The Importance of a Whole Lifecycle and Multidisciplinary Approach in Managing Hazardous Medicinal Products (HMPs)

Louise Church
Head of Health, Safety and Wellbeing, Royal College of Nursing

Louisa Knowles
Advanced Pharmacist for Technical Services, University Hospitals Birmingham NHS Foundation Trust

Royal College of Nursing

BOPA
British Oncology Pharmacy Association

What do we mean by the term ‘Hazardous Medicinal Products’ (HMPs)

Pharmaceutical substances used for:

- the treatment of cancer – cytotoxic/ cytostatic, antineoplastic drugs, and some immunotherapies

- non-cancer use for treating multiple sclerosis, HIV, psoriasis, rheumatoid arthritis, organ transplant. Includes biologic infusions, antivirals, vaccines and immunosuppressants and more.

- extends to other therapeutic groups and some antibiotics





Definition

No current UK accepted definition for ‘hazardous medicinal products’

European Union definition:

‘Hazardous medicinal products (HMPs) medicines containing substances that meet the classification criteria as:

- carcinogenic (category 1A or 1B),
- mutagenic (category 1A or 1B), or
- toxic for reproduction (category 1A or 1B)



Category 1A: known to have potential for humans, based on human evidence.

Category 1B: presumed to have potential for humans, based on animal evidence

Risks to Healthcare Staff from HMPs

HMPs cause effects in people other than the person being treated if unintentionally exposed to the substance

A European Commission study stated there are almost **1.8 million workers exposed** to relevant HMPs in the EU (European Commission, 2021).

When taking into account all those potentially exposed in the healthcare sector, that **number may be as high as 12.7 million exposed workers** in the EU, of which **7.3 million are nurses** (ETUI, 2022).



Requirement to ‘prevent worker exposure’

The Control of Substances Hazardous to Health Regulations do not apply to hazardous drugs

MYTH

The Summary of Product Characteristics is the main document that should be used when assessing the risks of hazardous drugs to workers

MYTH

If there is no evidence of harm or ill health to workers – there is no need to review the controls for the safe handling of hazardous drugs

MYTH

There are no UK based cytotoxic residue monitoring companies

MYTH

UK legislation and guidance

The Control of Substances Hazardous to Health Regs 2002 (COSHH)/

The Control of Substances Hazardous to Health Regulations (Northern Ireland) (COSHH) 2003

All hazardous substances (Reg 7(3))	Carcinogens and mutagens (Reg 7(5))
PREVENT EXPOSURE	
Designing & use of work processes and engineering controls	**Totally enclose the process, unless this is not reasonably practicable**
Control of exposure at source, including adequate ventilation	Prohibit eating, drinking and smoking
Provision of suitable personal protective equipment	Clean floors, walls and other surfaces regularly
	Warning signs
Regulation 10 – Monitoring Exposure at the Workplace	Storing, handling and disposing safely

What is ‘reasonably practicable’?

A H&S legal term requiring employers to balance the severity of a risk against the time, cost, and effort required to control it.

RISK v COST, TIME, EFFORT



It necessitates taking steps to minimise risks, but not at a cost that is "grossly disproportionate" to the safety benefit.

Key Aspects of ‘Reasonably Practicable’

Objective test: The judgment is based on *what a reasonable person would do*, not necessarily just what the employer can afford.

High risk vs. Low risk: greater risks warrant higher expenditure and effort to control.

HMP Pathway


PHARMACY / MANUFACTURING
Activities within pharmacy or medicines manufacturing facility
1 Procurement
2 Receipt
3 Storage
4 Preparation / Reconstitution
5 Dispensing / Release from pharmacy
6 Transport
POTENTIAL OCCUPATIONAL EXPOSURE AT ANY STAGE
Appropriate risk assessment and control measures should be applied throughout the medicines lifecycle.
11 Transport
10 Disposal
9 Waste & Excreta
8 Administration / Self Administration
7 Receipt and Storage
CYTOTOXIC WASTE
CYTOTOXIC WASTE
CLINICAL AREA / PATIENT CARE
Activities within clinical area, hospital ward, community or patient's home

Contamination on Vials

JOURNAL ARTICLE

Surface contamination of chemotherapy drug vials and evaluation of new vial-cleaning techniques: Results of three studies

Get access

Thomas H. Connor, Paul J. M. Sessink, Bruce R. Harrison, Jack R. Pretty, Byron G. Peters, Raul M. Alfaro, Appie Bilos, Gwendolyn Beckmann, Michael R. Bing, Lakisha M. Anderson, Robert DeChristoforo

American Journal of Health-System Pharmacy, Volume 62, Issue 5, 1 March 2005, Pages 475–484, https://doi.org/10.1093/ajhp/62.5.475

JOURNAL ARTICLE

Cyclophosphamide Contamination Observed on the External Surfaces of Drug Vials and the Efficacy of Cleaning on Vial Contamination

Get access

Karine Touzin, Jean-François Bussières, Éric Langlois, Michel Lefebvre, Claude Gallant

The Annals of Occupational Hygiene, Volume 52, Issue 8, November 2008, Pages 765–771, https://doi.org/10.1093/annhyg/men050

Published: 28 July 2008 **Article history**

Restricted access | Research article | First published online August 25, 2019 | Re-use permissions

External contamination of antineoplastic drug containers from a Canadian wholesaler

D Hilliquin and JF Bussières View all authors and affiliations

Volume 26, Issue 2 | https://doi.org/10.1177/1078155219868525



Contamination Generated During Preparation



Detection of contamination with antineoplastic agents in a hospital pharmacy department

Articles | Published: February 1992

Volume 14, pages 16–22 (1992) Cite this article

Save article

Paul J. M. Sessink, Rob B. Anzion, Petra H. H. Van den Broek & Rob P. Bos

Occupational exposure to antineoplastic drugs in four Italian health care settings

Cristina Sottani [a], Benedetta Porro [a], Marcello Imbriani [b c], Claudio Minoia [a]

Show more

Add to Mendeley Share Cite

https://doi.org/10.1016/j.toxlet.2011.03.028 Get rights and content View accessibility information

JOURNAL ARTICLE

Environmental Contamination with Cytotoxic Drugs in Healthcare Using Positive Air Pressure Isolators

Get access

S. CRAUSTE-MANCIET, P. J. M. SESSINK, S. FERRARI, J.-Y. JOMIER, D. BROSSARD

The Annals of Occupational Hygiene, Volume 49, Issue 7, October 2005, Pages 619–628, https://doi.org/10.1093/annhyg/mei045

Hosp Pharm. 2013 Mar 12;48(3):204–212. doi: 10.1310/hpj4803-204

Canadian monitoring program of the surface contamination with 11 antineoplastic drugs in 124 centers

Emma Pinet, Ciprian Mihai Cirtiu, [...], and Cynthia Tanguay +2 View all authors and affiliations

Volume 30, Issue 1 | https://doi.org/10.1177/10781552231167329

Reduction in Surface Contamination With Cyclophosphamide in 30 US Hospital Pharmacies Following Implementation of a Closed-System Drug Transfer Device

Paul JM Sessink *, Jason Trahan †, Joseph W Coyne ‡

Contamination on Ready to Administer Products

British Oncology Pharmacy Association

Open access | Research article | First published online December 13, 2024 | Re-use permissions

Workflow evaluation of environmental contamination with hazardous drugs during compounding and administration in an UK hospital

Paul JM Sessink, Beverley Barry, [...], and Karen Campbell +3 View all authors and affiliations

Volume 32, Issue 1 | https://doi.org/10.1177/10781552241285138 | View article versions

Restricted access | Research article | First published online May 15, 2024 | Re-use permissions

Assessment of the surface contamination of the primary packaging of oral antineoplastic drugs and secondary packaging of chemotherapy preparations at a Swiss hospital

Nathalie Nguyen, Virginie Vallet, [...], and Sandrine Fleury-Souverain +4 View all authors and affiliations

Volume 31, Issue 4 | https://doi.org/10.1177/10781552241250010 | View article versions

Int J Environ Res Public Health. 2023 Mar 11;20(6):4952. doi: 10.3390/ijerph20064952

Occupational Exposure to Antineoplastic Drugs in Twelve French Health Care Setting: Biological Monitoring and Surface Contamination

Sophie Ndaw [1,*], Aurélie Remy [1]



Contamination Generated during Administration (Connection / Disconnection)



Open access | Research article | First published online April 23, 2025 | Re-use permissions

Evaluation of the effect of closed system transfer device syringe adaptor connection in the isolator on cytotoxic residue contamination during intravenous administration

Louisa Knowles View all authors and affiliations

Volume 32, Issue 7 | https://doi.org/10.1177/10781552251334027 | View article versions

OPEN ACCESS | Professional | 28 May 2020

Use of a closed-system drug transfer device reduces contamination with doxorubicin during bolus injection

Authors: Tom Marler-Hausen, Chris Holt, Christine Headley, and Paul Sessink | AUTHORS INFO & AFFILIATIONS

Publication: British Journal of Nursing • Volume 29, Number 10 • https://doi.org/10.12968/bjon.2020.29.10.S15

2,535 / 14 PDF/EPUB

Oncol Nurs Forum. 2020 May 1;47(3):263-272. doi: 10.1188/20.ONF.263-272.

Surface Contamination With Antineoplastic Drugs on Two Inpatient Oncology Units

AnnMarie Lee Walton [1], Margaret A Bush [2], Christian Elizabeth Douglas [3], Deborah H Allen [4], Martha Polovich [5], Ivan Spasojevic [2]

Restricted access | Research article | First published online January 6, 2014 | Re-use permissions

Impact and appreciation of two methods aiming at reducing hazardous drug environmental contamination: The centralization of the priming of IV tubing in the pharmacy and use of a closed-system transfer device

Annie Guillemette, Hélène Langlois, [...], and Jean-François Bussières +5 View all authors and affiliations

Volume 20, Issue 6 | https://doi.org/10.1177/1078155213517127

CSTDs for Administration

- **Publication in 2020 – based at UCLH**
  - CSTD syringe adaptors were added by nurses immediately before administration
  - Reduction in contamination during administration
  - Contamination on nurses' gloves still seen



OPEN ACCESS | BY-NC | Professional | 28 May 2020

Use of a closed-system drug transfer device reduces contamination with doxorubicin during bolus injection

Authors: Tom Marler-Hausen, Chris Holt, Christine Headley, and Paul Sessink | AUTHORS INFO & AFFILIATIONS

Publication: British Journal of Nursing • Volume 29, Number 10 • https://doi.org/10.12968/bjon.2020.29.10.S15

2,535 / 14

PDF/EPUB

- **Publication in 2025 – based at UHB**
  - CSTD syringe adaptors were added in the pharmacy aseptic unit
  - Reduction in contamination:
    - During administration
    - On the surface of syringes
    - On the nurses' gloves



Open access | Research article | First published online April 23, 2025 | Re-use permissions

Evaluation of the effect of closed system transfer device syringe adaptor connection in the isolator on cytotoxic residue contamination during intravenous administration

Louisa Knowles View all authors and affiliations

Volume 32, Issue 7 | https://doi.org/10.1177/10781552251334027 | View article versions

Future Research

- **CSTDs added in pharmacy aseptic units for other routes of administration**
  - IV infusion bags
  - SC injections
  - Elastomeric devices
  - Intrathecal injections
  - Ophthalmic injections

- **Methods to reduce contamination on the prepared products**
  - Wiping down the product with an appropriate agent following preparation
  - The full use of CSTDs during preparation
  - Any other ideas?

Occupational Exposure to Personnel



Toxicology Letters
Volume 213, Issue 1, 13 August 2012, Pages 107-115

Occupational exposure to antineoplastic drugs in four Italian health care settings

Cristina Sottani [a], Benedetta Porro [a], Marcello Imbriani [b c], Claudio Minoia [a]

Assessment of primary, oxidative and excision repaired DNA damage in hospital personnel handling antineoplastic drugs

Get access

Milena Villarini, Luca Dominici, Renza Piccinini, Cristina Fatigoni, Maura Ambrogi, Gianluca Curti, Piero Morucci, Giacomo Muzi, Silvano Monarca, Massimo Moretti

Mutagenesis, Volume 26, Issue 3, May 2011, Pages 359–369,
https://doi.org/10.1093/mutage/geq102
Published: 26 November 2010 **Article history**

Int J Environ Res Public Health. 2023 Mar 11;20(6):4952. doi: 10.3390/ijerph20064952

Occupational Exposure to Antineoplastic Drugs in Twelve French Health Care Setting: Biological Monitoring and Surface Contamination

Sophie Ndaw [1,*], Aurélie Remy [1]

Editor: Paul B Tchounwou [1]

Micronuclei and chromosome aberrations in subjects occupationally exposed to antineoplastic drugs: a multicentric approach.

Moretti M [1], Grollino MG, Pavanello S, Bonfiglioli R, Villarini M, Appolloni M, Carrieri M, Sabatini L, Dominici L, Stronati L, Mastrangelo G, Barbieri A, Fatigoni C, Bartolucci GB, Ceretti E, Mussi F, Monarca S

Author information

International Archives of Occupational and Environmental Health. 02 Nov 2014, 88(6):683-695
https://doi.org/10.1007/s00420-014-0993-y PMID: 25362515

Environmental Contamination with Cytotoxic Drugs in Healthcare Using Positive Air Pressure Isolators

Get access

S. CRAUSTE-MANCIET, P. J. M. SESSINK, S. FERRARI, J.-Y. JOMIER, D. BROSSARD

The Annals of Occupational Hygiene, Volume 49, Issue 7, October 2005, Pages 619–628,
https://doi.org/10.1093/annhyg/mei045
Published: 26 August 2005 **Article history**

Toxicology Letters
Volume 316, November 2019, Pages 20-26

Antineoplastic drug occupational exposure: a new integrated approach to evaluate exposure and early genotoxic and cytotoxic effects by no-invasive Buccal Micronucleus Cytome Assay biomarker

C.L. Ursini [a], E. Omodeo Salè [b], A.M. Fresegna [a], A. Ciervo [a], C. Jemos [b], R. Maiello [a], G. Buresti [a], C. Colosio [c], F.M. Rubino [c], Stefan Mandić-Rajčević [c], P. Chiarella [a], D. Carbonari [a], P. Delrio [d], P. Maiolino [d], P. Marchetti [a], R. Boccia [a], S. Iavicoli [a], D. Cavallo [a]



Maximising the potential of the cancer Pharmacy team to optimise the care of people living with cancer

Pharmacy Aseptic Unit Guidance on PPE



7.7 Gowning

The operator is an essential part of the aseptic preparation process in hospitals. To minimise the risk of contaminating products with microorganisms and particles originating from the operators, it is essential to wear clean room clothing the quality of which should be appropriate for the process and the EU GMP grade of the working area (EC 2015).

GRADE OF ENVIRONMENT	MINIMUM CLOTHING REQUIREMENTS
D	■ Hair, and where relevant, facial hair, beards and moustaches including stubble should be completely covered, for example with a beard snood ■ A non-shedding protective coat or suit ■ Dedicated shoes or overshoes.
C	■ Hair, and where relevant, facial hair, beards and moustaches including stubble should be completely covered, for example with a beard snood ■ A single- or two-piece trouser suit (which sheds virtually no fibres or particulate matter), gathered at the wrists and with a high neck ■ Dedicated shoes or overshoes.
B	■ Headgear should totally enclose hair, and where relevant, facial hair; beards and moustaches including stubble; it should be tucked into the neck of the suit ■ A sterile face mask ■ Non-powdered sterile gloves ■ A single piece clean room coverall, gathered at the wrists and with a high neck ■ Trouser legs should be tucked inside the footwear and garment sleeves into the gloves ■ Dedicated footwear, e.g. clean room slippers ■ All clothing should shed virtually no fibres or particulate matter and should be sterilised*.

GUIDELINES

The Rules Governing Medicinal Products in the European Union
Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use

7.13 A description of typical clothing required for each cleanliness grade is given below:

i. Grade B (including access / interventions into grade A): appropriate garments that are dedicated for use under a sterilised suit should be worn before gowning (see paragraph 7.14). Appropriately sterilised, non-powdered, rubber or plastic gloves should be worn while donning the sterilised garments. Sterile headgear should enclose all hair (including facial hair) and where separate from the rest of the gown, it should be tucked into the neck of the sterile suit. A sterile facemask and sterile eye coverings (e.g. goggles) should be worn to cover and enclose all facial skin and prevent the shedding of droplets and particles. Appropriate sterilised footwear (e.g. over-boots) should be worn. Trouser legs should be tucked inside the footwear. Garment sleeves should be tucked into a second pair of sterile gloves worn over the pair worn while donning the gown. The protective clothing should minimize shedding of fibres or particles and retain particles shed by the body. The particle shedding and the particle retention efficiencies of the garments should be assessed during the garment qualification. Garments should be packed and folded in such a way as to allow operators to don the gown without contacting the outer surface of the garment and to prevent the garment from touching the floor.

ii. Grade C: Hair, beards and moustaches should be covered. A single or two-piece trouser suit gathered at the wrists and with high neck and appropriately disinfected shoes or overshoes should be worn. They should minimize the shedding of fibres and particles.

iii. Grade D: Hair, beards and moustaches should be covered. A general protective suit and appropriately disinfected shoes or overshoes should be worn. Appropriate measures should be taken to avoid any ingress of contaminants from outside the clean area.

iv. Additional gowning including gloves and facemask may be required in grade C and D areas when performing activities considered to be a contamination risk as defined by the CCS.

PPE in Pharmacy Aseptic Units

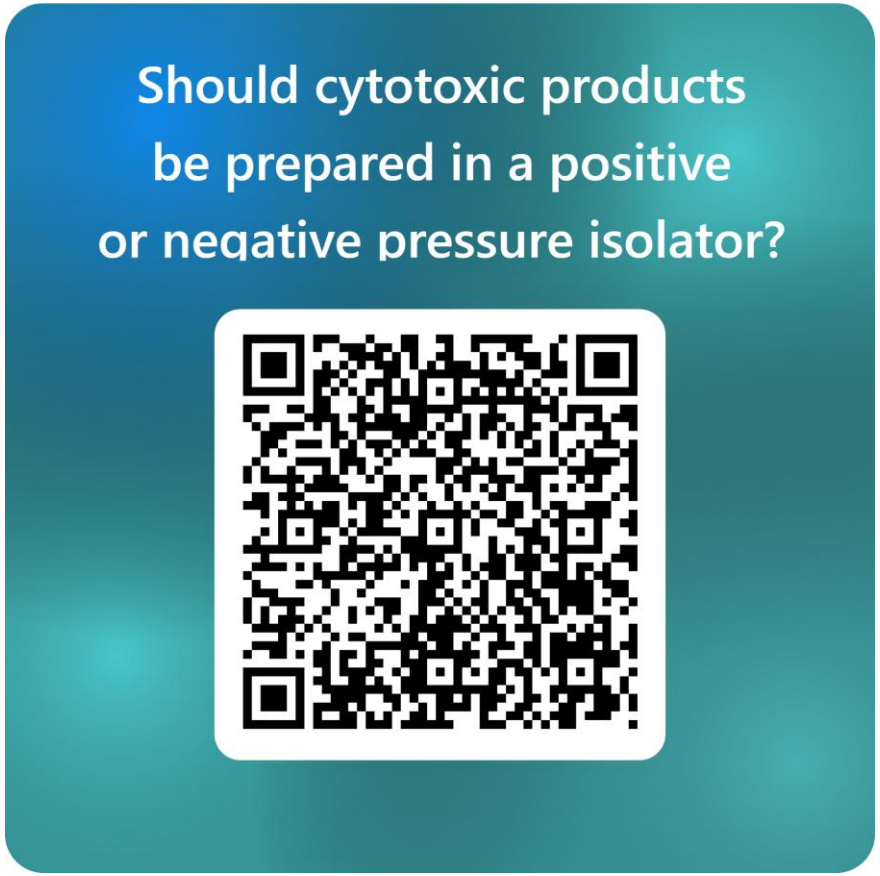


7.7 Gowning

The operator is an essential part of the aseptic preparation process in hospitals. To minimise the risk of contaminating products with microorganisms and particles originating from the operators, it is essential to wear clean room clothing the quality of which should be appropriate for the process and the EU GMP grade of the working area (EC 2015).

Designed to protect the product

Opinion on Isolators…



GUIDELINES

The Rules Governing Medicinal Products in the European Union
Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use

c. Negative pressure isolators should only be used when containment of the product is considered essential (e.g. radiopharmaceutical products) and specialized risk control measures should be applied to ensure the critical zone is not compromised.

Opinion on Isolators…

Safe Management of Hazardous Medicinal Products in UK Healthcare Settings

A UK Multidisciplinary Consensus Document

The document proposes five strategic recommendations:

1. Establish a UK Framework for Hazardous Medicinal Products (HMPs)
2. Prioritise Safer Product Design
3. Develop National PPE Standards
4. Improve Access to Occupational Health and Safety Risk Information
5. Improve Consistent Implementation Through Education and Collaboration

Thank you for listening

Any questions?



