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of hospital pharmacists

SIG - FINAL REPORT

Special Interest Group on Hazardous Medicinal Products

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The work of this Special Interest Group (SIG) was financially supported by Amgen.

Foreword by the President

The management of hazardous medicinal products is a complex process that requires sufficient human resources, safe handling procedures and appropriate training tailored to the conditions of the working environment and offered to all staff. The classification of medicinal products as hazardous plays an essential role in determining suitable handling procedures. However, unlike the United States, Europe does not have one single body that addresses all questions related to the classification of hazardous medicinal products similar to the National Institute for Occupational Safety and Health (NIOSH).

Consequently, the European Association of Hospital Pharmacists (EAHP) created a Special Interest Group (SIG) on Hazardous Medicinal Products (financially supported by Amgen). This SIG was tasked with investigating the different classification models that are used throughout Europe and examining whether these approaches are fit for their purpose.

This report summarises the findings of the SIG that were collected through desk research, horizon scanning activities, surveys of hospital pharmacists views at individual and national levels complimented by the knowledge and experience of the SIG participants. On behalf of EAHP, I would like to thank all SIG members for their valuable contributions and their engagement throughout the past year which led towards closing gaps by identifying classification systems around Europe, creating a European model and a definition of the term 'hazardous medicinal products' applicable to the European treatment landscape. My thanks also extend towards the chief pharmacists across Europe and EAHP's member associations that contributed to the survey activity in autumn 2021.

András Süle
President of the European Association of Hospital Pharmacists

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Executive Summary

This report presents the findings of the Special Interest Group on Hazardous Medicinal Products (financially supported by Amgen) set up by the European Association of Hospital Pharmacists (EAHP). The Special Interest Group (SIG) carried out an investigation into the classification systems that are used throughout Europe for hazardous medicinal products (HMPs).

A medicinal product is defined as hazardous when the intrinsic characteristics of the substance potentially jeopardise the well-being of healthcare workers and exposure presents a significant risk to users after consideration of measures that may eliminate or substantively reduce such risks during use which may be product preparation and administration by healthcare workers and subsequent patient care.

The risks associated with the intrinsic characteristics of a medicinal product may be further modified by good handling/manufacturing practices in the healthcare setting leading to an altered classification of the medicinal product at the point of handling (including activities such as proper storage, preparation, dispensing, administration, cleaning, transportation, etc.) and patient care.

There are many stakeholders with an interest in the topic of HMPs and all should be consulted with a view to enhancing the current management of HMPs in Europe including additional training for relevant professionals.

The exposure of healthcare workers to HMPs is a serious issue that in the view of EAHP needs to be addressed uniformly across the European Union and its Member States to ensure the protection of patients and healthcare personnel. The complex nature of handling HMPs requires training that is tailored to the conditions of the working environment which differ depending on the settings in the hospital or community, as well as from country to country, and the specific medicinal products, amounts, and formulations. To ensure the safety of patients and staff, hospital pharmacists contribute to, promote and implement safe practices for the handling of HMPs in institutions in Europe. To improve the current position and to support the work of hospital pharmacists proactive steps need to be taken to minimise the risks of HMPs for everyone. Therefore

EAHP calls on the European Commission and national governments across Europe to actively engage with hospital pharmacist representatives in the review and development of relevant Directives for the management of hazardous medicinal products (HMPs) in the healthcare environment.

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EAHP asks national governments and health system managers to immediately engage with the European Statements of Hospital Pharmacy and implement best practices relating to HMPs.

EAHP recommends an EU-wide standard approach to the classification and management of HMPs.

EAHP advises the European Commission and national governments across Europe to initiate best practice sharing on the classification and handling of HMPs between its Member States.

EAHP advocates for the revision of pharmacy curricula and the expansion of training opportunities for the pharmacy workforce to account for the growing demand for management of HMPs and related Health and Safety issues.

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Definition[1]

The EAHP Special Interest Group on Hazardous Medicinal Products has agreed the following definition of hazardous medicinal products (HMPs).

A medicinal product is defined as hazardous when the intrinsic characteristics of the substance potentially jeopardise the well-being of healthcare workers and exposure presents a significant risk to users after consideration of measures that may eliminate or substantively reduce such risks during product preparation and administration by healthcare workers and subsequent patient care. The risks associated with the intrinsic characteristics of a medicinal product may be further modified by good handling/manufacturing practices in the healthcare setting leading to an altered classification of the medicinal product at the point of handling (including activities such as proper storage, preparation, dispensing, administration, cleaning, transportation, etc.) and patient care.

A medicinal product is defined by the European Medicines Agency (EMA) as:

A substance or combination of substances that are intended to treat, prevent, or diagnose a disease, or to restore, correct or modify physiological functions by exerting a pharmacological, immunological or metabolic action. Once a marketing authorisation application (MAA) has been assessed by the European Medicines Agency (EMA), a scientific body with the expertise required to assess the benefits and risks of medicines, the European Commission takes a final legally binding decision on whether the medicine may be marketed in the EU. These decisions encompass the review and approval of medicinal products for paediatric use, orphan medicines, traditional herbal medicines, vaccines, and clinical trials for a candidate or authorised medicinal products approved under special rules by EMA.

[1] Resources used for the creation of a definition for HMPs:
European Medicines Agency. Definition medicinal product. Available at: https://www.ema.europa.eu/en/glossary/medicinal-product (last visited on 1 February 2022). Pharmaceutical Inspection Convention, Guide to Good Manufacturing Practice for Medicinal Products Part I. Available at: https://picscheme.org/docview/4205 (last visited on2 February 2022). NIOSH (2020), Managing Hazardous Drug Exposures: Information for Healthcare Settings. Available at: https://www.cdc.gov/niosh/docket/review/docket233c/pdfs/DRAFT-Managing-Hazardous-Drug-Exposures_Information-for-Healthcare-Settings.pdf (last visited on 2 February 2022). EU Strategic Framework on Health and Safety at Work 2021—2027, Occupational safety and health in a changing world of work. Available at: https://eu-osh-framework-2021.osha.europa.eu/upload_ftp/nirestream/euoshahybrid/pdf/eu-strategic-framework-on-safety-and-health-2021-27-pdf.pdf?updated=1624886105 (last visited on 2 February 2022). EU OSHA guidance. Available at: https://osha.europa.eu/en/safety-and-health-legislation/european-guidelines (last visited on 2 February 2022). Directive (EU) 2019/983 of the European Parliament and of the Council of 5 June 2019 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work OJ L 164/23.

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Intrinsic Hazardous Qualities

Consistent with the NIOSH definition of a "hazardous drug", a substance approved for use as a medicinal product may be classified as hazardous when it possesses any one of the following five characteristics:

- Genotoxicity, or the ability to cause a change or mutation in genetic material;
- Carcinogenicity, or the ability to cause cancer in humans, animal models, or both;
- Teratogenicity, or developmental toxicity, the ability to interfere with normal development, either before or after birth.
- Fertility impairment.
- Serious organ toxicity at low doses in humans or animal models.

Subsequent modification of risk

The risks associated with the classification of a substance as hazardous may be modified by the formulation of the final medicinal product as well as exposure opportunities for either healthcare workers or other individuals (for example family members or care givers exposed to the hazardous medicinal product). Modification factors include:

- Concentration
- Formulation
- Route of administration
- Molecule size
- Manipulation/compounding steps required
- Adherence to good handling/manufacturing practices
- Exposure – frequency, duration and intensity
- Daily dose

Risk Assessment

The potential risks to healthcare workers handling hazardous medicinal products are a combination of the intrinsic hazardous qualities of the product and the specific handling requirements (including

activities such as proper storage, preparation, dispensing, administration, cleaning, transportation, etc.) and patient care. Guidance on the requirements for risk assessments should be provided at EU level and implemented together with the practices in force at the local, regional and/or national level.

A risk assessment is informed by the available evidence. Consideration of the reliability of the evidence should be a feature of the assessment. Studies undertaken for a MAA process will have been conducted according to, or consistent with established methods to identify hazards. Other studies without prior external review will require expert analysis and the use of tools to evaluate study reliability,[2] and the direction, magnitude, and importance of individual biases identified prior to inclusion in the risk assessment[3] [4] including pre-clinical data provided by independent research groups or agencies. This evidence is more difficult to evaluate and may give rise to the application of the precautionary principle[5] in instances where the types and degrees of risk are not well understood and may be serious or irreversible. The precautionary principle shall be informed by three specific principles:

- the fullest possible scientific evaluation, the determination, as far as possible, of the degree of scientific uncertainty;
- a risk evaluation and an evaluation of the potential consequences of inaction;
- the participation of all interested parties in the study of precautionary measures, once the results of the scientific evaluation and/or the risk evaluation are available.

The precautionary principle may be invoked when a phenomenon, product or process may have a dangerous effect, identified by a scientific and objective evaluation, if this evaluation does not allow the risk to be determined with sufficient certainty.

[2] Arroyave, W. D., Mehta, S. S., Guha et al. (2021). Challenges and recommendations on the conduct of systematic reviews of observational epidemiologic studies in environmental and occupational health. J Expo Sci Environ Epidemiol, 31(1), 21-30. doi:10.1038/s41370-020-0228-0. NTP. (2019). Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Available at: http://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookjan2015_508.pdf (last visited on 1 February 2022). Savitz, D. A., Wellenius, G. A., & Trikalinos, T. A. (2019). The Problem With Mechanistic Risk of Bias Assessments in Evidence Synthesis of Observational Studies and a Practical Alternative: Assessing the Impact of Specific Sources of Potential Bias. Am J Epidemiol, 188(9), 1581-1585. doi:10.1093/aje/kwz131.

[3] Joint Research Center. (2017). ToxRTool - Toxicological data Reliability Assessment Tool European Commission. available at: https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool (last visited on 19 January 2022).

[4] Schneider, K., Schwarz, M., Burkholder, I., Kopp-Schneider, A., Edler, L., Kinsner-Ovaskainen, A., . . . Hoffmann, S. (2009). "ToxRTool", a new tool to assess the reliability of toxicological data. *Toxicol Lett, 189*(2), 138-144. doi:10.1016/j.toxlet.2009.05.013.

[5] Summary of Communication (COM(2000) 1final) on the precautionary principle, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=LEGISSUM%3Al32042 (last visited on 17 January 2022).

Background

Medicines are an essential component of patient care and must be readily available. Some medicines have intrinsic hazardous qualities and as such must be handled and managed to meet the requirements of national and European legislation and guidelines.[6]

Managing HMPs and ensuring the safety of staff in the hospital is part of the role of the hospital pharmacist. With the knowledge that in September 2020, the European Commission proposed a fourth update of the Carcinogens and Mutagens Directive[7] EAHP believes that the input of hospital pharmacists into any such review is essential for practical application of any proposed changes and contribute to the provision of high quality, safe and efficacious care.

Hospital pharmacists are dealing with HMPs in their daily work. Their safe handling is of uttermost importance for the health and safety of healthcare workers and individuals (for example family members or care givers exposed to the hazardous medicinal product). Their classification plays an essential role in determining suitable handling procedures. However, Europe does not have one single body similar to the National Institute for Occupational Safety and Health (NIOSH) in the United States, that addresses all questions linked to the classification of hazardous medicinal products.

To better understand the landscape for HMPs in Europe, the European Association of Hospital Pharmacists (EAHP) established a Special Interest Group (SIG)[8] on Hazardous Medicinal Products to

a) Examine national strategies and national requirements across Europe for the management of hazardous medicines.
b) Identify best practices and promote better sharing and implementation of these practices between countries, including the operation of information portals and awareness of the topic via education and advocacy.

[6] Council 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 OJ L 183/1. Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work OJ L 131/11. 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 OJ L 158/50. Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency OJ L136/1. Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products OJ L311/1.
[7] Consolidated text: 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 (Sixth individual Directive within the meaning of Article 16(1) of Council Directive 89/391/EEC), available at: https://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX%3A02004L0037-20140325 (last visited on 4 January 2022).
[8] SIG membership Appendix I – SIG membership.

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c) Promote heightened awareness by governments and EU regulators of the critical impacts HMPs may have in relation to healthcare workers' and individuals' health and safety, and the accompanying need for urgent action on the topic.

The SIG started its work in December 2020, with the first meeting taking place in February 2021, and concluded its activities in January 2022. Throughout this period, the SIG members undertook a horizon scanning to collect information on the existing classification systems, conducted a literature review to examine national and international definitions of HMPs and solicited information by way of two surveys (one to national associations and one for individual chief pharmacists) to better inform the group of the range of handling practices, conditions, and knowledge of HMPs in Europe today. This report summarises the findings of the SIG.

European Statements of Hospital Pharmacy[9]

In 2014, EAHP adopted the European Statements of Hospital Pharmacy that express commonly agreed objectives which every European health system should aim for in the delivery of hospital pharmacy services. The topic of HMPs is linked to a number of statements in the European Statements of Hospital Pharmacy cited verbatim, below:

SECTION 2 Selection, Procurement and Distribution

2.6. Hospital pharmacies should have responsibility for all medicines logistics in hospitals. This includes proper storage, preparation, dispensing, distribution and disposal conditions for all medicines, including investigational medicines.

SECTION 3 Production and Compounding

3.2. Medicines that require manufacture or compounding must be produced by a hospital pharmacy, or outsourced under the responsibility of the hospital pharmacist.

3.3. Before making a pharmacy preparation, the hospital pharmacist must undertake a risk assessment to determine the best practice quality requirements. These must consider premises, equipment, pharmaceutical knowledge and labelling.

[9] EAHP, European Statements of Hospital Pharmacy, available at https://statements.eahp.eu/statements/european-statements-hospital-pharmacy (last visited on 4 January 2022).

3.4. Hospital pharmacists must ensure that an appropriate system for quality control, quality assurance and traceability is in place for pharmacy prepared and compounded medicines.

3.5. Hazardous medicines should be prepared under appropriate conditions to minimise the risk of contaminating the product and exposing hospital personnel, patients and the environment to harm.

> *Additional information included in the commented version of the European Statements of Hospital Pharmacy – To achieve this there will need to be a multidisciplinary risk assessment of the hazardous medicines to determine where and how it is best prepared.*

SECTION 5 Patient Safety and Quality Assurance

5.6. Hospital pharmacists should identify high-risk medicines and ensure appropriate procedures are implemented in procurement, prescribing, preparing, dispensing, administration and monitoring processes to minimise risk.

5.9. Hospital pharmacists should ensure that the information needed for safe medicines use, including both preparation and administration, is accessible at the point of care.

Horizon scanning

Classification systems within Europe and the US

The members of the SIG started their work by gathering information on the existing classification systems within Europe. This activity specifically focused on the countries covered by the SIG membership, namely Austria, Croatia, Ireland, Poland, Spain, Sweden, the Netherlands and the United Kingdom. Classification in the **Netherlands** is linked to the Pharmaceutical Substances Risk Assessment (Risico instrument Farmaceutische Stoffen (RiFaS). RiFaS calculates the risk of manufacturing or compounding a drug, based on the internal risk of the drug itself combined with the risk of being exposed to the drug during handling. RiFaS is used nationwide by all community and hospital pharmacies. Further details were provided by way of a presentation to the SIG which is discussed later in the document. In **Austria,** no standardized classification system exists but normally hospital pharmacies take into account information from different databases and resources (for example the European Chemicals Agency (ECHA), the European Directorate for the Quality of Medicines & HealthCare (EDQM), the Food and Drug Administration FDA, the International Agency for Research on Cancer (IARC), NIOSH, the Employer's Liability Insurance Association for Health Services and Welfare Care (BGW) and prescription information/information from the European Public Assessment Report

(EPAR). The information is shared between hospital pharmacies. Based on the discussions within the SIG, it was concluded that the Dutch and the Austrian approach are very similar with the difference being the number of categories that are being looked at (5 categories in the Netherlands; 11 categories in Austria because of the differentiation between secured versus potential HMP-status).

In **Spain**, the National Institute for Safety and Health at Work (INSST) published in 2016 in collaboration with the Spanish Society of Hospital Pharmacists (SEFH) the document "Hazardous drugs: Prevention measures for their preparation and administration". As a continuation and update to this document INSST and SEFH developed the INFOMEP database. As outlined in the technical document, the preparation of the INFOMEP database has been based on the information periodically published by NIOSH, supplemented with the information available on the drugs used in Spain, including recommendations for preparation and administration of drugs. Both resources are not binding but rather used as a guideline and plans are in place to regularly update them.

The **United Kingdom** does not have a classification system for HMPs. Handling of carcinogens and mutagens are covered by the Control of Substances Hazardous to Health (COSHH regulations 2002 (as amended), but for classification, like in **Ireland** the NIOSH list is used. The **Polish** legal framework regulating chemical substances, their mixtures, agents or technological processes with carcinogenic or mutagenic impacts is very comprehensive. Hence, it covers all types of hazardous products and chemical substances. There are, however, no dedicated regulations for HMPs. They are covered by general regulations. In **Croatia**, the classification of HMPs refers to the GHS classification (Globally Harmonized System of Classification and Labelling of Chemicals), IARC and locally most to the NIOSH list.

In **Germany**, there is no specific list of hazardous medicinal products. However, during the handling of HMPs, the Chemicals Law and the Hazardous Substances Ordinance are applicable. Additionally, the Federal Institute for Occupational Health and Safety (BAuA) provides Technical Rules for Hazardous Substances that provide guidance, i.e. TRGS 525: Hazardous Substances in Health System Institutions, which describes measures to protect employees when handling hazardous medicinal products as well as the obligation of the employer to conduct a risk assessment and to maintain a list of carcinogenic, mutagenic or toxic to reproduction (CMR) compounds handled by employees. In **Portugal**, there are several documents about occupational health, the most important being the Decree-Law 24/2012. This legal document consolidates the minimum requirements regarding the protection of workers against risks to health and safety due to exposure to chemical agents at work and is the transposition of the EU Directive 2009/161/EU. It's annex contains a list of hazardous products. There is no other

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list of HMPs in Portugal. The Decree-Law 24/2012 mentions that for the handling of carcinogenic or mutagenic products there should be a special law on exposure limits put in place, but nothing has been published yet.

In **Sweden**, no standardized classification system for HMPs exists. The Swedish legislation regulates the handling of HMPs based on their effects and provides examples highlighting which anatomical therapeutic chemical codes (ATC codes) are more likely to cause harm for occupational healthcare workers.

As part of the horizon scanning, the SIG also looked at the NIOSH website and compared the 2016 NIOSH List of Antineoplastic & other hazardous drugs in healthcare settings, with the draft NIOSH lists of 2018 and 2020. It was noted that in the 2020 draft the definition was updated. The NIOSH draft list (2020) noted that many of the drugs currently used to treat cancer function differently than those previously used and that antineoplastic drugs are no longer all cytotoxic, genotoxic, and highly hazardous chemicals. Properties of a drug molecule that may limit adverse health effects are typically chemical, physical, and structural properties that affect its absorption (e.g. molecular weight). The NIOSH list (2016) of hazardous drugs differentiated between cancer and non-cancer drugs without looking at mechanisms of action or properties that could modify the risk to healthcare workers. As a result, drugs that required different protective measures were grouped together. The NIOSH draft list (2020) groups drugs by hazard. Drugs are further grouped into two tables. One table comprises drugs that contain special handling information specified by the manufacturer or meet the NIOSH definition of a hazardous drug and are classified as “known to be a human carcinogen” by the National Toxicology Program (NTP) or as “carcinogenic” or “probably carcinogenic” by IARC. The second table lists drugs that meet the agency’s definition of a hazardous drug but do not have special handling instructions and are not classified as carcinogenic by NTP or IARC.

Although the SIG did not identify a European classification of hazardous medicines, there is other literature that at least provides some guidance about the handling of such products, such as “PE 010-4 Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments”[10], a document used by the competent authorities to verify the conditions and facilities of healthcare institutions.

[10] PE 010-4 Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments”, available at: picscheme.org (last visited on 27 January 2022).

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Stakeholders

Loosely defined, a stakeholder is a person or group of people who can affect or be affected by a given project. The SIG was aware that the topic of HMPs was of interest to a broad range of stakeholders, some of whom are directly impacted by the topic, some of whom have legislative responsibilities, some with commercial interests and some who are indirectly affected. As for all topics, there are stakeholders at the European, national, regional and local level.

A list of stakeholders was compiled to identify many of the relevant national and European institutions as well as non-political stakeholders who have previous involvement in the topic of carcinogens and mutagens (see Appendix II – List of relevant stakeholders). The list is not exhaustive and exists to inform the EAHP communication and advocacy strategy on the topic of HMPs, should the need arise.

Management of HMPs in the Netherlands

The Risk Instrument for Pharmaceutical Substances (RiFaS) is the national approach to the management of HMPs in the Netherlands[11]. Developed and managed under the auspices of the Professional Association of Pharmacists in the Netherlands (KNMP)[12] and in particular its Special Interest Group on Product Care and Preparation. This group consists of pharmacists who are interested in all facets of the medicinal product as a product (product care): from the receipt of a product or its preparation in the pharmacy to its administration to the patient and for whom handling hazardous substances is an important topic.

RiFaS adopts the approach that actual risk = intrinsic hazard x exposure opportunities[13]. RiFaS provides individual advice on request on the safe handling of products via Rifas.nl. The advice is tailored to the equipment available in the requesting pharmacy, such as a dust extractor or a safety bench. It also takes into account how long the healthcare worker will be working with the substance. The theoretical underpinning for the risk classification of pharmaceutical substances consists of a number of reports from TNO (Netherlands Organisation for Applied Scientific Research)[14] and KNMP. RiFaS is suitable for

[11] Information about the Risk Instrument for Pharmaceutical Substances (RiFaS), available at: https://www.knmp.nl/producten/producten-diversen/risico-instrument-farmaceutische-stoffen-rifas (last visited on 19 January 2022).
[12] Information about the Professional Association of Pharmacists in the Netherlands, available at: https://www.knmp.nl/knmp (last visited on 19 January 2022).
[13] Presentation on file. Please contact EAHP (info@eahp.eu) for further information.
[14] Information about the Netherlands Organisation for Applied Scientific Research, available at: http://www.tno.nl/en/ (last visited on 19 January 2022).

queries arising from compounding and non-compounding pharmacies in institutions (universities and hospitals) as well as community pharmacies.

This standardised national approach to each hazardous substance while enabling consideration of local factors such as equipment and workload ensures appropriate safeguards regardless of the workplace and individual knowledge level. It enhances efficiency by minimising unnecessary reproduction of the same work in each location. The system is funded on a subscription basis.

EAHP's SIG on Hazardous Medicinal Products considers the Dutch model to be an exemplar and that this model should be used as a reference for future development.

Literature review

The SIG undertook a literature review to identify common definitions of HMPs and guidance on the handling of HMPs. The literature review identified the NIOSH guidelines as an internationally recognised definition. With regard to the handling of HMPs, the NIOSH guidelines, national frameworks based on the NIOSH guidelines and Chapter 800 of the USP were the most commonly referenced sources found in the review. In turn, NIOSH identifies IARC, and the U.S. NTP as governmental agencies that review and identify chemicals (including drugs) that are considered as known, probably, or possibly carcinogenic to humans. The EDQM Resolution CM/Res (2016)2 on good reconstitution practices in health care establishments for medicinal products for parenteral use was identified as a potential aid to assessment of handling requirements, however, it did not appear to be used as a reference source for national guidance, where such exist.

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Survey of national organisations of Hospital Pharmacists (Members of EAHP)

Survey design

A brief survey to identify the understanding of the governance of HMPs was undertaken. This brief survey sought to identify the classification and/or handling guidelines where such exist and the involvement of the national association of hospital pharmacists on the topic of HMPs. The survey contained 6 questions.

Respondents

EAHP has 35 country members.[15] The survey was answered by 26 out of the 35 member associations. No feedback was shared by Denmark, Finland, Greece, Latvia, Lithuania, Montenegro, Switzerland, the Netherlands and the United Kingdom. However, the work undertaken by the Netherlands was shared separately as part of the horizon scanning activity of the SIG (see section 'Horizon scanning').

Survey findings

Do guidelines (at local/ regional/country level) exist in relation to minimum handling requirements for HMPs? Please include the link and/or the name of the document you are referring to.

This question was an open question for which several different responses were shared. 6 member associations decided to leave this question blank (Austrian Association of Hospital Pharmacists, Section for hospital/clinical pharmacy of Bosnia and Herzegovina, French Collective for Hospital Pharmacy, Malta Association of Hospital Pharmacists, Pharmaceutical Association of Serbia, Hospital Pharmacy Section and Spanish Society of Hospital Pharmacists), while 3 (Bulgarian Association of Hospital Pharmacy, Hospital Pharmacy Group of the Pharmaceutical Society of Iceland and Italian Society of Hospital Pharmacy) indicated that no guidelines exist at the local, regional or country level and 1 (Macedonian Hospital Pharmacy Association) outlined that no feedback could be provided. The remaining 16 member associations provided additional feedback.

[15] Information about EAHP's member associations available at: https://www.eahp.eu/members (last visited 4 January 2022).

The Hospital Pharmacists Association of Ireland stated that at the country level there are regulations about the classification of packaging and labelling regulations. Within these regulations, the classification of carcinogenic and mutagenic substances are classified into different categories. For further information, the link to the Guideline on the Safe Handling and Use of Cytotoxic Drugs was shared.[16] The Turkish Pharmacists' Association[17] and the Hungarian Society of Hospital Pharmacists[18] both provided links to guidelines in their national languages. The Czech Association of Hospital Pharmacists mentioned two national laws, Act No. 350/2011 Coll. - Act on Chemical Substances and Chemical Mixtures and on the Amendment of Certain Acts (Chemical Act) and NV 361/2007 Sb. - Government Decree laying down health protection conditions at work.

The German Association of Hospital Pharmacists referred to TRGS 525 Handbook M620, while the Association of Hospital Pharmacists of Luxembourg pointed out that guidelines exist at the local level. The Polish Pharmaceutical Chamber remarked that regulations are set at the national level, but that there is no HMP guideline yet. However, the topic is somewhat covered by the Polish Standards on Oncology Pharmacy. The Swedish Pharmaceutical Society's Section of Hospital Pharmacy shared that there are numerous guidelines regarding hazardous medications, mostly local or regional guidelines. There are too many to list. Thus, a link to the national database of children's monographs in ePed, the experience and evidence-based database for paediatric medicines, was provided.[19]

The Portuguese Association of Hospital Pharmacists communicated that the Cytotoxic Preparation Manual by the Board of the College of Hospital Pharmacy Specialty contains information on guidelines. The Slovak Chamber of Pharmacists - Section of Hospital Pharmacists reported that the International Society of Pharmacovigilance (ISOP) standards translation from 2008 is used, while the Croatian Pharmaceutical Society - Hospital Pharmacy Section pointed out that the guidelines are only existing in the paper format and therefore no link could be shared. The Estonian Society of Hospital Pharmacists indicated that guidelines in their country only exist at the hospital level and not at the national level.

[16] Irish Guideline on the Safe Handling and Use of Cytotoxic Drugs, available at: https://www.hse.ie/eng/staff/safetywellbeing/healthsafetyand%20wellbeing/hse%20guideline%20on%20the%20safe%20handling%20and%20use%20of%20cytotox%20drugs%20%20aug%202016.pdf (last visited 4 January 2022).

[17] Turkish Antineoplastic (Cytotoxic) Guide to Working Safely with Medications available at: https://www.thd.org.tr/thdData/userfiles/file/antineoplastikrehberi.pdf (last visited on 4 January 2022).

[18] The Hungarian National Institute of Pharmacy and Food Health (OGYÉI) methodological letter - Cytostatic mixture infusion and injection ordering, preparation, inspection, delivery, available at: https://www.ogyei.gov.hu/dynamic/ogyei%20p%2064_200807_2021.docx (last visited on 4 January 2022).

[19] Swedish ePed database, available at: https://eped.se/backup/eped/lists/17546907492254303423.html (last visited on 4 January 2022).

The Belgian Association of Hospital Pharmacists shared the link to a webpage developed by the VZA (Flemish Association of Hospital Pharmacists) about crushing medications.[20] In addition, it was mentioned that at the hospital level guidelines concerning the handling of cytotoxic medications exist that are different in each hospital. In relation to the level of the medication, a reference was made to PIF (Product Information Fiches). The Slovenian Pharmaceutical Society, Section of Hospital Pharmacists reported that only local lists of HMPs, specified by a single hospital (for local use) exist and that there is no possibility to share these. The Norwegian Association of Hospital Pharmacists remarked that guidelines existed for cytotoxic drugs and antibiotics. These are local guidelines, but they are published on the internet and can be used by other hospitals as well.[21] The National Hospital Pharmacists Association of Romanian explained that information about HMPs is shared via the Ministry of Labour, Family and Social Protection which is the competent authority in the field of occupational safety and health.[22]

Is your association active in the area of 'hazardous medicinal products (HMPs)' (e.g. by advocating in the field, contributing to guidelines, developing guidelines, conducting research, etc.)?

16 out of 25 confirmed that their member association is active in the area of HMPs, while 8 indicated that no work in this field is being carried out. 2 member associations were not able to answer this question and consequently ticked the option 'I don't know'.

Are there any projects (at local level, regional level, country level, etc.) underway in the area of HMPs?

In relation to specific projects that are being carried out at national level, 12 out of 25 member associations shared that projects are being conducted.

The Hospital Pharmacists Association of Ireland explained that the new national guideline concerning the management of waste medicines in the hospital pharmacy department is currently being finalised in which hospital pharmacists have been involved. The final publication is awaited. It is entitled -

[20] Information about crushing created by the Flemish Association of Hospital Pharmacists, available at: www.pletmedicatie.be (last visited on 4 January 2022).
[21] Cytostatics (chemotherapy / chemotherapy) - pregnant, breastfeeding and other special considerations, available at: https://ehandboken.ous-hf.no/document/13340 (last visited on 4 January 2022). Handling of antimicrobial drugs (incl. Antibiotics), available at: https://ehandboken.ous-hf.no/document/10316 (last visited on 4 January 2022).
[22] National Research and Development Institute of Occupational Safety (INCDPM), available at: http://www.inpm.ro (last visited on 4 January 2022).

Guidelines for Segregation, Packaging & Removal of Waste Medicines from HSE Pharmacy Departments and Aseptic Units. For hazardous medicines, there is a national guideline in place since 2016 entitled "Guideline on the handling and use of cytotoxic drugs".

The German Society of Hospital Pharmacists pointed out that projects are carried out on a regular basis. The update of important guidelines for healthcare institutions was named as one example. The Pharmaceutical Association of Serbia, Hospital Pharmacy Section mentioned that within the guidelines of good pharmacy practice, one of the standards is dedicated to the centralized preparation of cytotoxic drugs and that standard refers to the NIOSH list of drugs. The French Collective for Hospital Pharmacy in Europe commented that there is a scientific society, called SFPO, which is specialized in the field of hazardous medicinal products.[23]

The Polish Pharmaceutical Chamber shared that there is a national legislative project on dangerous substances and the development of maximum allowable concentration levels for dangerous drugs currently ongoing. The Swedish Pharmaceutical Society's Section of Hospital Pharmacy reported about the ePed best practice initiative that is a national project to assess medicines for children in terms of safety and promote safe handling and reconstitution.[24]

The Portuguese Association of Hospital Pharmacists reported that hospital pharmacists have developed some interesting work in the area of hazardous medicines in recent years including occupational exposure to cytotoxics in ambulatory care that was shared during the national congress in 2019.[25] The Belgian Association of Hospital Pharmacists remarked that oncologic therapy at home is a project that is started by the National Working Group of the Belgian Oncology Pharmacy Practitioners. There is also a Flemish Working group for the crushing of medications within the Flemish Association. The members maintain a website where practitioners can find information about crushing or not or alternatives for medication therapy that cannot be swallowed.[26]

The Hospital Pharmacy Group of the Pharmaceutical Society of Iceland participated in a project on safe handling, with wipe tests for chemotherapy in different areas, which is being carried out with the European Society of Oncology Pharmacy (ESOP). The Austrian Association of Hospital Pharmacists

[23] French Society of Psycho-Oncology, available at: www.sfpo.fr (last visited on 4 January 2022).
[24] Best practice materials share by the Swedish ePed initiative, available at: https://eped.se/best-practice/ (last visited on 4 January 2022).
[25]12 National Congress of the Portuguese Association of Hospital Pharmacists, available at: https://www.apfh.pt/congresso2019/?targetPage=resumos (last visited on 4 January 2022).
[26] Information about crushing created by the Flemish Association of Hospital Pharmacists, available at: www.pletmedicatie.be (last visited on 4 January 2022).

mentioned that some contributions are made in their country with regard to occupational safety with oncological drugs. The National Hospital Pharmacists Association of Romanian explained that they are working on a joint project for a course for pharmacists and nurses to dissolve hazardous solutions in pharmacy and administer them to patients.

The Czech Association of Hospital Pharmacists outlined that a project on the monitoring of carcinogenic antineoplastic drugs in the environment has been organised by the Masaryk University and the Masaryk Memorial Cancer Institute in Brno.[27] A second project focuses on the development of integrative risk assessment approaches for hazardous chemicals.[28] In addition, the establishment of the National Centre for Toxic Compounds was mentioned.[29]

No projects existed in the countries covered by the other 7 member associations (Bulgarian Association of Hospital Pharmacy, Croatian Pharmaceutical Society - Hospital Pharmacy Section, Hungarian Society of Hospital Pharmacists, Italian Society of Hospital Pharmacy, Association of Hospital Pharmacists of Luxembourg, Malta Association of Hospital Pharmacists, Slovak Chamber of Pharmacists - Section of Hospital Pharmacists) that responded to the survey, while the remaining 6 member associations (Section for hospital/clinical pharmacy of Bosnia and Herzegovina, Macedonian Hospital Pharmacy Association, Norwegian Association of Hospital Pharmacists, Slovenian Pharmaceutical Society, Section of Hospital Pharmacists, Spanish Society of Hospital Pharmacists and Turkish Pharmacists' Association) did not know. The Estonian Society of Hospital Pharmacists indicated that none of the projects are available online.

Is there a standardised list regarding the classification of HPMs in your country?

19 out of 25 member associations indicated that no list regarding the classification of HMPs exists in their country. 3 did not know and 1 left this question blank. There were only 3 member associations, the Bulgarian Association of Hospital Pharmacy, the Czech Association of Hospital Pharmacists and the Italian Society of Hospital Pharmacy, that could confirm that a list exists. In Italy, this list is issued by the Ministry of Health, while in Bulgaria it comes from the Drug Agency. The Italian Society of Hospital Pharmacy was not able to share a link and indicated that exposure limits are not always included. The

[27] Information about the project, available at: https://www.cytostatika.cz/ (last visited on 18 January 2022).
[28] Information about the PRORISK - European Training Network, available at: https://www.recetox.muni.cz/prorisk (last visited on 18 January 2022).
[29] Information about the National Centre for Toxic Compounds, available at: https://www.recetox.muni.cz/en/cooperation/science-and-society/national-centre (last visited on 18 January 2022).

Bulgarian Association of Hospital Pharmacy remarked that the list is part of Ordinance 28 to the Ministry of Health about pharmacies and that no exposure limits are included. The Czech Association of Hospital Pharmacists referred to the National Public Health Institute[30] and hygiene services at the regional level[31].

Are standards for the handling of HMPs included in the curriculum for pharmacists in your country?

13 out of 25 member associations mentioned that there is no specific training, while 2 outlined that standards for the handling of HMPs are taught during undergraduate training. Specialised health and safety courses covered these types of training for 4 member associations. Postgraduate training on handling standards was the option chosen by 2 member associations.

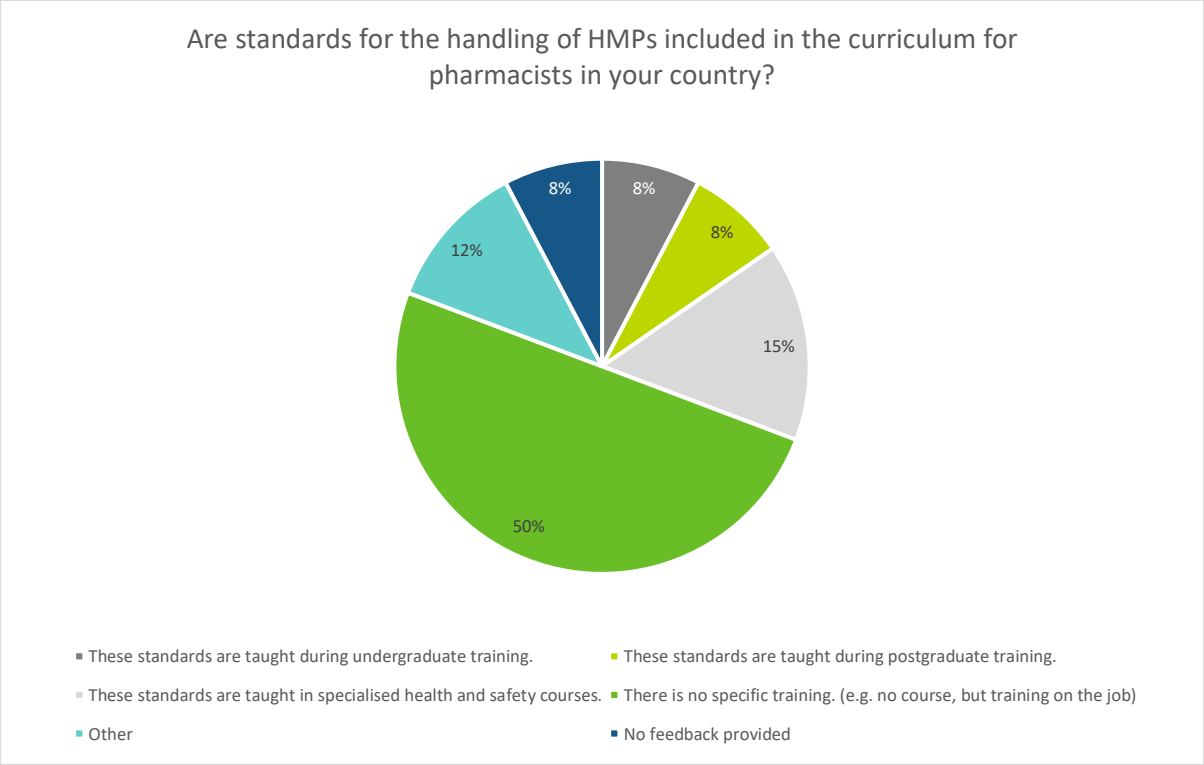

***Figure 1** - Percentage of responses by member associations to the question 'Are standards for the handling of HMPs included in the curriculum for pharmacists in your country?.*

[30] Czech National Public Health Institute, available at: http://szu.cz/index.php?lang=2 (last visited on 18 January 2022).
[31] Information about regional hygiene services, available at: https://www.mzcr.cz/krajske-hygienicke-stanice/ (last visited on 18 January 2022).

Out of the remaining 5 member associations, 2 decided not to provide feedback to this question, while 3 ticked the option 'other' and provided additional feedback. The Polish Pharmaceutical Chamber remarked that the standards are a part of the national legislation, one gets familiar with them in the workplace. Also, the topic is introduced from time to time at industry-specific conferences. The Portuguese Association of Hospital Pharmacists pointed out that these standards are taught mostly on the job and that the association also carried out some training linked to this subject. The Bulgarian Association of Hospital Pharmacists stated that the standards are part of the Rules of Good Pharmacy Practice about Cytotoxic Drugs and that they are also taught via masterclasses on oncology pharmacy.

If the EU were to develop a classification system for HMPs, do you see the potential for your country to reference this list in developing handling guidelines?

21 out of 26 member associations welcomed the development of a classification system for HMPs by the European Union and saw the potential to reference this list when developing handling guidelines. 1 member association selected 'no', while 2 did not know or kept the response to this question blank.

The work of this Special Interest Group (SIG) was financially supported by Amgen.

Survey on Hazardous Medicinal Products for Individual Chief Pharmacists

In addition to the survey for EAHP's 35 member associations, the SIG also prepared a more detailed survey for individual chief pharmacists working across Europe. EAHP's member associations helped with the dissemination of this survey.

Survey design

The purpose of the survey to individual chief pharmacists was to obtain an understanding of hospital pharmacy practice and relevant knowledge of HMPs. It was agreed that the survey should be informative without being overly time consuming given the extraordinary demand on hospital pharmacy services during the COVID-19 pandemic. As the handling of HMPs has multi-departmental implications and may have governance external to an individual institution, questions were designed to elicit responses regarding institution wide and national approaches to HMPs. There were a total of 28 questions which in the case of positive responses would potentially lead to another 8 questions.

The section survey finding has grouped the answers by theme rather than in order of the questions included in the survey. The survey questions are annexed to this report (see Appendix III – Questions included in the Survey on Hazardous Medicinal Products for Individual Chief Pharmacists).

Respondents

The survey was available to all chief pharmacists, as identified by each EAHP member country association. There were 545 responses to the survey with 277 surveys fully completed and a further 268 partially completed. Hospital pharmacists that only responded to the first 3 questions touching on their background and hospital information were excluded, leaving 384 responses to be assessed. More than three-quarters of respondents worked in either a teaching or general hospital while the remainder worked in specialist hospitals, including geriatric, neurology, oncology, orthopaedic/traumatology, psychiatric, paediatric and rheumatology hospitals. The general questions also collected information on the number of hospital beds served by the institution as well as on the country of the respondent.

Survey Findings

Standards for the handling of hazardous medicines

Out of the respondents that answered this question 58% (N=224/384) identified national standards for the handling of hazardous medicines in hospital pharmacy and two-fifths (39% | N=151/384) policies in specialised wards/units. There was a lower response rate for other departments. However, this finding is tempered by 19% (74/384) of pharmacists not having detailed knowledge of policies in other hospital departments. Only 6% (24/384) of respondents identified an absence of national standards for hospital pharmacy handling of hazardous medicines.

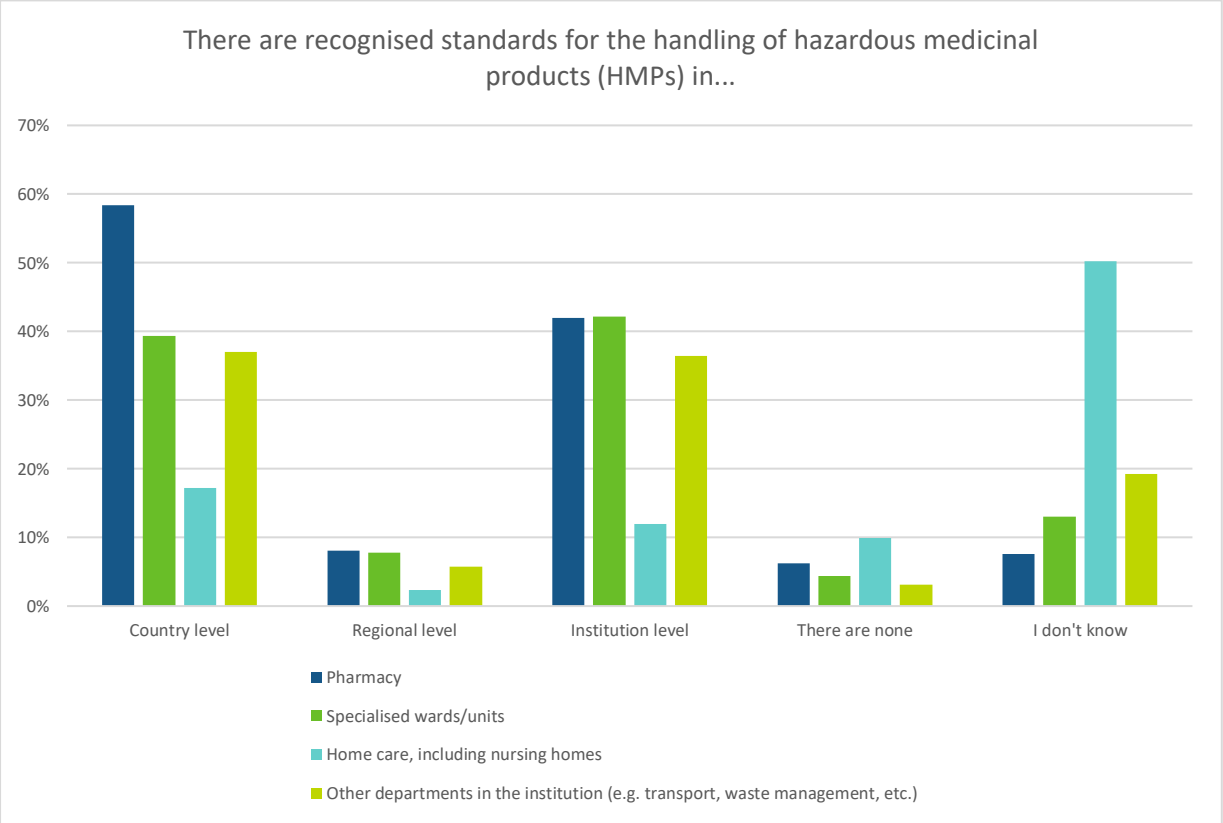

***Figure 2** - Percentage of responses by chief pharmacists (N=384) to question 4 'There are recognised standards for the handling of hazardous medicinal products (HMPs) in…'.*

While HMP policies exist, it is unclear how these apply to everyday practice as only 55% (14% (52/384) in electronic format and 41% (159/384) in paper format) identified that their institution had a list of hazardous medicines in place. A supplementary question to those who had a list and were willing to provide further information showed 74% (145/197) prepared these internally in the institution while 23% (N=46/197) received these from an external source, with 3% (6/197) uncertain of the information source.

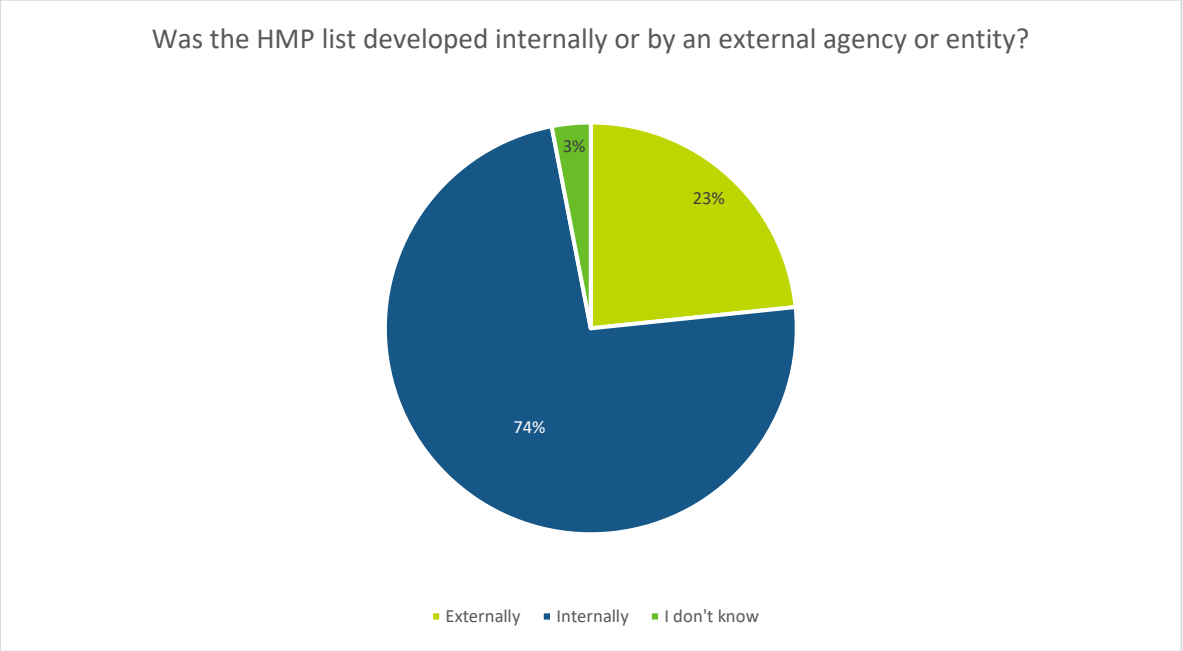

***Figure 3** - Percentage of responses by chief pharmacists (N=197) to question 7 'Was the HMP list developed internally or by an external agency or entity?'.*

There is a high dependence on the list generated by NIOSH. However, during the horizon scanning activity of the SIG it was also confirmed that there are other entities in Europe that influence the classification landscape (see section 'Horizon scanning').

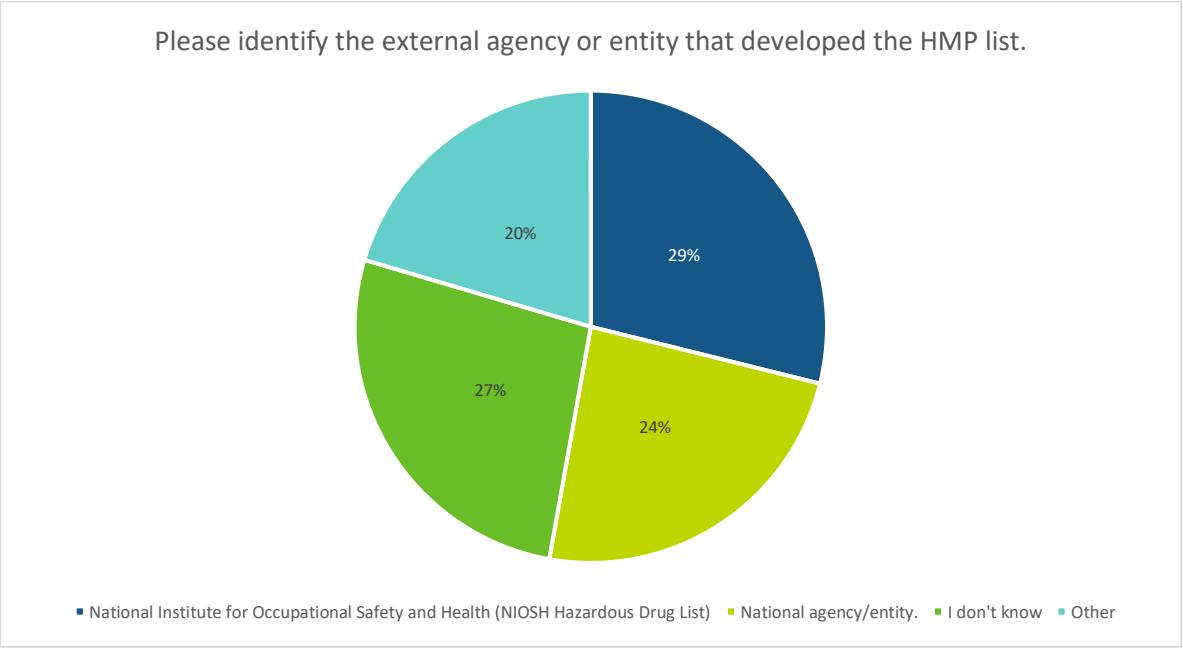

***Figure 4** - Percentage of responses by chief pharmacists (N=142) to the question 8 'Please identify the external agency or entity that developed the HMP list.'.*

The question relating to the identification of HMPs throughout the whole chain of usage was a question for which respondents could select one or multiple of the eleven answer options, ranging from administration to unpacking. In line with the institutional approach hazardous medicines across the entire medication management process was examined with preparation 77% (N=254/331), storage 75% (N=247/331), administration 69% (N=227/331) and clinical waste 64% (N=212/331) scoring the highest percentages for active identification. Only 9% (N=30/331) of respondents identified that hazardous medications are not identified.

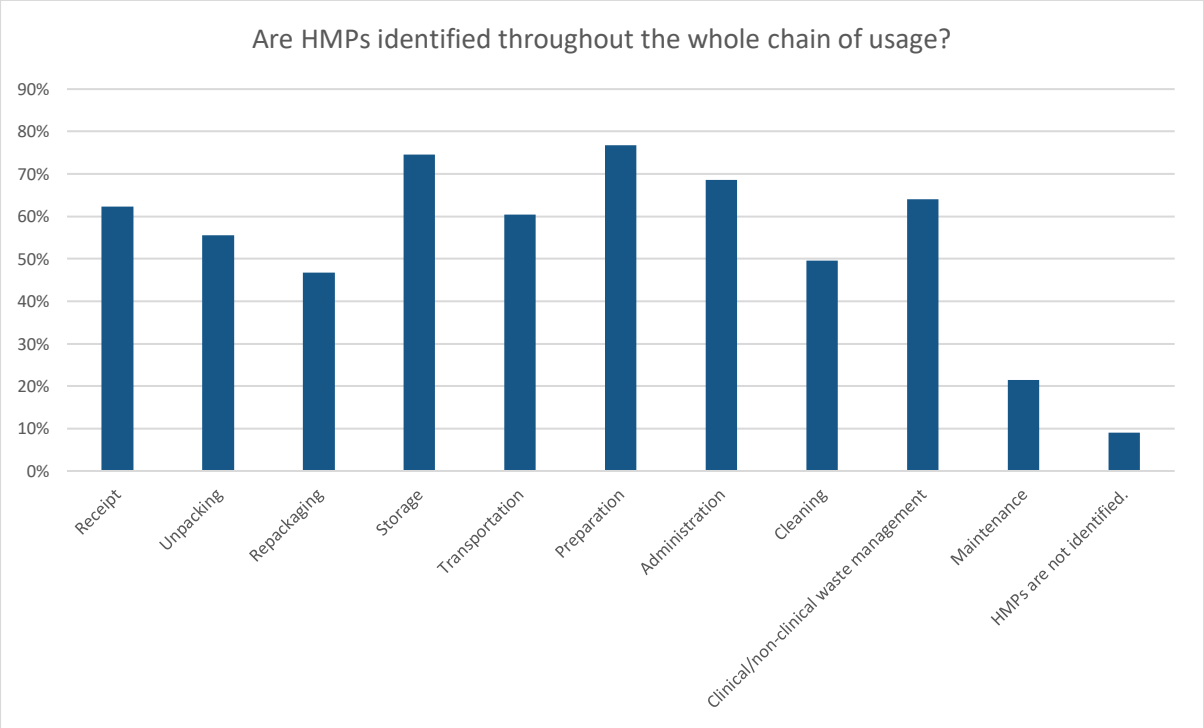

Figure 5 - *Percentage of responses by chief pharmacists (N=331) to question 9 'Are HMPs identified throughout the whole chain of usage?'. (Note that this was a tick all that apply question)*

Lists and symbols were the main tools used for informing staff about HMPs. Other types of tools mentioned by the 17% (N=52/311) of respondents that opted for 'Other' included training, standard operating procedures and product information labelling.

The work of this Special Interest Group (SIG) was financially supported by Amgen.

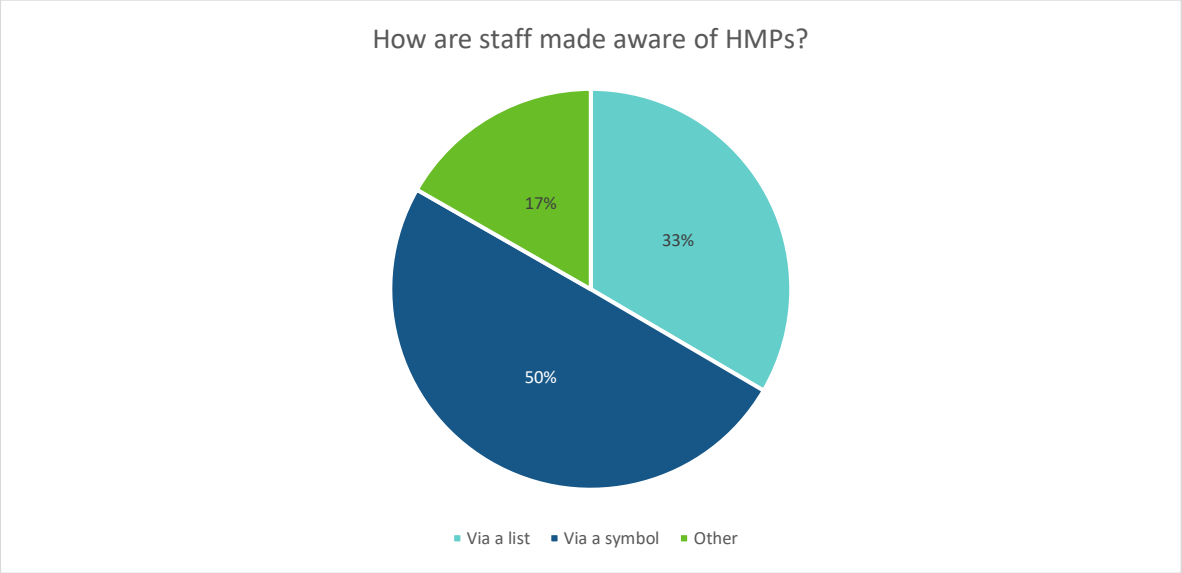

***Figure 6** - Percentage of responses by chief pharmacists (N=311) to question 10 'How are staff made aware of HMPs?'.*

As indicated by the responses to this question, for which respondents could select one or multiple of the nine answer options, there was a correlation between the areas with policies and the staff members who received training with pharmacy staff and nursing staff most frequently in receipt of training.

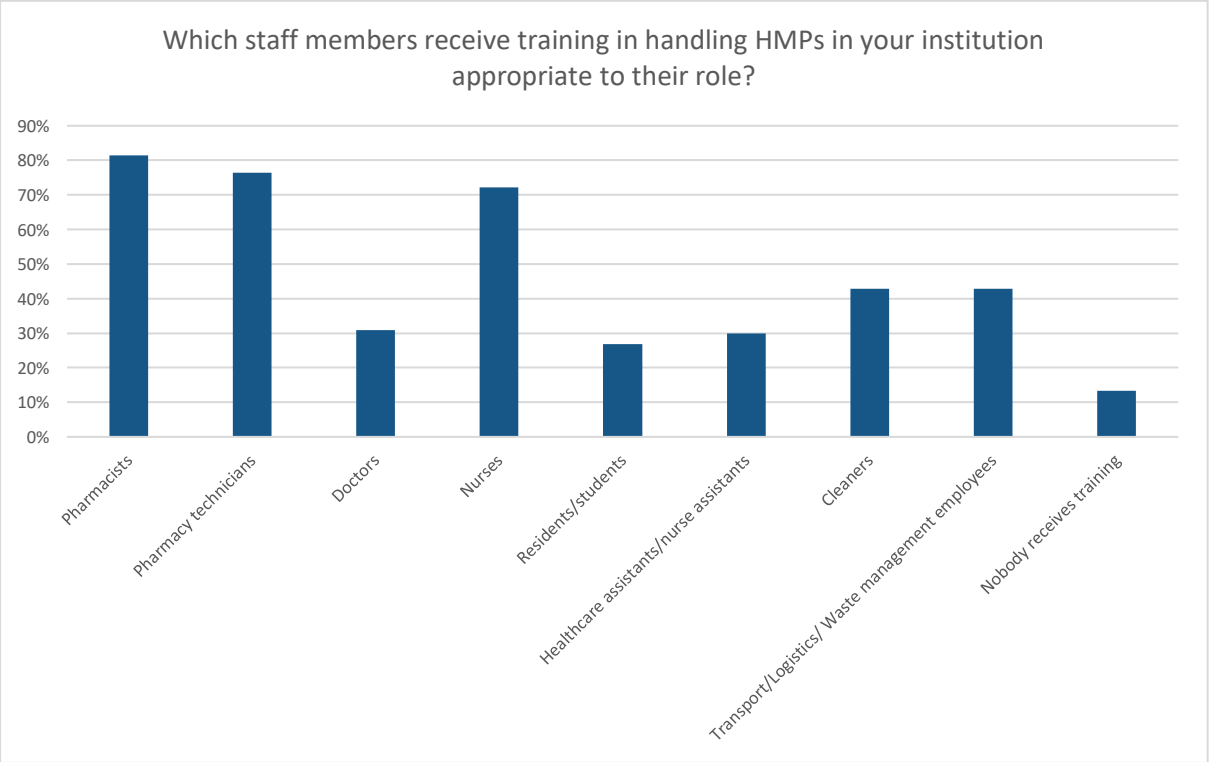

***Figure 7** - Percentage of responses by chief pharmacists (N=317) to question 11 'Which staff members receive training in handling HMPs in your institution appropriate to their role?'. (Note that this was a tick all that apply question)*

The identification of hazardous medicines was found to be supported in 75% (N=234/313) of the cases by written protocols for either some (37% | N=115/313) or all stages (38% | N=119/313).

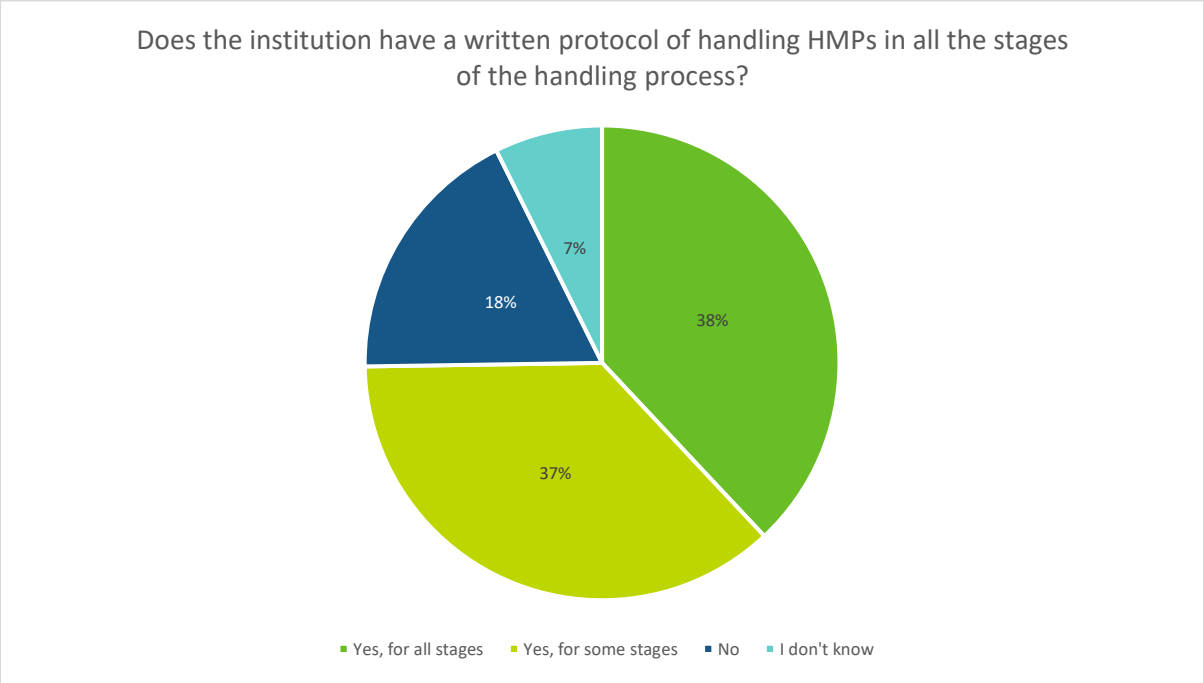

***Figure 8** - Percentage of responses by chief pharmacists (N=313) to question 13 'Does the institution have a written protocol of handling HMPs in all the stages of the handling process?'.*

The 75% (N=234/313) of respondents that indicated that their institution had either a written protocol for all the stages of the handling process (38% | N=119/313) or for some of them (37% | N=115/313) were asked to provide additional insights on the access thereto. Pharmacy and nursing staff were identified as having a high level of access to these protocols while other staff averaged around 50% access. In relation to this question, it should be noted that respondents could tick one or multiple of the eight answer possibilities that were provided. All but one, selected the option 'pharmacists'.

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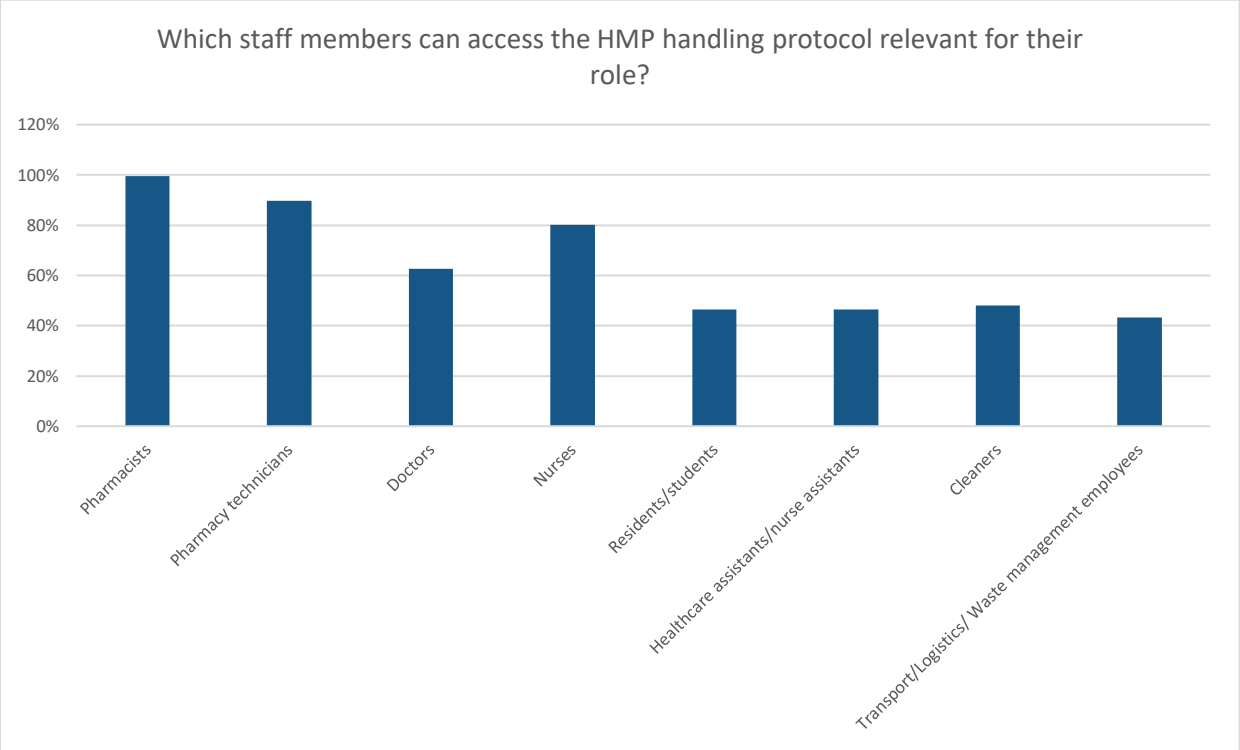

***Figure 9** - Percentage of responses by chief pharmacists (N=233) to question 14 'Which staff members can access the HMP handling protocol relevant for their role?'. (Note that this was a tick all that apply question)*

Documentary evidence of the training was required by the national competent authority in 9% of responses, 25% (N=69/279) by the institution, retained in a personnel record in 33% (N=91/279) while 26% (N=72/279) had no requirement for documentation of training and 18% (N=51/279) did not know if this was a formal requirement. It should be noted that respondents were provided with the possibility to select one or multiple of the five answer options provided for this question.

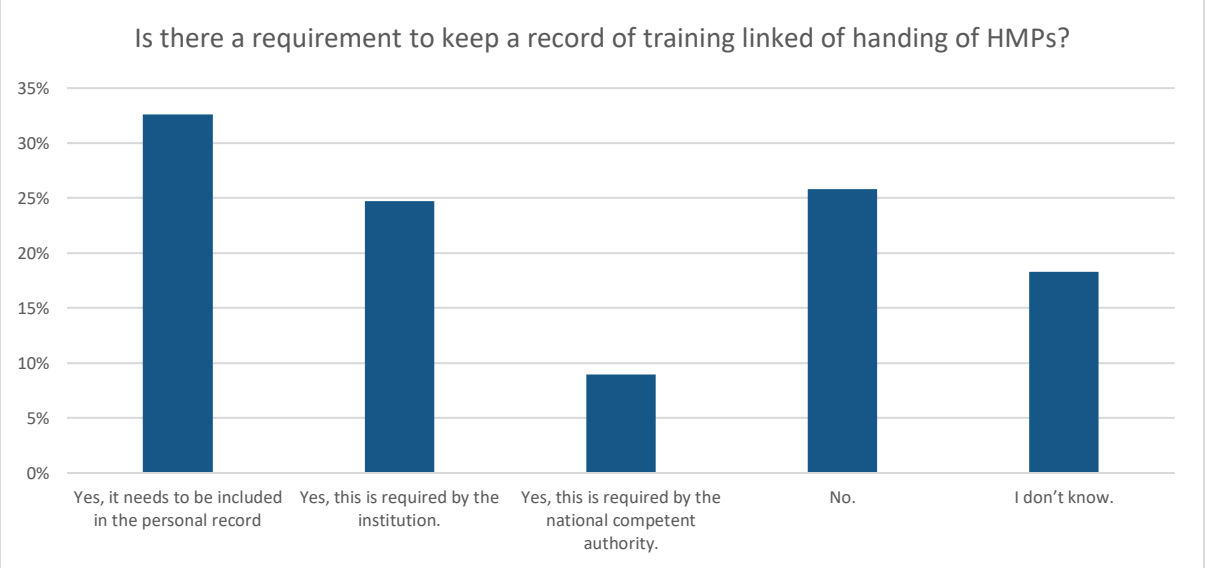

***Figure 10** - Percentage of responses by chief pharmacists (N=279) to question 32 'Is there a requirement to keep a record of training linked of handing of HMPs?'. (Note that this was a tick all that apply question)*

Regardless of the policies and training in place, there was a lower level of risk identification of HMPs with manipulation at the patient level e.g. crushing of oral medications.

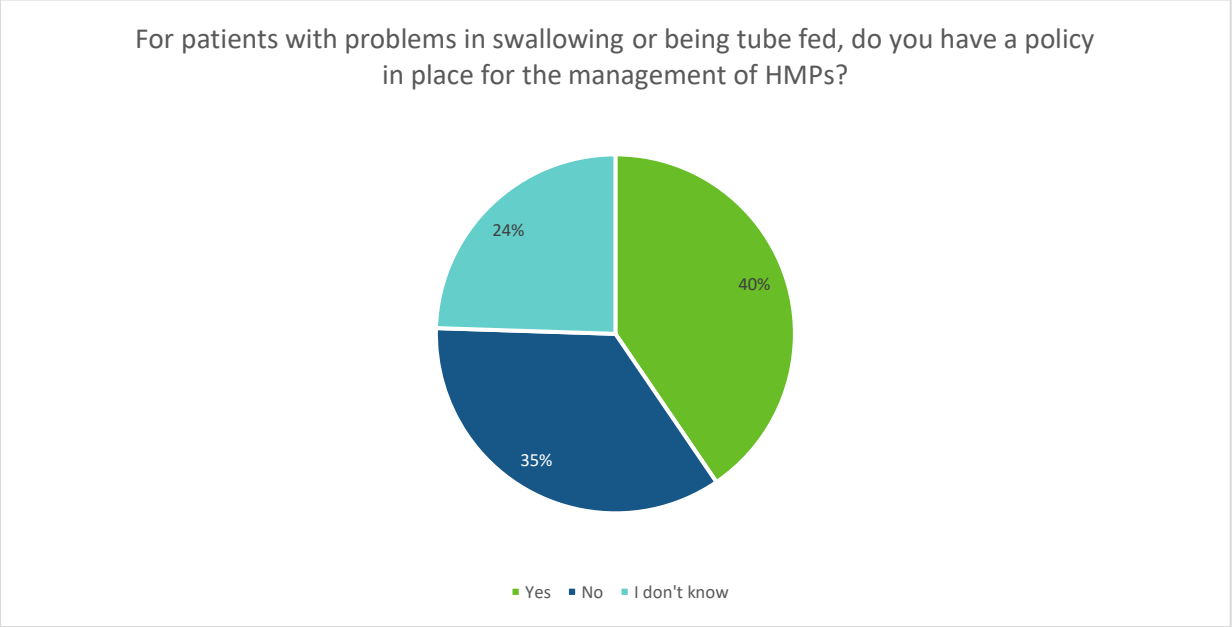

***Figure 11** - Percentage of responses by chief pharmacists (N=294) to question 25 'For patients with problems in swallowing or being tube fed, do you have a policy in place for the management of HMPs?'.*

Equipment

Moving the focus of the survey to the equipment it was found that 75% prepare HMPs in the pharmacy in either a biological safety cabinet (BSC) (46% | N=135/295) or an isolator (23% | N=67/295) or a combination of both 6% (18/295). 23% (N=68/295) of respondents identified that the pharmacy did not prepare HMPs while 2% (N=6/295) said there were no specific preparation measures in place. In the absence of additional questioning, it is not clear if the pharmacies do not prepare HMPs in their pharmacy because of the services provided at the institution or because the preparation took place elsewhere. It is also unclear for the 2% (N=6/295) that have no specific measures in place.

When examining only the feedback provided by respondents working in university/teaching hospitals and oncology hospitals, no significant difference was noted.

Considerable variation in the type of cabinet in use was identified. The practice in institutions is not governed in the same way as for manufacturers of medicinal products for whom negative pressure is

specified for relevant workflow.[32] [33] Institutions are permitted to consider the health and safety issues for operators and institutional guidance may derive in part from PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments.[34]

When asked what systems were considered by the pharmacist to provide protection for workers against exposure respondents could choose between needles, spikes, closed system transfer devices (CSTDs), BSCs and Isolators. Respondents had the possibility to select one or multiple of the five options provided for this question.

Looking at respondents that selected BSCs in combination with one or multiple of the other options it was observed that 45% (N=131/292) deem BSCs together with CSTDs the most effective way to protect workers followed by 15% (N=44/292) that thought the combination of BSCs and spikes is the most effective. 9% (N=26/292) believed that BSCs used with spikes and CSTDs would offer the best protection from potential exposure to HMPs.

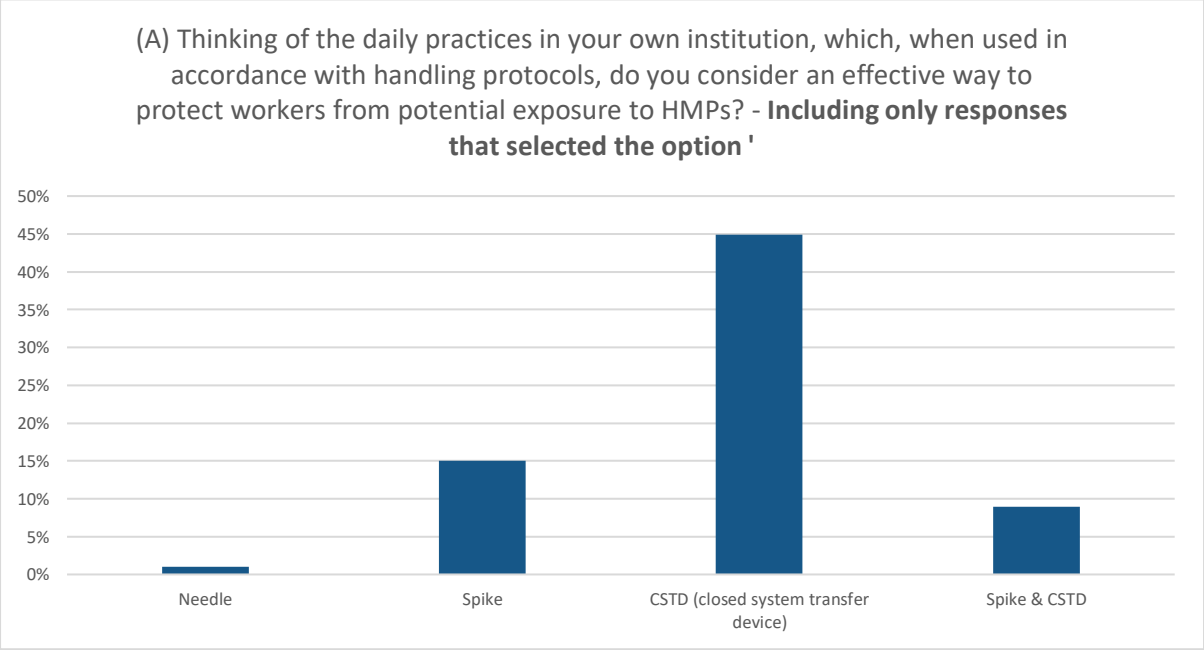

***Figure 12** - Percentage of responses by chief pharmacists (N=292) to question 16 'Thinking of the daily practices in your own institution, which, when used in accordance with handling protocols, do you consider an effective way to protect workers from potential exposure to HMPs?' that selected the option 'biological safety cabinet' in combination with the others. (Note that this was a tick all that apply question)*

[32] EU GMP Annex 1 Revision 2020, Manufacture of Sterile Medicinal Products, available at: https://www.honeymangroup.com/training/articles/annex-1-revision-2020/ (last visited on 16 January 2022).
[33] World Health Organization, WHO Technical Report Series, No. 957, 2010, Annex 3, WHO good manufacturing practices for pharmaceutical products containing hazardous substances, available at: https://www.who.int/medicines/areas/quality_safety/quality_assurance/GMPPharmaceuticalProductsCcontainingHhazardousSubstances TRS957Annex3.pdf (last visited on 10 January 2022).
[34] Pharmaceutical Inspection Co-operation Scheme (PIC/S), Publications, available at: https://picscheme.org/en/publications (last visited on 4 January 2022).

Isolators were considered effective in combination with CSTDs by 35% (N=103/292) of the respondents. 9% (26/292) of respondents deemed spikes when used with an isolator as a good option for offering protection against the potential exposure to HMPs. A small group (5% | N=16/292) also considered isolators in combination with both CSTDs and spikes effective.

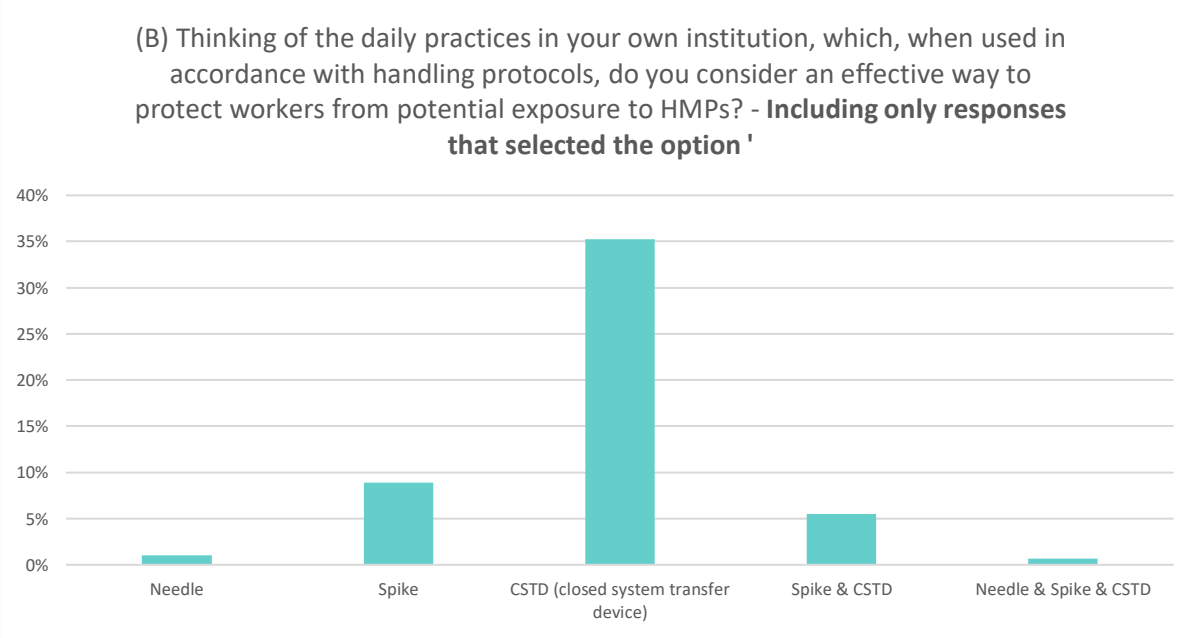

***Figure 13** - Percentage of responses by chief pharmacists (N=292) to question 16 'Thinking of the daily practices in your own institution, which, when used in accordance with handling protocols, do you consider an effective way to protect workers from potential exposure to HMPs?' that selected the option 'isolator' in combination with the others. (Note that this was a tick all that apply question)*

When assessing the responses to the five options for this question individually, it could be deduced that 14% (N=41/292) of respondents believe that CSTDs offer the best protection against the exposure to HMPs, followed by 10% (N=28/292) selecting isolator and 5% (N=15/292) opting for BSC.

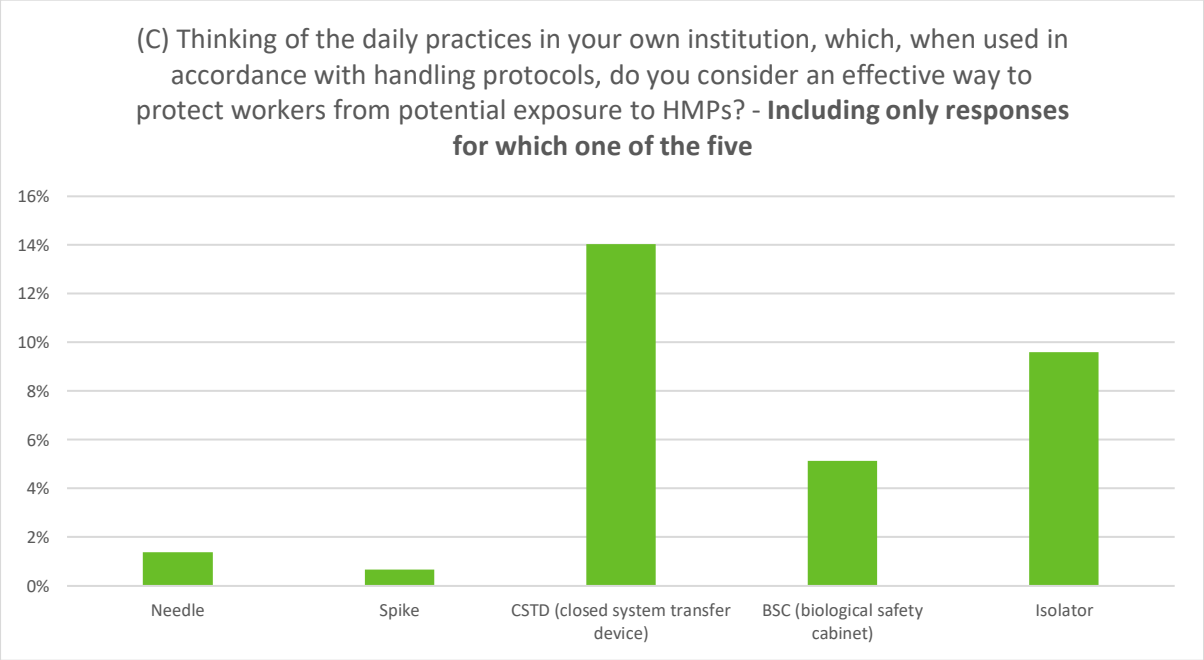

Figure 14 - *Percentage of responses by chief pharmacists (N=292) to the question 16 'Thinking of the daily practices in your own institution, which, when used in accordance with handling protocols, do you consider an effective way to protect workers from potential exposure to HMPs?' that ticked only 1 option. (Note that this was a tick all that apply question)*

When asked about the availability of spill kits 61% (N=178/293) of respondents indicated these were available in both the pharmacy and the relevant wards. A further 16% (N=47/293) has spill kits only in the pharmacy and 3% (N=9/293) only on the wards and 19% (N=55/293) of respondents indicated they do not have spill kits available at all in their institution.

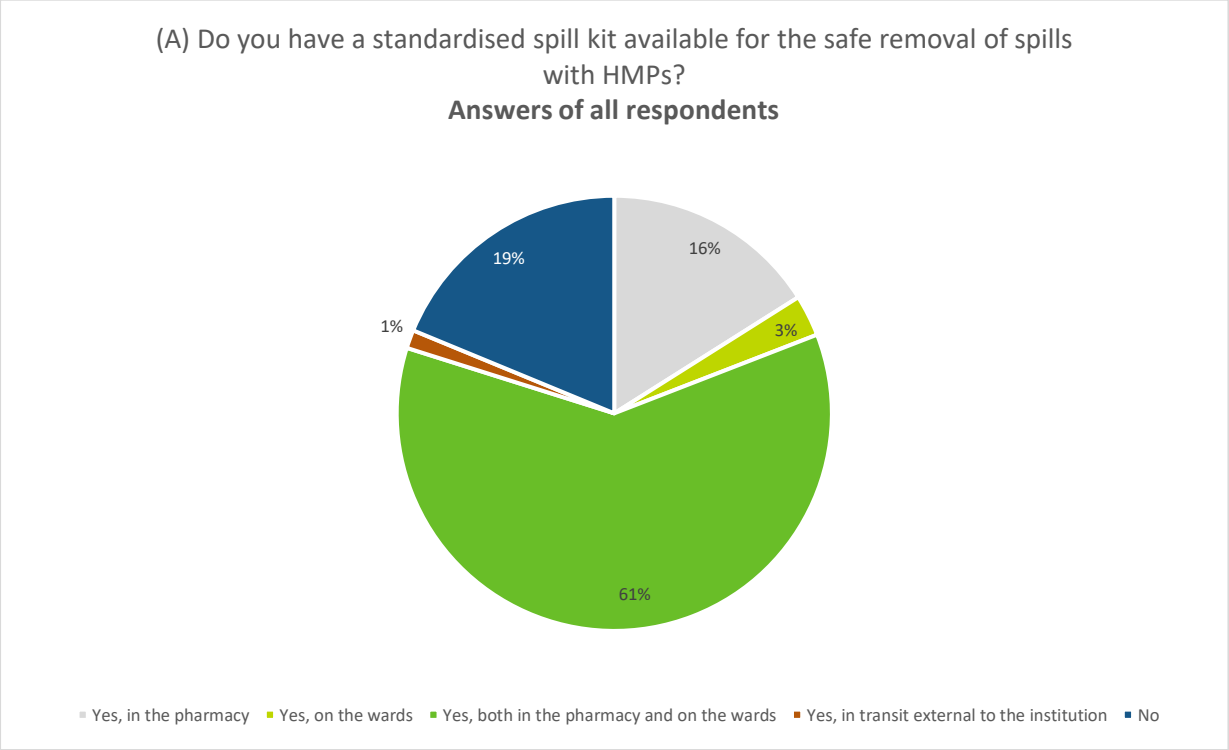

Figure 15 – *Percentage of responses by all chief pharmacists (N=293) to question 24 'Do you have a standardised spill kit available for the safe removal of spills with HMPs?'.*

When looking only at respondents working in university/teaching hospitals and oncology hospitals the number of respondents indicating that no spill kits existed went down to 6% (N=5/87) and those that reported spill kits were available in both the pharmacy and other relevant wards went up to 75% (N=65/87).

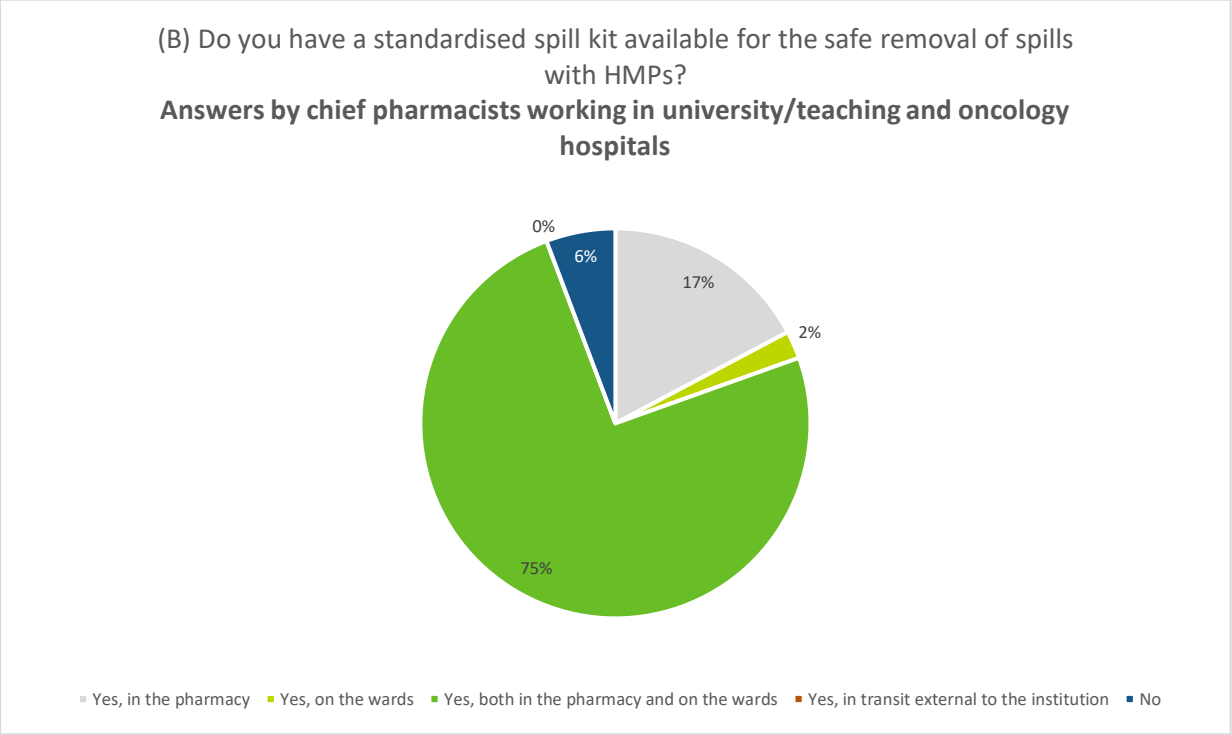

Figure 16 *– Percentage of responses by all chief pharmacists (N=87) working in university/teaching hospitals and oncology hospitals to question 24 'Do you have a standardised spill kit available for the safe removal of spills with HMPs?'.*

Warning labels were found to be widely used with 69% (N=191/282) having specific warning labels. 8% (N=33/282) considered that this question did not apply to them which may arise from the institution type in which the respondent works.

Yes, we use the "Yellow Hand" label	23%
Yes, we use a warning label, other than the "Yellow Hand"	44%
No, we don't use any special warning label	24%
Not applicable	8%

Table 1 *– Percentage of responses by chief pharmacists (N=282) to question 27 'Do you use in your institution a special warning label for HMPs?'.*

Education

75% (N=221/294) of respondents consider that differences in occupational hazards exist between biological/targeted small molecule oncology drugs versus traditional chemotherapeutic drugs while 78% (N=220/283) would welcome further post-graduate education on the topic.

The work of this Special Interest Group (SIG) was financially supported by Amgen.

When asked to summarise their views the hospital pharmacists' respondents were asked to rank the following 9 statements:

- I know where to find information about the handling of HMPs
- I know who is responsible for the risk assessment of handling HMPs
- I know what type of protection to use when handling HMPs
- I have access to proper protection when handling HMPs
- I know how to safely dispose of HMPs
- I am offered regular education on how to handle HMPs
- I know where to access education on HMPs
- I provide education to other healthcare practitioners on HMPs
- My staff are informed/have received training in all of the above

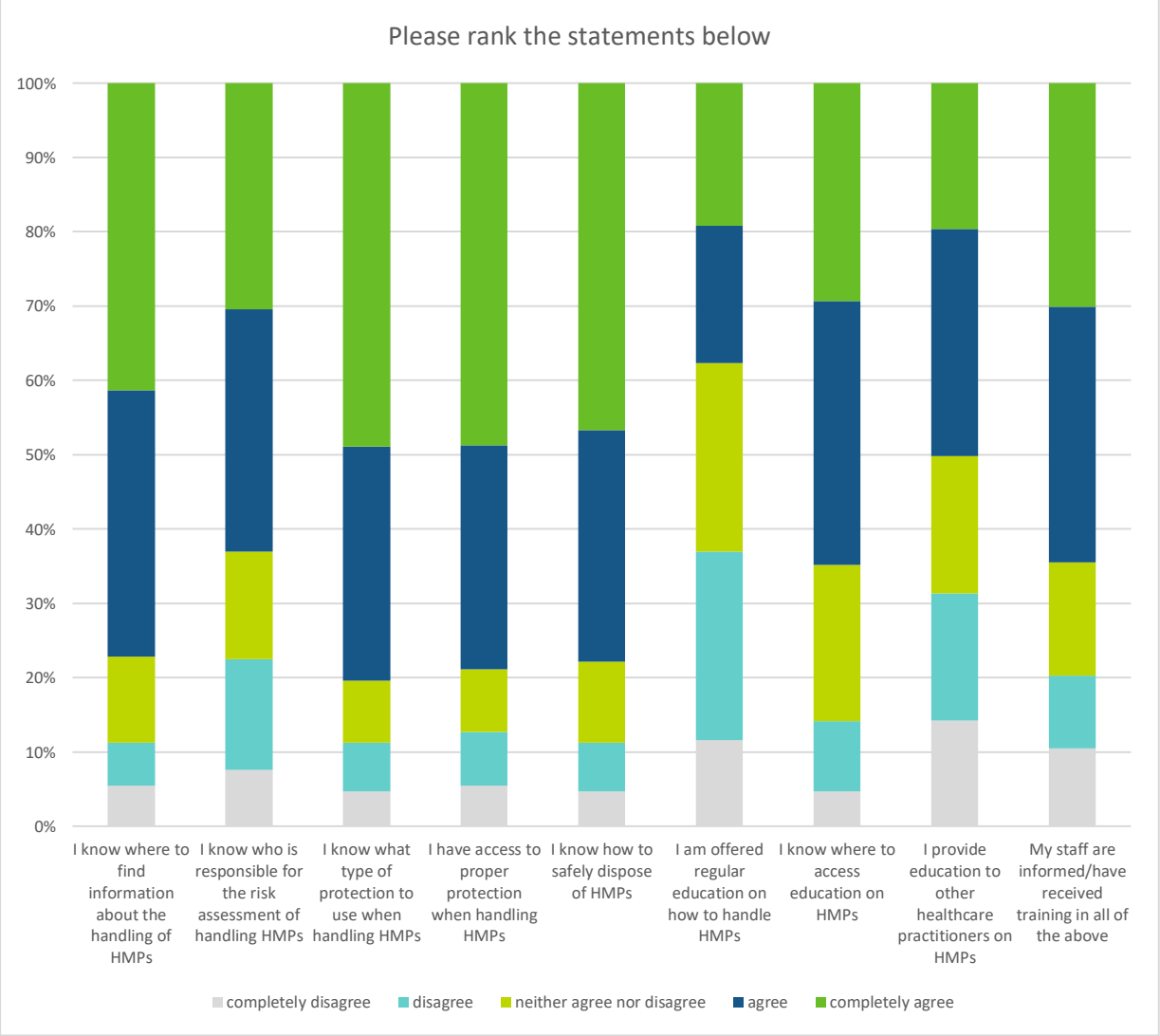

***Figure 17** – Percentage of responses by chief pharmacists (N=276) to question 28 'Please rank the statements below'.*

The work of this Special Interest Group (SIG) was financially supported by Amgen.

The ranking received for this overarching question confirms the responses submitted earlier by the respondents. It reinforces the need for additional education and training on the handling of HMPs, with a 62% (N=172/276) non-positive response received, 37% (N=102/276) not being offered additional post-graduate training and another 25% (N=70/276) not agreeing or disagreeing with the statement ' I am offered regular education on how to handle HMPs'.

Quality Assurance

The survey examined the topic of quality assurance of the environment in which HMPs are prepared and used. Only 26% (N=77/298) identified that surface contamination monitoring for traditional chemotherapeutic drugs was conducted on a regular basis with 41% (N=122/298) of respondents, coming mainly from Croatia, France, Poland, Portugal, Serbia, Spain and the United Kingdom, never having undertaken such monitoring.

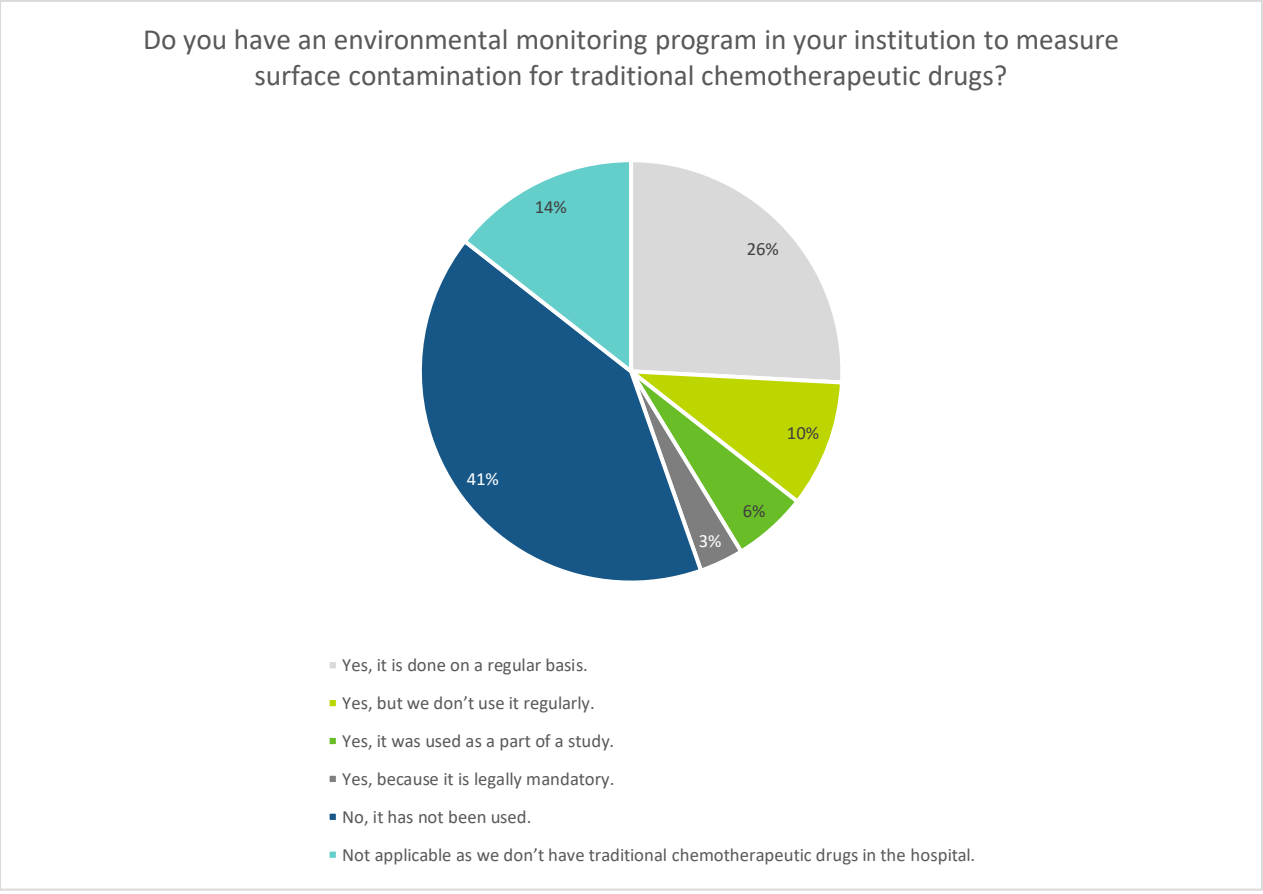

***Figure 18** – Percentage of responses by chief pharmacists (N=298) to question 19 'Do you have an environmental monitoring program in your institution to measure surface contamination for traditional chemotherapeutic drugs?'.*

Surface monitoring undertaken in all of the institutions identifying regular use of a surface contamination review showed 52% (N=53/102) of the institutions having an annual review, 6 monthly reviews in another 23% (N=23/102) and more frequently in the remainder. There was almost an even divide with those institutions who only undertook surface swabbing in the pharmacy compared with all possible areas where traditional chemotherapeutic medicines are used.

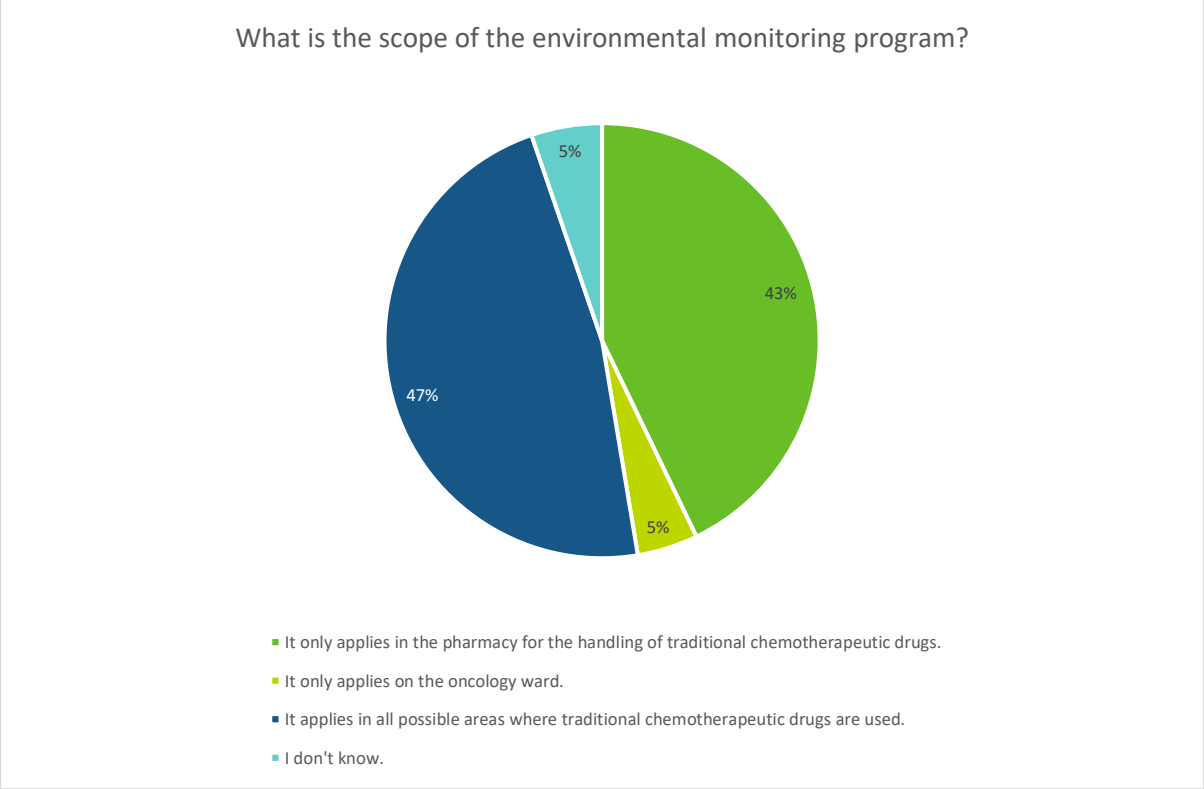

***Figure 19** – Percentage of responses by chief pharmacists (N=133) to question 21 'What is the scope of the environmental monitoring programme?'.*

The pharmacy department takes the lead in the management of the quality improvement programmes arising from the environmental programme most of the time as outlined by figure 20. However, a shared responsibility for implementation is noted from the respondents that included departments such as Occupational Health, Quality Management and/or Hospital Management by selecting multiple choices when answering (see figures 21 and 22). It should be noted that respondents were able to select one or multiple of the five answer options for this question.

The work of this Special Interest Group (SIG) was financially supported by Amgen.

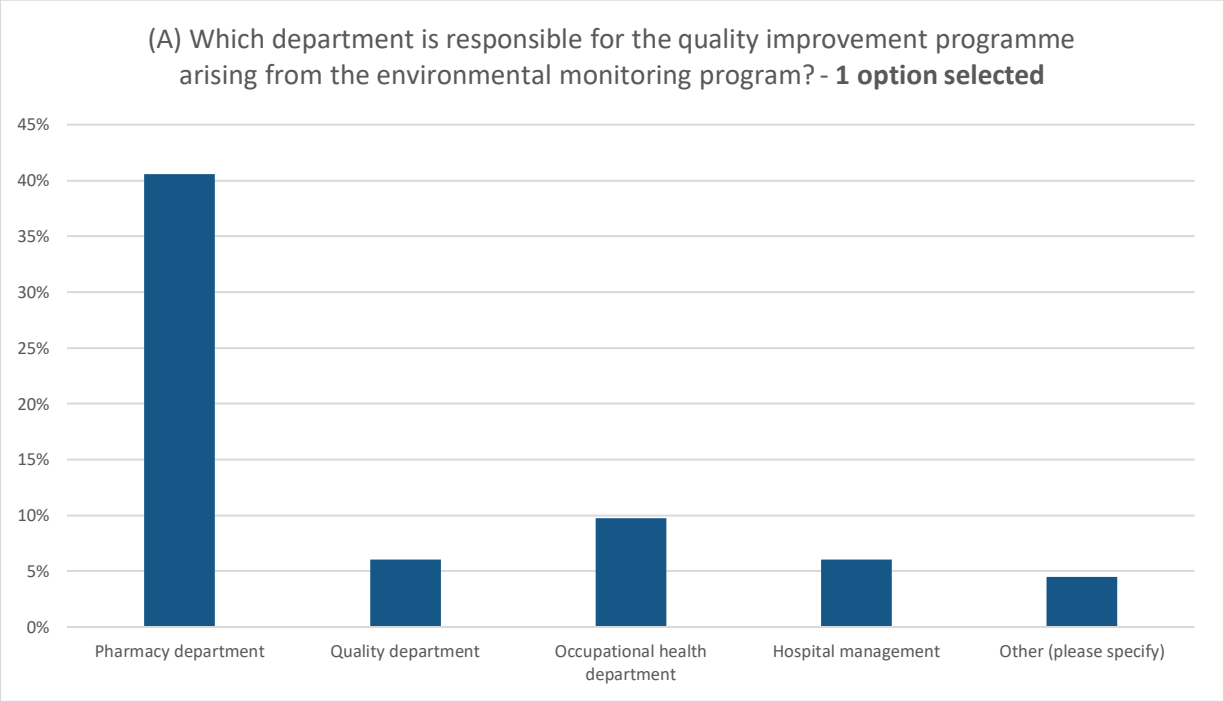

Figure 20 *– Percentage of responses by chief pharmacists (N=133) to question 22 'Which department is responsible for the quality improvement programme arising from the environmental monitoring program?' that ticked 1 option. (Note that this was a tick all that apply question)*

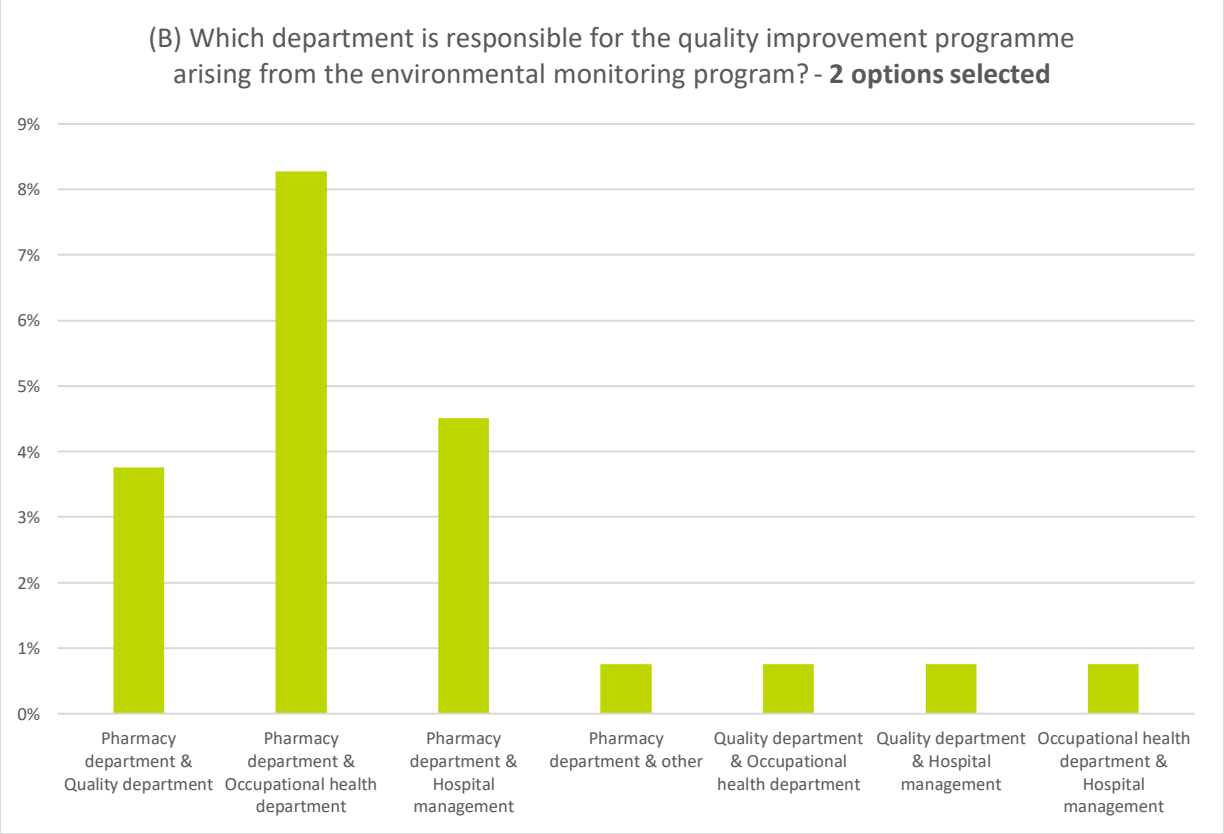

Figure 21 *– Percentage of responses by chief pharmacists (N=133) to question 22 'Which department is responsible for the quality improvement programme arising from the environmental monitoring program?' that ticked 2 options. (Note that this was a tick all that apply question)*

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***Figure 22** – Percentage of responses by chief pharmacists (N=133) to question 22 'Which department is responsible for the quality improvement programme arising from the environmental monitoring program?' that ticked multiple options. (Note that this was a tick all that apply question)*

35% (N=98/249) of respondents with a surface contamination monitoring system were required to report findings, however only an individual Polish respondent reported to an external organisation. The remaining reported to an internal group with some respondents commenting that a hierarchy of risk assessments influenced their reporting requirements. Some 14% (N=34/249) did not know if reporting was mandated. 51% (N=127/249) of responses appear to indicate there is no requirement to report findings (31% (N=76/249) no and 20% (N=51/249) not applicable). Detailed examination of these responses was outside of the scope of this survey.

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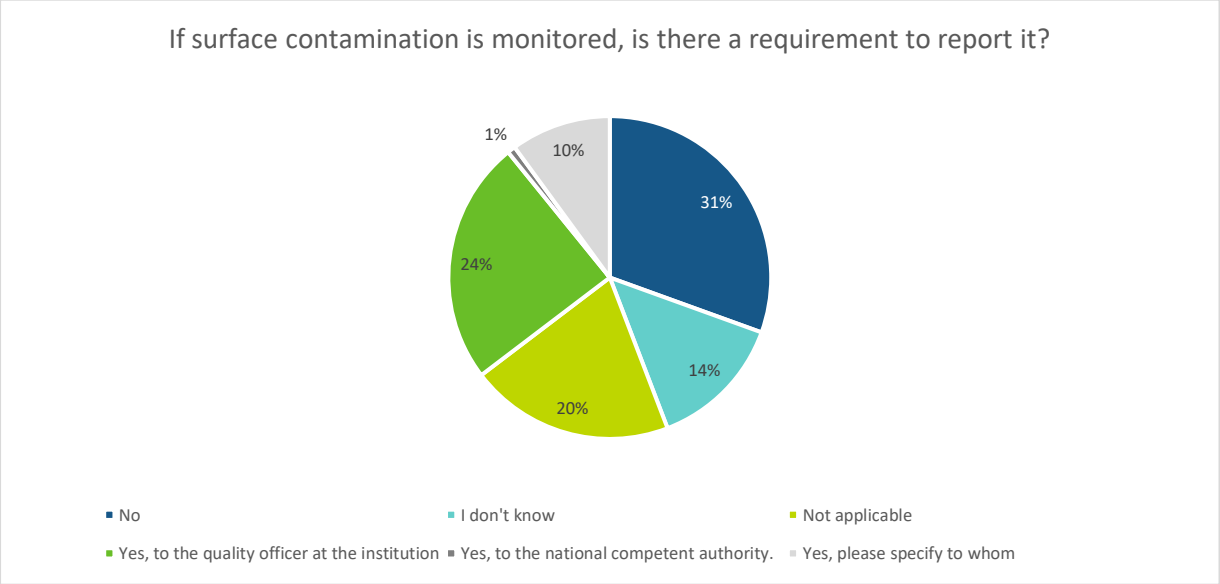

***Figure 23** – Percentage of responses by chief pharmacists (N=249) to question 34 'If surface contamination is monitored, is there a requirement to report it?'.*

Medical Assessment

There is no standard approach to the medical assessment of staff identified from respondents. Only 11% (N=30/280) require an assessment on recruitment while 34% (N=96/280) have regular reviews.

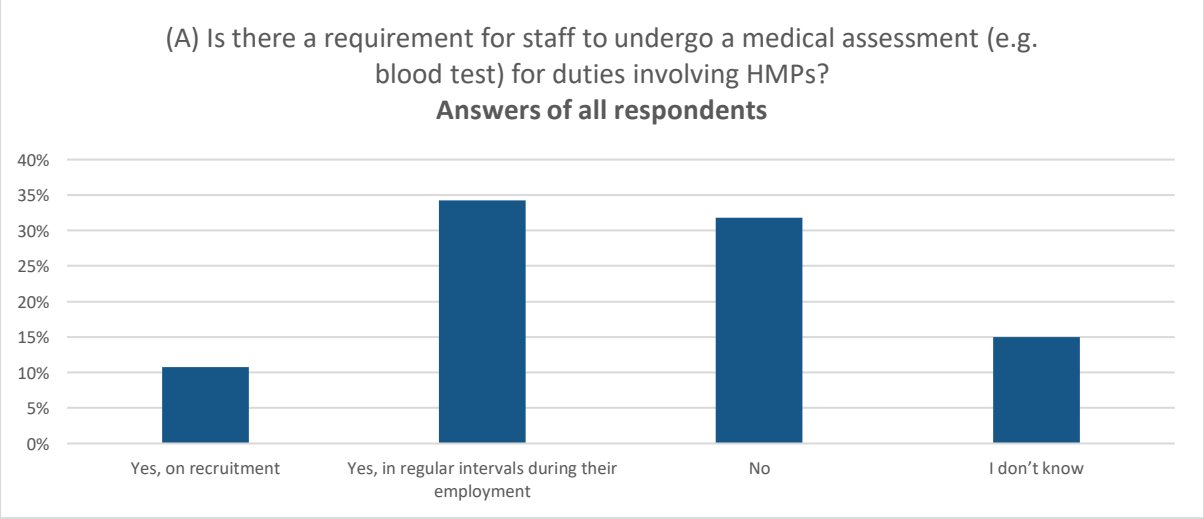

***Figure 24** – Percentage of responses by all chief pharmacists (N=280) to question 33 'Is there a requirement for staff to undergo a medical assessment (e.g. blood test) for duties involving HMPs?'.*

When looking only at chief pharmacists working at university/teaching and oncology hospitals no significant differences in the response pattern was observed. Only 5% (N=8/160) of staff in these types of hospitals are required to undergo an assessment on recruitment while 26% (N=41/160) have regular reviews.

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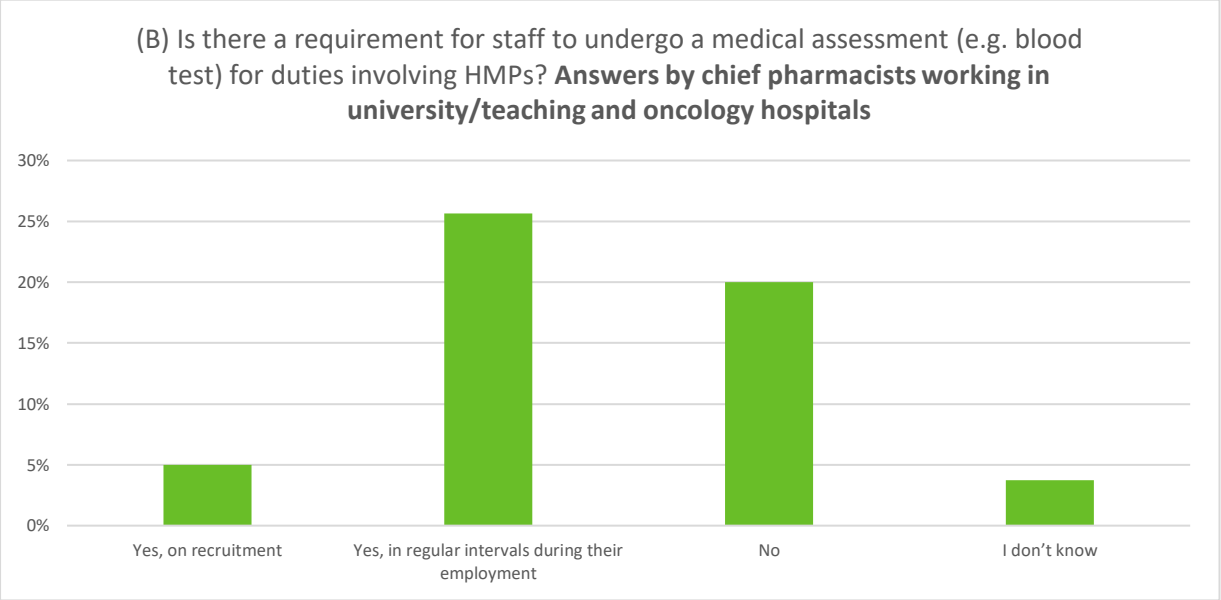

Figure 25 – *Percentage of responses by chief pharmacists (N=160) working in university/teaching hospitals and oncology hospitals to question 33 'Is there a requirement for staff to undergo a medical assessment (e.g. blood test) for duties involving HMPs?'.*

External Audit

30% (N=82/279) of replies indicated that there is an external audit of the processes for the handling of HMPs. This was surprising as only 1 respondent reported surface contamination to an external agency and only 9% (N=25/279) reported evidence of training to competent authorities (in relation to the question inquiring about the requirement to keep a record of training linked of handing of HMPs).

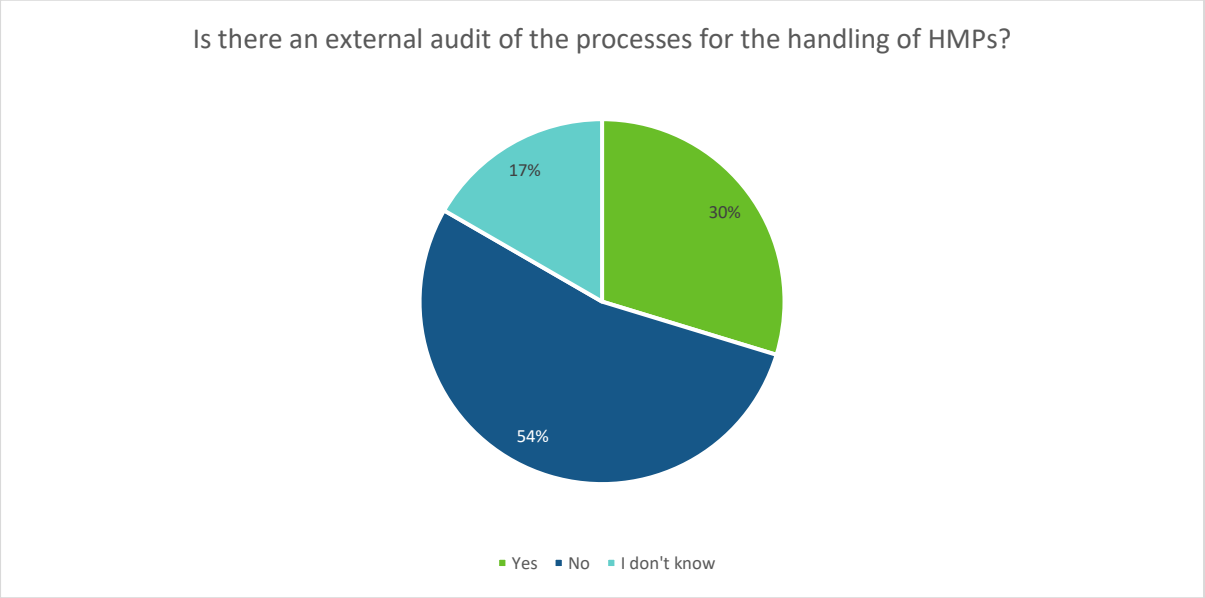

Figure 26 – *Percentage of responses by chief pharmacists (N=279) to question 35 'Is there an external audit of the processes for the handling of HMPs?'.*

19 different countries gave further information by way of comment to the question asking who conducts the audit. The audit groups included

a) National Professional Association of hospital pharmacists
b) National Peer Audit group – various
c) Medicine Agency
d) Hospital validation team – accreditation agency
e) Hospital validation team - internal
f) Department of Health
g) Department of Labour
h) Labour Related Authorities

There was almost universal (95% | N=267/281) approval for the adoption of a harmonised approach by the EU to HMPs.

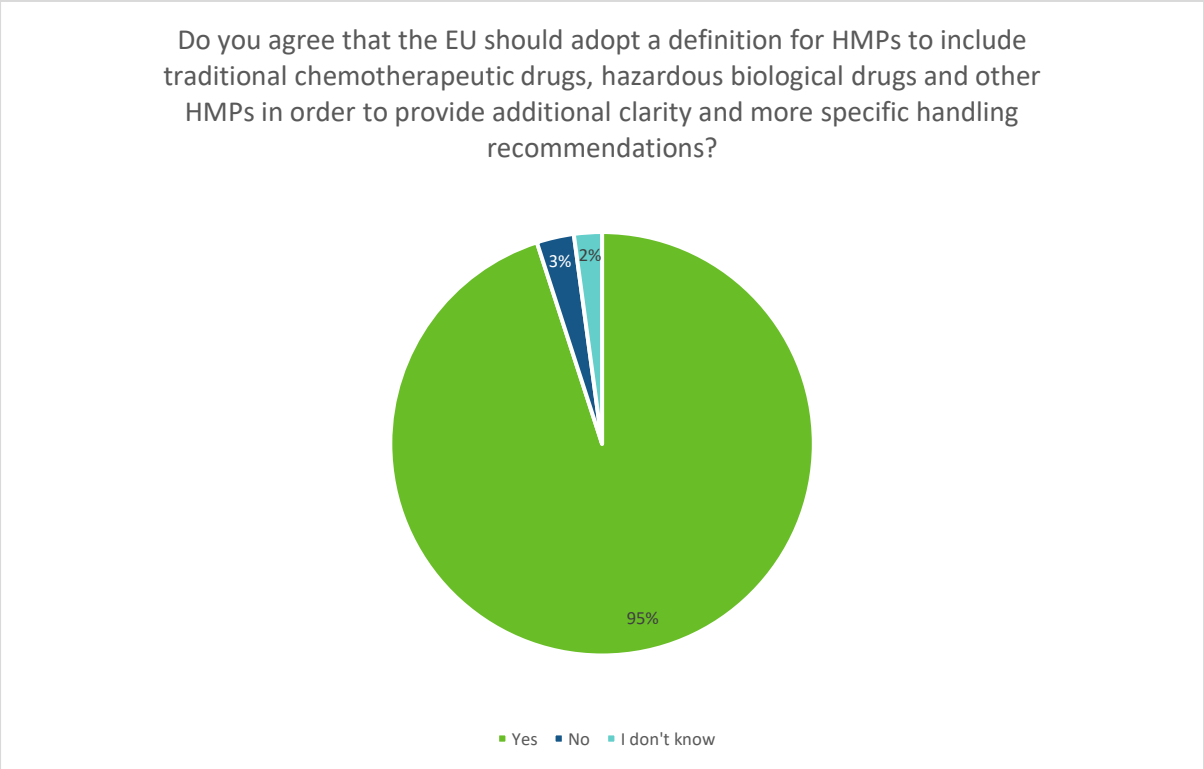

Figure 27 – *Percentage of responses by chief pharmacists (N=281) to question 29 'Do you agree that the EU should adopt a definition for HMPs to include traditional chemotherapeutic drugs, hazardous biological drugs and other HMPs in order to provide additional clarity and more specific handling recommendations?'.*

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The survey respondents indicated a high level of potential use for an EU wide classification system for HMPs.

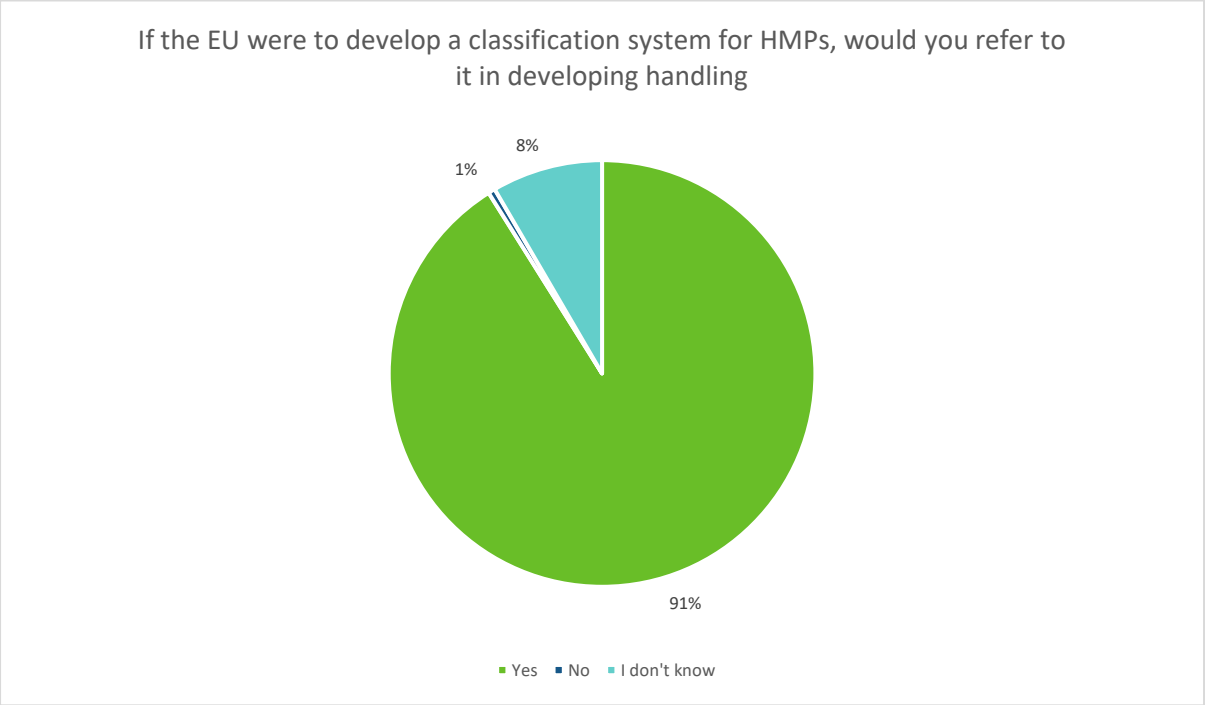

Figure 28 – *Percentage of responses by chief pharmacists to question 5 'If the EU were to develop a classification system for HMPs, would you refer to it in developing handling guidelines?'.*

Other improvements that could be adopted included additional advice from manufacturers (both in the SmPC and as educational sessions), classification system e.g. NIOSH or EU guidance on biologics as well as further guidance from EDQM. In relation to this question, it should be noted that respondents were provided with the possibility to choose between one or multiple of the five different answer options.

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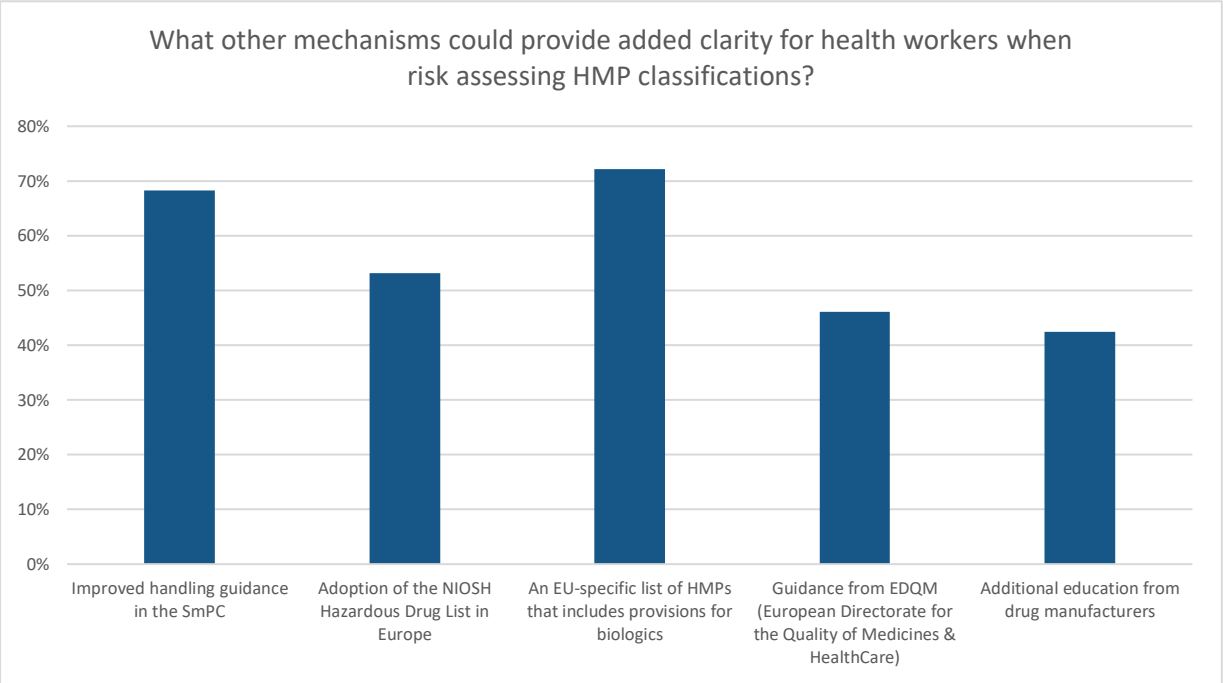

***Figure 29** – Percentage of responses by chief pharmacists to question 30 'What other mechanisms could provide added clarity for health workers when risk assessing HMP classifications?'.*

Discussion

This first survey of European hospital pharmacists views on and knowledge of hazardous medicinal products demonstrates a high awareness of and significant effort into the management of these products at the institutional level. The emphasis appears to be placed on HMPs used for the treatment of malignancy. The safety precautions for handling HMPs in the oncology and haematology setting are well identified in the literature and the survey responses, whereas a less clear understanding of the safe handling of HMPs for other conditions. The EDQM Resolution states 'that health professionals should be supported by appropriate guidance to prevent risk of healthcare damage by inappropriate reconstitution in healthcare establishments in Europe'. The resolution also supports appropriate training for healthcare workers.

The absence of a European definition for and clear guidance on the management of HMPs is noted. Hospital pharmacists would welcome further work in this area. In lieu of a European approach considerable emphasis has been placed on the NIOSH definition. Institutions using HMPs identify these HMPs internally and then consider several European documents such as Health and Safety

documents and directives[35] in conjunction with the NIOSH guidelines. The definition developed by this SIG encompasses the intrinsic hazardous nature of a substance while recognising modifications that alter the risk profile of a medicine during use. The SIG recommends that this definition should be used as a basis for a discussion with European authorities and other healthcare professionals working with HMPs for the development of a European definition.

While the NIOSH guidelines are internationally recognised by many European countries as a reference document they are not without practical problems in everyday use. These would include a significant time lag between updates, insufficient detail for multiple factors that modify exposure risk to healthcare workers and caregivers as well as a rapid response system to appropriately identify the inherent hazard level of new technologies and potential for modification. In practice it appears that hospital pharmacists recognise the different hazards relating to technologies such as monoclonal antibodies although the survey did not identify how these views affect practices. The SIG recommends further presentation of the Dutch model for consideration at a European level. This model provides practical support to users, is flexible for the introduction of new products, recognises and assesses new evidence in a timely manner, promotes standard approach to risk management of HMPs and enables efficiency in the health system by reducing duplication at the institutional level. The SIG considers that national systems should be developed with a linkage at the European level to inform shared practice and standardisation. One example of such an approach is seen in the European approach to medicine shortages[36], adaption of this model may enhance handing of HMPs across Europe.

Many of the institutions rely appropriately on the hospital pharmacist for management of HMPs. The survey findings show a significant interest in further education on the topic and a significant number advised that they had not received post graduate education on the topic. The SIG recommends that

[35] Council 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 OJ L 183/1. Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work OJ L 131/11. 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 OJ L 158/50. Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency OJ L136/1. Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products OJ L311/1. COM/2021/323 final Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions EU strategic framework on health and safety at work 2021-2027 Occupational safety and health in a changing world of work. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52021DC0323 (last visited on 2 February 2022). Framework Agreement on prevention from sharp injuries in the hospital and healthcare sector concluded by HOSPEEM and EPSU, available at: https://www.epsu.org/article/framework-agreement-prevention-sharp-injuries-hospital-and-health-care-sector (last visited on 19 January 2022).

[36] European Medicines Agency. Shortages catalogue, available at: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/availability-medicines/shortages-catalogue (last visited 18 January 2022).

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further education is required at both under graduate and post graduate level to inform this role at the institutional level and enhance the institutional responsibility to worker wellbeing. The SIG considers that further engagement with and implementation of the European standards of hospital pharmacy will enhance safety.

> The European Statements of Hospital Pharmacy; Section 3 Production and Compounding
>
> *3.5 Hazardous medicines should be prepared under appropriate conditions to minimise the risk of contaminating the product and exposing hospital personnel, patients and the environment to harm.*

The survey findings show that there is minimal oversight at the institutional level for governance of HMPs. The European Statements of Hospital Pharmacy, in particular statement 5.3, support more accountability in this area.

> The European Statements of Hospital Pharmacy; Section 5: Patient Safety and Quality Assurance
> *5.3 Hospital pharmacists should ensure their hospitals seek review of their medicines use processes by an external quality assessment accreditation programme, and act on reports to improve the quality and safety of these processes.*

The SIG recommends that consideration be given to a structured approach in Europe to the topic and recommend a closer examination and adaptation of the Dutch model to support institutional practice in other EU countries.

Conclusion and Recommendations

The SIG considers that while there is evidence of much ongoing work and activity on the topic of hazardous medicinal products (HMPs) there is an absence of a coherent approach to the management of HMPs in Europe. Much of the risk assessment activity takes place at the institutional level with guidance from the national levels but little further oversight of implementation. The exposure of healthcare workers to hazardous medicinal products is a serious issue that in the view of the European

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Association of Hospital Pharmacists (EAHP) needs to be addressed uniformly across the European Union and its Member States to ensure the protection of patients and healthcare personnel.

The complex nature of handling HMPs requires training that is tailored to the conditions of the working environment which differ depending on the settings in the hospital or community as well as from country to country.

To ensure the safety of patients and staff in the handling of HMPs hospital pharmacists contribute and promote their safe handling in institutions in Europe. To improve the current position and to support the work of hospital pharmacists proactive steps need to be taken to minimise the risks of HMPs for everyone. The SIG believes that additional guidance at the European level to promote healthcare workers wellbeing is desirable. This guidance should

- Promote the implementation of best practice;
- Recognise and support training and education of the workforce;
- Permit all available processes to reduce exposure to hazardous medicinal products in the workplace; and
- Allow for adaptability as new products or new evidence become available.

This guidance should also factor in efficiency and cost-effectiveness for the healthcare sector.

Therefore, EAHP's SIG on Hazardous Medicinal Products makes the following recommendations.

EAHP calls on the European Commission and national governments across Europe to actively engage with hospital pharmacist representatives in the review of relevant Directives for the management of hazardous medicinal products (HMPs) in the healthcare environment.

EAHP asks national governments and health system managers to immediately engage with the European Statements of Hospital Pharmacy and implement best practices relating to HMPs.

EAHP recommends an EU wide standard approach to the classification and management of HMPs.

EAHP advises the European Commission and national governments across Europe to initiate best practice sharing on the classification and handling of HMPs between its Member States.

EAHP advocates for the revision of pharmacy curricula and the expansion of training opportunities for the pharmacy workforce to account for the growing demand for management of HMPs and related Health and Safety issues.

The work of this Special Interest Group (SIG) was financially supported by Amgen.

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Appendix I – SIG membership

Name	Role	Country
Emelie Ahnfelt	Pharmacist, Uppsala University Hospital	Sweden
Aida Batista	Director of Pharmacy at Centro Hospitalar do Médio Ave, EPE (CHMA)	Portugal
Oscar Breukels	Hospital pharmacist at the Meander Medical Centre	The Netherlands
Mirjam Crul	Hospital pharmacist at the Department of Clinical Pharmacology and Pharmacy of the Amsterdam University Medical Center	The Netherlands
David Dolan	Occupational, Environmental & Quality Toxicologist at Amgen	United States
Josep Guiu	Director of Pharmacy and Medicines. Consortium of Health and Social care of Catalonia	Spain
Kathryn Jackson (from November 2021 onwards)	Director, Global Regulatory and R&D Policy Global Oncology at Amgen	United States
Brad Jordan (until summer 2021)	Director, Global Regulatory and R&D Policy Global Oncology at Amgen	United States
Ewelina Korczowska	Senior Pharmacist at Clinical Hospital of Lord's Transfiguration in Poznan	Poland
Maja Koroman	Specialist of Clinical Pharmacy- hospital pharmacy at the General Hospital Pula	Croatia
Mari Kuuttila	Hospital pharmacist at Åland's Health and Medical Care (ÅHS)	Finland
Joan Peppard	Chair of the SIG and Chief Pharmacist and Head of Department in the Midland Regional Hospital Tullamore	Ireland
Mark Santillo	Regional Quality Assurance Officer at the Torbay & South Devon NHS Foundation Trust, Torbay Hospital	United Kingdom
Falko Schüllner	Representative Director and Head of Quality Assurance at the Tirol Kliniken Hospital Pharmacy	Austria
Birgitte Simon-Hettich	Head of Early Chemical and Preclinical Safety at Merck Healthcare KGaA	Germany
Maria Jose Tames	Assistant Director at the Pharmacy Department of the Onkologikoa Foundation in San Sebastian	Spain

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Appendix II – List of relevant stakeholders

Authorities, entities and organisations at national level

Country	National competent authority in the field of labour	National competent authority in the field of health/healthcare	National body responsible for occupational health and safety	Others
Austria	Federal Ministry for Labour, Family and Youth (Bundesministerium für Arbeit, Familie und Jugend)	Federal Ministry of Social Affairs, Health, Care and Consumer Protection (Bundesministerium für Soziales, Gesundheit, Pflege und Konsumerschutz) Austrian Agency for Health and Food Safety (AGES)	Austrian Labour Inspectorate	Pharmacy Association Austria (Apothekerkammer) General Accident Insurance (AUVA Allgemeine Unfallversicherungsanstalt)
Belgium	Federal Public Service Employment, Labour and Social Dialogue (Service public fédéral Emploi, Travail et Concentration Sociale)	Ministry of Health (Ministère de la Santé)		
Bosnia and Herzegovina	Federal Ministry of Labour and Social Policy (Federalno ministarstvo radi I socijalne politike)	Federal Ministry of Health (Federalno ministarstvo zdravstva)		
Bulgaria	Ministry of Labour and Social Policy	Ministry of Health		

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Country	National competent authority in the field of labour	National competent authority in the field of health/healthcare	National body responsible for occupational health and safety	Others
Croatia	Ministry of Labour, Pension System, Family and Social Policy (Ministarstvo rada, mirovinskog sustava, obitelji i socijalne politike)	Ministry of Health (Ministarstvo zdravstva)	Institute for the Improvement of Occupational Safety (Zavod za unapređivanje zaštite na radu)	Croatian Chamber of Pharmacists (Hrvatska ljekanrička komora) Section of Oncology Pharmacy at Croatian Pharmaceutical Society (Sekcija za onkološko ljekarništvo Hrvatskog Farmaceutskog društva)
Cyprus	Department of Labour Inspection, Ministry of Labour, Welfare and Social Insurance	Ministry of Health		
Czech Republic	Ministry of Labour and Social Affairs (Ministerstvo práce a sociálních věcí)	Ministry of Health (Ministerstvo zdravotnictví)		
Denmark	Ministry of Employment (Beskæftigelsesministeriet)	Ministry of Health and the Elderly (Sundheds- og Ældreministeriet)	Danish Working Environment Authority	
Estonia	Social Ministry (Sotsiaalministeerium)	*Social Ministry also covers health*	Labour Inspectorate of Estonia (Tööinspektsioon)	
Finland	Ministry of Economic Affairs and Employment (Työ- ja elinkeinoministeriö)	Ministry of Social Affaris and Health (Sosiaali- ja terveysministeriö)	National Institute of Occupational Health (Työterveyslaitos)	

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Country	National competent authority in the field of labour	National competent authority in the field of health/healthcare	National body responsible for occupational health and safety	Others
France	Ministry of Labour (Ministère du Travail)	Ministry of Solidarity and Health (Ministère des Solidarités et de la Santé)		
Germany	Federal Ministry of Labour and Social Affairs (Bundesministerium für Arbeit und Soziales)	Federal Ministry of Health (Bundesgesundheits-ministerium)	Federal Institute for Occupational Safety and Health (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin)	German Society for Oncological Pharmacy (Deutsche Gesellschaft für onkologische Pharmazie (DGOP)) Association of Cytostatic Drug Producing Pharmacists (Verband der Zytostatika herstellenden Apothekerinnen und Apotheker (VZA))
Greece	Ministry of Labour and Social Affairs	Ministry of Health		
Hungary	Ministry for Innovation and Technology (Innovációs és Technológiai Minisztérium)	Ministry of Human Resources (Emberi Erőforrások Minisztériuma)		
Iceland	Ministry of Social Affairs	Ministry of Health		
Ireland	Department of Jobs, Enterprise, and Innovation	Department of Health	Health and Safety Authority	
Italy	Ministry of Labour and Social Policies (Ministero del Lavoro e delle Politiche Sociali)	Ministry of Health (Ministero della Salute)	Italian Agency for Vocational Education and Training, Employment and Social Policies	
Latvia	Ministry of Welfare (Labklājības Ministrija)	Ministry of Health (Veselības ministrija)	State Labour Inspection (Valsts darba inspekcija)	

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Country	National competent authority in the field of labour	National competent authority in the field of health/healthcare	National body responsible for occupational health and safety	Others
Lithuania	Ministry of Social Security and Labour (Socialinės Apsaugos ir Darbo Ministerija)	Ministry of Health (Sveikatos Apsaugos Ministerija)		
Luxembourg	Ministry of Labour, Employment and the Social and Solidarity Economy (Ministère du Travail, de l'Emploi et de l'Économie sociale and solidaire)	Ministry of Health (Ministère de la Santé)	Inspection of Labour and Mines (Inspection du Travail et des Mines)	
Malta	Ministry of Finances and Employment	Ministry of Health	Occupational Health and Safety Authority	
Montenegro	Ministry of Labour and Social Welfare (Ministarstvo rada I socijalnog staranja)	Ministry of Health (Ministarstvo zdravlja)		
Netherlands	Ministry of Social Affairs and Employment (Ministerie van Sociale Zaken en Werkgelegenheid)	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport)		
North Macedonia	Ministry of Labour and Social Policy	Ministry of Health		
Norway	Ministry of Labour and Social Affairs (Arbeids- og sosialdepartementet)	Ministry of Health and Care Services (Helse- og omsorgsministeren)	Labour Inspection Authority (Arbeidstilsynet)	

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Country	National competent authority in the field of labour	National competent authority in the field of health/healthcare	National body responsible for occupational health and safety	Others
Poland	Ministry of Labour and Social Policy (Ministerstwo Pracy i Polityki Społecznej)	Ministry of Health (Ministerstwo Zdrowia)	Central Institute for Labour Protection - National Research Institute (Centralny Instytut Ochrony Pracy - Panstwowy Instytut Badawczy)	
Portugal	Ministry of Labour, Solidarity and Social Security (Ministério do Trabalho, Solidariedade e Segurança Social)	Ministry of Health (Ministério da Saúde)	Authority for Working Conditions (Autoridade para as Condições do Trabalho)	
Romania	Ministry of Social Welfare and Protection (Ministerul Muncii și Protecției Sociale)	Ministry of Health (Ministerului Sănătății)		
Serbia	Ministry of Labour, Employment, Veteran and Social Policy (Ministarstvo rada, zapošljavanja, boračke i socijalne politike)	Ministry of Health (Ministarstvo zdravlja)		
Slovakia	Ministry of Education, Social Affairs and Family (Ministerstvo práce, sociálnych vecí a rodiny)	Ministry of Health (Ministerstvo zdravotníctva)	National Labour Inspectorate (Národný inšpektorát práce)	
Slovenia	Ministry of Labour, Family, Social Affairs and Equal Opportunities (Ministrstvo za delo, družino, socialne zadeve in enake možnosti)	Ministry of Health (Ministrstvo za zdravje)		

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Country	National competent authority in the field of labour	National competent authority in the field of health/healthcare	National body responsible for occupational health and safety	Others
Spain	Ministry of Labour, Migrations and Social Security (Ministerio de Trabajo y Economía Social)	Ministry of Health (Ministerio de Sanidad)	National Institute for Safety, Health and Wellbeing at Work (Instituto Nacional de Seguridad, Salud y Bienestar en el Trabajo)	
Sweden	Ministry of Labour (Arbetsmarknadsdepartemente t)	Ministry of Health and Social Affairs (Socialdepartementet)	Work Environment Authority (Arbetsmiljöverket)	
Switzerland		Federal Office of Public Health		
Turkey	Ministry of Family, Labour and Social Services (Aile, Çalışma ve Sosyal Hizmetler Bakanlığı)	Ministry of Health (Sağlık Bakanlığı)		
United Kingdom	Department for Work and Pensions	Department of Health and Social Care		

European stakeholders

Type of organisation/entity	Name of the organisation/entity
European institution	Council of the European Union
European institution	European Agency for Safety and Health at Work (EU OSHA)
European institution	European Commission - DG Employment, Social Affairs and Inclusion (EMPL), Unit B.3
European institution	European Parliament - Committee on Employment and Social Affairs (EMPL)
European institution	European Parliament - Committee on the Environment and Public Health (ENVI)

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European institution	European Parliament - Committee on Legal Affairs (JURI)
	Business Europe
	European Biosafety Network
Healthcare professional organisation	European Oncology Nursing Society
	European Public Service Union
Healthcare professional organisation	European Society of Oncology Pharmacy
	European Trade Union Confederation

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Appendix III – Questions included in the Survey on Hazardous Medicinal Products for Individual Chief Pharmacists

Hospital pharmacists and members of the multidisciplinary team – such as nurses, pharmacy technicians and others – are dealing with hazardous medicinal products in their daily work. Their safe handling is of uttermost importance for the safety of healthcare workers and patients treated with these medicines. Their classification plays an essential role in determining suitable handling procedures. However, unlike the United States, Europe does not have one single body similar to the National Institute for Occupational Safety and Health (NIOSH) that addresses all questions linked to the classification of hazardous medicinal products.

To better understand the classification landscape for hazardous medicinal products in Europe, the European Association of Hospital Pharmacists (EAHP) has established a Special Interest Group (SIG) on Hazardous Medicinal Products which is seeking further input for their work by means of this survey.

We thank all chief pharmacists for participating in the EAHP Survey on Hazardous Medicinal Products.

It takes approximately 20 to 25 minutes to complete the survey.
This survey will be closed on the 10th of October 2021.

In the absence of a European definition of the term 'hazardous medicinal product', EAHP's SIG reserves the right to propose a definition arising from the work of the group.

The definition of the term 'hazardous medicinal product (HMP)' used throughout this survey is a modification of the definition used by NIOSH chosen because of its familiarity:

Drugs are classified as hazardous when they possess any one of the following five characteristics regardless of the proposed formulation and recommended route of administration

- *Genotoxicity, or the ability to cause a change or mutation in genetic material; a mutagen.*
- *Carcinogenicity, or the ability to cause cancer in humans, animal models, or both; a carcinogen.*
- *Teratogenicity, or developmental toxicity, the ability to interfere with normal development, either before or after birth.*
- *Fertility impairment.*
- *Serious organ toxicity at low doses in humans or animal models.*

Note: This also covers medicines that should not be crushed but are crushed by a healthcare worker in a home setting.

Section 1 – Introduction/General questions

1. I work in …

- ○ Albania
- ○ Andorra
- ○ Armenia
- ○ Austria
- ○ Azerbaijan
- ○ Belgium
- ○ Bosnia and Herzegovina
- ○ Bulgaria
- ○ Croatia
- ○ Cyprus
- ○ Czech Republic
- ○ Denmark
- ○ Estonia
- ○ Finland
- ○ France
- ○ Georgia
- ○ Germany
- ○ Greece
- ○ Hungary
- ○ Iceland
- ○ Ireland
- ○ Italy
- ○ Latvia
- ○ Lichtenstein
- ○ Lithuania
- ○ Luxembourg
- ○ Malta
- ○ Monaco
- ○ Montenegro
- ○ Netherlands
- ○ North Macedonia
- ○ Norway
- ○ Poland
- ○ Portugal
- ○ Romania
- ○ Russia
- ○ Serbia
- ○ Slovakia
- ○ Slovenia
- ○ Spain
- ○ Sweden
- ○ Switzerland
- ○ Turkey
- ○ Ukraine
- ○ United Kingdom
- ○ Other (please specify)

2. My institution is a ….

- ○ General hospital
- ○ Teaching/university hospital
- ○ Psychiatric hospital
- ○ Paediatric hospital
- ○ Geriatric hospital
- ○ Oncology hospital
- ○ Orthopaedic/traumatology hospital
- ○ Other (please specify)

3. How many beds are served by your institution?

- ○ Fewer than 100 beds
- ○ 101 to 500 beds
- ○ 501 to 1000 beds
- ○ More than 1000 beds

Section 2 – Classification and Standards

4. There are recognised standards for the handling of hazardous medicinal products (HMPs) in…

	Country level	Regional level	Institution/local level	There are no standards	I don't know
Pharmacy	☐	☐	☐	☐	☐
Specialised wards/units	☐	☐	☐	☐	☐
Home care, including nursing homes	☐	☐	☐	☐	☐
Other departments in	☐	☐	☐	☐	☐

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the institution (e.g. transport, waste management, etc.)					

Please specify the types of 'other departments in the institution':

5. If the EU were to develop a classification system for HMPs, would you refer to it in developing handling guidelines?
   - Yes
   - No
   - I don't know.

6. Has your institution evaluated HMPs and is there a list of them?
   - Yes, in electronic format (Please share the link).
   - Yes, in paper format.
   - No.
   - I don't know.

Please share the link:

7. Was the HMP list developed internally or by an external agency or entity?
   - Internally
   - External
   - I don't know.

8. Please identify the external agency or entity that developed the HMP list.
   - National Institute for Occupational Safety and Health (NIOSH Hazardous Drug List)
   - National agency/entity.
   - I don't know.
   - Other (please specify)

9. Are HMPs identified throughout the whole chain of usage? Please tick all areas where HMPs are identified:
   - ☐ Receipt
   - ☐ Unpacking
   - ☐ Repackaging
   - ☐ Storage
   - ☐ Transportation
   - ☐ Preparation
   - ☐ Administration
   - ☐ Cleaning
   - ☐ Clinical/non-clinical waste management
   - ☐ Maintenance
   - ☐ HMPs are not identified.

10. How are staff made aware of HMPs?
   - Via a list.

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- Via a symbol (e.g. the yellow hand).
- Other, please specify.

11. Which staff members receive training in handling HMPs in your institution appropriate to their role?
- ☐ Pharmacists
- ☐ Pharmacy technicians
- ☐ Doctors
- ☐ Nurses
- ☐ Residents/students
- ☐ Healthcare assistants/nurse assistants
- ☐ Cleaners
- ☐ Transport/Logistics/ Waste management employees
- ☐ Nobody receives training

12. Does your institution differentiate biological (e.g., monoclonal antibodies)/ targeted small molecule oncology drugs (e.g., kinase inhibitors, proteasome inhibitors) from traditional chemotherapeutic drugs (e.g., alkylating agents, antimicrotubule agents) in the risk management procedures?
- Yes
- No
- I don't know

Section 3 – Implementation/guidelines on handling

13. Does the institution have a written protocol for handling HMPs in all the stages of the handling process?
- Yes, for all stages.
- Yes, for some stages.
- No
- I don't know.

14. Which staff members can access the HMP handling protocol relevant for their role?
- ☐ Pharmacists
- ☐ Pharmacy technicians
- ☐ Doctors
- ☐ Nurses
- ☐ Residents/students
- ☐ Healthcare assistants/nurse assistants
- ☐ Cleaners
- ☐ Transport/Logistics/ Waste management employees

15. What is used most frequently in the pharmacy for the reconstitution and preparation of HMPs?
- Needle
- Spike
- CSTD (closed system transfer device)

16. Thinking of the daily practices in your own institution, which, when used in accordance with handling protocols, do you consider an effective way to protect workers from potential exposure to HMPs?
- ☐ Needle
- ☐ Spike
- ☐ CSTD (closed system transfer device)
- ☐ BSC (biological safety cabinet)
- ☐ Isolator

17. Where do you prepare HMPs in the pharmacy?
- BSC (biological safety cabinet)
- Isolator
- A combination of the above.
- We don't prepare them in the pharmacy.
- There are no specific preparation measures in place.

18. What type of isolator/biological safety cabinet do you use?
- ☐ Positive pressure isolator.
- ☐ Negative pressure isolator.
- ☐ Controlled pressure room conditions for biological safety cabinet.
- ☐ I don't know.

19. Do you have an environmental monitoring program in your hospital to measure surface contamination for traditional chemotherapeutic drugs?
- Yes, it is done on a regular basis.
- Yes, but we don't use it regularly.
- Yes, it was used as a part of a study.
- Yes, because it is legally mandatory.
- No, it has not been used.
- Not applicable as we don't have traditional chemotherapeutic drugs in the hospital.

20. Please define what regularly/on a regular basis means. Please tick the nearest box.
- Weekly.
- Monthly.
- Every 6 months
- Yearly.

21. What is the scope of the environmental monitoring program?
- It only applies in the pharmacy for the handling of traditional chemotherapeutic drugs.
- It only applies on the oncology ward.
- It applies in all possible areas where traditional chemotherapeutic drugs are used.
- I don't know.

22. Which department is responsible for the quality improvement programme arising from the environmental monitoring program?
- ☐ Pharmacy department
- ☐ Quality department
- ☐ Occupational health department
- ☐ Hospital management
- ☐ Other (please specify)

23. In your professional opinion, are there differences in the occupational hazards of biological (e.g., monoclonal antibodies)/targeted small molecule oncology drugs (e.g., kinase inhibitors, proteasome inhibitors) versus traditional chemotherapeutic drugs (e.g., alkylating agents, antimicrotubule agents)?
- Yes
- No
- I don't know.

24. Do you have a standardised spill kit available for the safe removal of spills with HMPs?
- Yes, in the pharmacy
- Yes, on the wards

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- Yes, both in the pharmacy and on the wards
- Yes, in transit external to the institution
- No

25. For patients with problems in swallowing or being tube fed, do you have a policy in place for the management of HMPs?

- Yes
- No
- I do not know.

26. If your institution uses electronic patient records are HMPs identified therein?

- Yes
- No
- I don't know.
- Not applicable.

Section 4 – Awareness

27. Do you use in your hospital a special warning label for HMPs?

- Yes, we use the "Yellow Hand" label
- Yes, we use a warning label, other than the "Yellow Hand"
- No, we don't use any special warning label
- Not applicable

28. Please rank the statements below (5 = completely agree | 4 = agree| 3 = neither agree nor disagree | 2 = disagree | 1 = completely disagree)

	1	2	3	4	5
I know where to find information about the handling of HMPs	☐	☐	☐	☐	☐
I know who is responsible for the risk assessment of handling HMPs	☐	☐	☐	☐	☐
I know what type of protection to use when handling HMPs	☐	☐	☐	☐	☐
I have access to proper protection when handling HMPs	☐	☐	☐	☐	☐
I know how to safely dispose of HMPs	☐	☐	☐	☐	☐
I am offered regular education on how to handle HMPs	☐	☐	☐	☐	☐
I know where to access education on HMPs	☐	☐	☐	☐	☐
I provide education to other healthcare practitioners on HMPs	☐	☐	☐	☐	☐
My staff are informed/have received training in all of the above	☐	☐	☐	☐	☐

29. Do you agree that the EU should adopt a definition for HMPs to include traditional chemotherapeutic drugs, hazardous biological drugs and other HMPs in order to provide additional clarity and more specific handling recommendations?

- Yes
- No
- I don't know.

30. What other mechanisms could provide added clarity for health workers when risk assessing HMP classifications?

- ☐ Improved handling guidance in the SmPC
- ☐ Adoption of the NIOSH Hazardous Drug List in Europe
- ☐ An EU-specific list of HMPs that includes provisions for biologics

- ☐ Guidance from EDQM (European Directorate for the Quality of Medicines & HealthCare)
- ☐ Additional education from drug manufacturers

31. Do you consider that there is a need for further post-graduate education on HMPs, for example on the difference between hazardous biological drugs, traditional chemotherapy drugs and other HMPs?
- ○ Yes
- ○ No
- ○ I don't know.

Section 5 – Monitoring/supervision by healthcare institutions

32. Is there a requirement to keep a record of training linked to the handling of HMPs?
- ☐ Yes, it needs to be included in the personal record
- ☐ Yes, this is required by the institution.
- ☐ Yes, this is required by the national competent authority.
- ☐ No.
- ☐ I don't know.

33. Is there a requirement for staff to undergo a medical assessment (e.g. blood test) for duties involving HMPs?
- ☐ Yes, on recruitment
- ☐ Yes, in regular intervals during their employment
- ☐ No
- ☐ I don't know

34. If surface contamination is monitored, is there a requirement to report it?
- ○ No.
- ○ I don't know.
- ○ Not applicable.
- ○ Yes, to the quality officer at the institution.
- ○ Yes, to the national competent authority.
- ○ Yes (please specify to whom)

35. Is there an external audit of the processes for the handling of HMPs?
- ○ Yes
- ○ No
- ○ I don't know.

36. Who conducts the audit?

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SIG - FINAL REPORT

Special Interest Group on Hazardous Medicinal Products

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