-Torner M, Alonso-Herreros J, Cercós-Lletí A, Poveda-Andrés, JL et al. Monitorización de las superficies de trabajo de medicamentos peligrosos en los Servicios de Farmacia. Documento de consenso. Guía de práctica farmacéutica de la Sociedad Española de Farmacia Hospitalaria (SEFH). Farm Hosp [Internet]. 2021;45(2):96–107. Available from: https://www.sefh.es/fh/208_10consenso0111655esp.pdf

7. Nunnally J. Psychometric Theory [Internet]. New York: McGraw-Hill Interamericana de España S.L.; 1978 [cited 2021 Jul 15]. Available from: https://scholar.google.com/scholar_lookup?title=+Psychometric+theory&author=Nunnally+J&publication_year=1978

8. Polit D, Beck C. Investigación en enfermería: Principios y métodos [Internet]. Philadelphia.: JB Lippincott and Co; 1999 [cited 2021 Jul 15]. Available from:

https://books.google.com/books?hl=es&lr=&id=5g6VttYWnjUC&oi=fnd&pg=PA3&ots=_0iRrIllxA&sig=wLJ-w8KtQ8cxbbD4iJChSB6Jj84

9. Kiffmeyer TK, Tuerk J, Hahn M, Stuetzer H, Hadtstein C, Heinemann A, et al. Application and assessment of a regular environmental monitoring of the antineoplastic drug contamination level in pharmacies - the MEWIP project. Ann Occup Hyg [Internet]. 2013 May [cited 2021 Jul 16];57(4):444–55. Available from: https://pubmed.ncbi.nlm.nih.gov/23125441/

10. CDC. CDC - Publicaciones de NIOSH - Lista de NIOSH de antineoplásicos y otros fármacos tóxicos en entornos de atención médica, 2010, Apéndice A, (2010-167) [Internet]. DHHS. 2015 [cited 2021 Jul 13]. Available from: https://www.cdc.gov/spanish/niosh/docs/2010-167_sp/apendice.html

11. Connor TH, McDiarmid MA. Preventing occupational exposures to antineoplastic drugs in health care settings. CA Cancer J Clin [Internet]. 2006 Sep 1 [cited 2021 Jul 16];56(6):354–65. Available from: https://www.cdc.gov/niosh/docs/2004-165/

12. United States Department of Labor. Occupational Safety & Health Administration (OSHA) Technical Manual (OTM) [Internet]. 20/01/1999. 1999 [cited 2021 Jul 16]. p. Section III Chapter 2. Available from: https://www.osha.gov/otm

13. Departamento de Salud y Servicios Humanos, Centros para la Prevención y el Control de las Enfermedades, Instituto Nacional para la Salud y Seguridad Ocupacional. Vigilancia médica para los trabajadores de la salud expuestos a medicamentos peligrosos [Internet]. NIOSH. 2013 [cited 2020 Dec 9]. p. 4. Available from: https://www.cdc.gov/spanish/niosh/docs/wp-solutions/2007-117_sp/default.html

X. Appendices

Appendix 1. Expert invitation letter

Madrid,[ ] [ ] 2021

Dear Expert Mr/Ms.....

Due to your experience and level of expertise, you have been selected to evaluate the risk assessment instrument for the monitoring of hazardous drugs, which is part of a Guide for the Monitoring of Hazardous Drugs of the Spanish Institute for Nursing Research, part of the Spanish General Council of Nursing.

The risk assessment proposal examined establishes the Expert Judgement Review technique as one of the main sources to evaluate the validity of the content of instruments under construction. Instrument evaluation is very important to ensure that they are valid and that their results are efficiently used.

We would be very grateful for your valuable collaboration, if you could spend a few minutes evaluating these tables in terms of sufficiency, clarity, coherence, and relevance criteria for each of its items, on the basis of the definitions and indicators given below.

We would be very grateful if you could complete these documents are soon as possible.

Thank you very much.
c/o

Table 47 Personal data

Expert identification:
Name and surname:
Telephone and email:
Hospital, service, and current position:
Education:
Areas of professional experience:
Years working:

Appendix 2A. Hazardous Drugs

Please state if you agree to monitor the following hazardous drugs.

SO1. - To identify the most frequent hazardous drugs to be monitored.

Hazardous Drugs	**Completely disagree 1**	**Somewhat disagree 2**	**Agree 3**	**Quite agree 4**	**Strongly agree 5**	**Remarks**
Cyclophosphamide						
Methotrexate						
Doxorubicin						
5-Fluorouracil (5-FU)						

RECOMMENDATION

It is recommended to monitor at least cyclophosphamide as a subrogated market for control of surface contamination in administration areas.

Do you agree with this statement? Yes/no

Remarks:

Appendix 2B. Hazardous Drugs (II)

The results of the first review by the expert group establish monitoring the following hazardous drugs: at least Cyclophosphamide, as well as Methotrexate, Doxorubicin, 5-Fluorouracil (5-FU). Other very important drugs in nursing services were also mentioned that should be monitored.

Please write down those hazardous drugs that you believe should be monitored in addition to those stated in the first review.

SO1. - To identify the most frequent hazardous drugs to be monitored.(II)

Hazardous Drugs	Completely disagree 1	Somewhat disagree 2	Agree 3	Quite agree 4	Strongly agree 5	Remarks

RECOMMENDATION

It is recommended to monitor at least cyclophosphamide as a subrogated market for control of surface contamination in administration areas. If not all the hazardous drugs used in each nursing service can be monitored, at least the following should be monitored (stating those that are most frequent by expert consensus).

Do you agree with this statement? Yes/no

Remarks:

Source to view the list of hazardous drugs: NIOSH [2016]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138). Retrieved from: https://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf?id=10.26616/NIOSHPUB2016161

Appendix 3. Locations to monitor

The locations that it are recommended to at least sample are listed below. Please state whether you agree with each item.

SO2. - To confirm risk areas in the administration of hazardous drugs.

The locations to be sampled will be defined on the basis of the manipulation circuit and the location of administration of the hazardous drug. It is recommended to monitor at least the following locations:

Nursing workstations or rooms

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Medication rooms

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Areas where fluid/drug IV bags are stored

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Counters and medication trolleys

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Keyboard and computer mouse

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Floor in patient care areas

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Bathroom floors

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Intravenous infusion pumps

Completely disagree1	Somewhat disagree2	Agree3	Quite agree4	Strongly agree5

Chairs

Completely disagree1 Somewhat disagree2 Agree3 Quite agree4 Strongly agree5

Intravenous therapy equipment

Completely disagree1 Somewhat disagree2 Agree3 Quite agree4 Strongly agree5

Do you agree with this statement? Yes/no

Remarks:

Appendix 4A. Template for the assessment of the risk of surface contamination by hazardous drugs

The various hazardous drugs administration areas and contamination risk assessment areas are specified below. Please review the risk level defined in the first table under the text to analyse each item and state your degree of agreement in table 2 below. You can specify the classification and score that you would give in the remarks, if they differ from those given.

Administration areas	Likelihood	Seriousness	Prevention	EXAMPLE
Room counter/medication room	1	2	3	
Room counter/medication room	2	2	3	
Room counter/medication room	2	2	3	
Room counter/medication room	2	2	3	
Room counter/medication room	1	2	2	
Counter in the patient's room	1	3	2	
Counters in the nursing staff's room	1	2	3	
Graph room outside the room	1	2	3	
Night stand	1	3	2	
Medication trolley	1	2	3	
Intravenous pump	2	2	2	
Floor under the intravenous pump	3	3	2	
Keyboard in the patient's room	1	2	3	
Patient's bathroom (sink, wall, floor, doorknob, toilet seat)	2	3	2	
Chair armrest	2	3	2	
Floor under the chair	2	3	2	
Hazardous rug residue container	3	2	3	
Floor in front of the hazardous drug residue container?	3	2	3	

Low
Medium
High

Table 48 Administration areas

SO4.- To approve classification in the monitoring of hazardous drugs according to the risk level allocated to the area during the risk assessment.

	Completely disagree 1	Somewhat disagree 2	Agree 3	Quite agree 4	Strongly agree 5	Remarks
Do you agree with the classification of the counter in the medication room/area?						
Do you agree with the classification of containers in the medication room/area?						
Do you agree with classification of the refrigerator in the medication room/area?						
Do you agree with classification of the trolley in the mediation room/area?						
Do you agree with the classification of the floor in the room/medication room?						
Do you agree with the classification of the counter in the patient's room?						
Do you agree with classification of the counter in the nursing staff's room?						
Do you agree with classification of the graph room outside the room?						
Do you agree with the classification of the nightstand?						

	Completely disagree 1	Somewhat disagree 2	Agree 3	Quite agree 4	Strongly agree 5	Remarks
Do you agree with the classification of the intravenous pump?						
Do you agree with classification of the floor under the chair?						
Do you agree with the classification of the counter in the patient's room?						
Do you agree with the classification of the patient's bathroom?						
Do you agree with classification of Chair armrest?						
Do you agree with classification of Floor under the chair?						
Do you agree with the classification of Drug residue container?						
Do you agree with the classification of Floor in front of the hazardous drug residue container?						
Remarks						

Appendix IV.B. Template for the assessment of the risk of surface contamination by hazardous drugs (II)

The results of the first review by the expert group specify the risk levels for the areas agreed and marked in grey, such as: containers in the medication room/area, refrigerator in the medication room/area, trolley in the medication room/area, etc. For the following areas, marked in red, a consensus must be reached in a second review by the expert group.

The various hazardous drugs administration areas and contamination risk assessment areas sent in the first review, to which two or more experts have given scores between 1 (completely disagree) and 2 (quite disagree) are specified below. Please review the risk level defined in the first table under the text to analyse the item about which consensus has not been reached and must be re-evaluated. Please state your degree of agreement in table 2 below. **You can specify the classification and score that you would give in the remarks.** Please describe any other areas that you believe it is important to evaluate, together with the risk level assigned.

Table 49 Administration areas

SO4.- To approve classification in the monitoring of hazardous drugs according to the risk level allocated to the area during the risk assessment.

	Completely disagree 1	Somewhat disagree 2	Agree 3	Quite agree 4	Strongly agree 5	Remarks What classification and score would you give: likelihood, seriousness, Prevention
Do you agree with the classification of the counter in the medication room/area?						
Do you agree with the classification of containers in the medication room/area?	Expert group consensus: Likelihood 2, Seriousness 2, Prevention 2. HIGH risk					
Do you agree with the classification of containers in the medication room/area?	Expert group consensus: Likelihood 2, Seriousness 2, Prevention 2. HIGH risk					
Do you agree with the classification of the trolley in the mediation room/area?	Expert group consensus: Likelihood 2, Seriousness 2, Prevention 2. HIGH risk					
Do you agree with the classification of the floor in the room/medication room?						
Do you agree with the classification of the counter in the patient's room?	Expert group consensus: Likelihood 2, Seriousness 3, Prevention 2. Medium Risk					
Do you agree with classification of the counter in the nursing staff's room?						
Do you agree with classification of the graph room outside the room?						

	Completely disagree 1	Somewhat disagree 2	Agree 3	Quite agree 4	Strongly agree 5	Remarks What classification and score would you give: likelihood, seriousness, Preventión
Do you agree with the classification of the nightstand?						
Do you agree with the classification of the medication trolley?						
Do you agree with the classification of the intravenous pump?						
Do you agree with classification of the floor under the chair?	Expert group consensus: Likelihood 3, Seriousness 3, Prevention 2. HIGH risk					
Do you agree with the classification of the counter in the patient's room?						
Do you agree with the classification of the patient's bathroom?	Expert group consensus: Likelihood 2, Seriousness 3, Prevention 2. HIGH risk					
Do you agree with classification of Chair armrest?	Expert group consensus: Likelihood 2, Seriousness 3, Prevention 2. HIGH risk					
Do you agree with classification of Floor under the chair?	Expert group consensus: Likelihood 2, Seriousness 3, Prevention 2. HIGH risk					
Do you agree with the classification of Drug residue container?	Expert group consensus: Likelihood 3, Seriousness 2, Prevention 3. HIGH risk					
Do you agree with the classification of Floor in front of the hazardous drug residue container?	Expert group consensus: Likelihood 3, Seriousness 2, Prevention 3. HIGH risk					

Appendix V. Risk determination and sampling plan Monitoring frequency

The risk assessment classification is displayed below. Please state whether you agree with each item.

Table 50 Risk assessment (1): Contamination likelihood

Classification	Contamination likelihood
Low(1)	Low level of handling of hazardous drugs, none or very occasional manipulation and administration (e.g. orally administered drugs) **More than once a month**
Medium(2)	Medium level of handling of hazardous drugs, with some manipulation or administration by means of safe practices. **2 or 3 times a month**
High(3)	High level of hazardous drugs with frequent manipulation or administration with less safe practices (e.g., intravenous infusion bags) **1 or more times a week**

SO4.- To reach an agreement of the assessment of the risk, classified by likelihood, seriousness, and contamination prevention into low, medium, and high.

Contamination likelihood	**Completely disagree 1**	**Somewhat disagree 2**	**Agree 3**	**Quite agree 4**	**Strongly agree 5**
Do you agree with classification as low?					
Do you agree with classification as medium?					
Do you agree with classification as high?					

Remarks:

Table 51 Risk assessment (2): Contamination seriousness

Classification	Contamination seriousness
Low(1)	Restricted and highly limited access (e.g. trained staff)
Medium(2)	Semi-controlled access (e.g. staff only)
High(3)	Open access (e.g., public areas)

Source: Adapted from HD Guide Risk Assessment Pharmacy Report

SO4.- To reach an agreement of the assessment of the risk, classified by likelihood, seriousness, and contamination prevention into low, medium, and high.

Contamination seriousness	**Disagree 1**	**Somewhat disagree 2**	**Agree 3**	**Quite agree 4**	**Strongly agree 5**
Do you agree with classification as low?					
Do you agree with classification as medium?					
Do you agree with classification as high?					

Remarks:

Table 52 Risk assessment (3): Contamination prevention

Classification	**Contamination prevention**
Low(1)	Engineering controls, administrative controls, and PPE
Medium(2)	Administrative controls and PPE
High(3)	PPE only

Source: Adapted from HD Guide Risk Assessment Pharmacy Report

SO4.- To reach an agreement of the assessment of the risk, classified by likelihood, seriousness, and contamination prevention into low, medium, and high.

Contamination prevention	**Disagree 1**	**Somewhat disagree 2**	**Agree 3**	**Quite agree 4**	**Strongly agree 5**
Do you agree with classification as low?					
Do you agree with classification as medium?					
Do you agree with classification as high?					

Remarks:

Appendix VI. Risk level and sampling frequency

The risk level by area and its correspondence with the sampling frequency are shown below. Please state whether you agree with each item.

Table 53 Risk level and sampling frequency

Risk level of the area	Sampling frequency
High	Weekly
Medium	Monthly
Low	Quarterly

Source: Own work

SO5.- To validate the risk level defined according to the sample taking frequency.

	Disagree 1	**Somewhat disagree 2**	**Agree 3**	**Quite agree 4**	**Strongly agree 5**
Do you agree with the weekly sampling frequency at the high risk level?					
Do you agree with the weekly sampling frequency at the medium risk level?					
Do you agree with the weekly sampling frequency at the low risk level?					

Remarks:

SO5.- To validate the risk level defined according to the sample taking frequency.

RECOMMENDATION
Sampling frequency should be established on the basis of the risk level assigned to the area during the risk assessment, in accordance with the table below.

Do you agree with this statement? Yes/no

Remarks:

SO6.- To reach an agreement on the suitable time for the taking of samples in work surfaces.

RECOMMENDATION
It is recommended to take the samples at the end of the working day, before the usual cleaning protocols and/or decontamination are conducted and after them.

Do you agree with this statement? Yes/no

Remarks:

Appendix VII. Final assessment

The indicators that will provide content validity as quality criteria for the various measurement instruments are specified below. Please state whether you agree and any remarks you might want to make.

Table 54 Validation aspects

Indicators	Criteria	Completely disagree 1-20	Somewhat disagree 21-40	Agree 41-60	Quite agree 61-80	Strongly agree 81-100	Remarks
1. Clarity	It is written in adequate language, it is easy to understand						
2. Objetivity	Suitability for the research topic						
3. Topicality	It is suitable for the research context						
4. Organisation	The questionnaire contains a logical and sequential organisation of the questions						
5. Sufficient	Is the instrument sufficient to measure all the indicators?						
6. Consistency	It is suitable for the problem posed						
7. Coherence	There is a correlation between indicators and dimensions						
8. Metodology	The instrument suits the research methodology						

Remarks:

CONSEJO GENERAL DE ENFERMERÍA

INSTITUTO ESPAÑOL
DE INVESTIGACIÓN
ENFERMERA