Italian perspectives on the safe handling of hazardous drugs and closed systems

Safety measures, research and technological innovation for handling hazardous drugs: guarantee of protection with the evolving standard

Ledda A, Castellano P, Lombardi R, et al. *INAIL* 2023.

Directive 2004/37/EC[1] on the protection of workers from risks deriving from occupational exposure to carcinogens or mutagens was updated in March 2022

Directive 2022/431/EU[2]

- Specifically lists hazardous drugs (HDs) as a risk to workers
- Emphasises the obligation to protect workers from toxic substances affecting reproduction (so-called reprotoxic substances)
- Instructs employers to evaluate the risk of, and implement measures to prevent, exposure to HDs
- In the EU, a list similar to the existing list of HDs compiled by National Institute for Occupational Safety and Health (NIOSH), adapted to the realities of the Member States will also be compiled
- Mandates Member States to implement the necessary legislative, regulatory, and administrative provisions to comply with the directive's guidelines by April 5th, 2024
- Risk assessment is paramount to all the measures that should be taken

Italian reference legislation

- Italian reference legislation has already addressed the risk arising from the manipulation of hazardous medicinal products (HMPs) in several documents prior to the publication of Directive 2022/431/EU2
- Legislative Decree 81/20083 and subsequent amendments (Title IX "Hazardous Substances"), national decrees and technical guidance documents related to anticancer drugs outline prevention and protection measures that employers must implement to protect the health of workers
- Environments for the preparation of HMPs
  - Centralise preparation areas within hospital pharmacy, with access through a filter zone, effective air exchanges, and outgoing air treated with filter systems
- Collective protection measures
  - Hoods/biosafety cabinets
  - Isolators
  - Robotic systems
  - Closed-system drug-transfer devices (CSTDs)
  - Disposal containers
- Individual protection devices
  - Personal protective equipment (PPE)

Closed System Drug Transfer Devices (CSTDs)

CSTDs were highlighted as a useful tool to reduce worker exposure

- A CSTD limits microbial and chemical contamination, as it mechanically prevents exchanges between the external and internal environment of the system itself and vice versa
- CSTDs should be used when handling hazardous drugs

Performance evaluation for CSTDs

- To assess the effectiveness and efficiency of barrier-type CSTDs to contain vapor, NIOSH has established a testing protocol (NIOSH Docket Number 288, CDC - 2015-0075) that has to be considered the reference standard for their evaluation[4,5]
- According to NIOSH testing protocol / standard, systems that use filters are not considered "barrier systems" and cannot be considered "closed systems"
- To ensure that contaminants are prevented from entering and escaping the CSTD, available studies should be considered, and the entire system in all of its components have to be carefully analysed
- It is the responsibility of the hospital pharmacy and hospital managers to identify devices that guarantee the best protection for employees

Regulatory references

1 Directive 2004/37/EC. Available at: https://bit.ly/3N7ykHJ [Accessed Jan 2024]
2 Directive 2022/431/EU. Available at: https://bit.ly/3TaWZ27 [Accessed Jan 2024]
3 Legislative Decree no. 81 of April 9, 2008, as amended. Available at: https://bit.ly/47SvrCO [Accessed Jan 2024]
4 NIOSH Docket Number 288, CDC-2015-0075. Available at: https://bit.ly/3ShsZkr [Accessed Jan 2024]
5. TAR Region Sicily reg. prov. coll. n. 00136/2022, 04/04/2023

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Safe Handling of Hazardous Drugs

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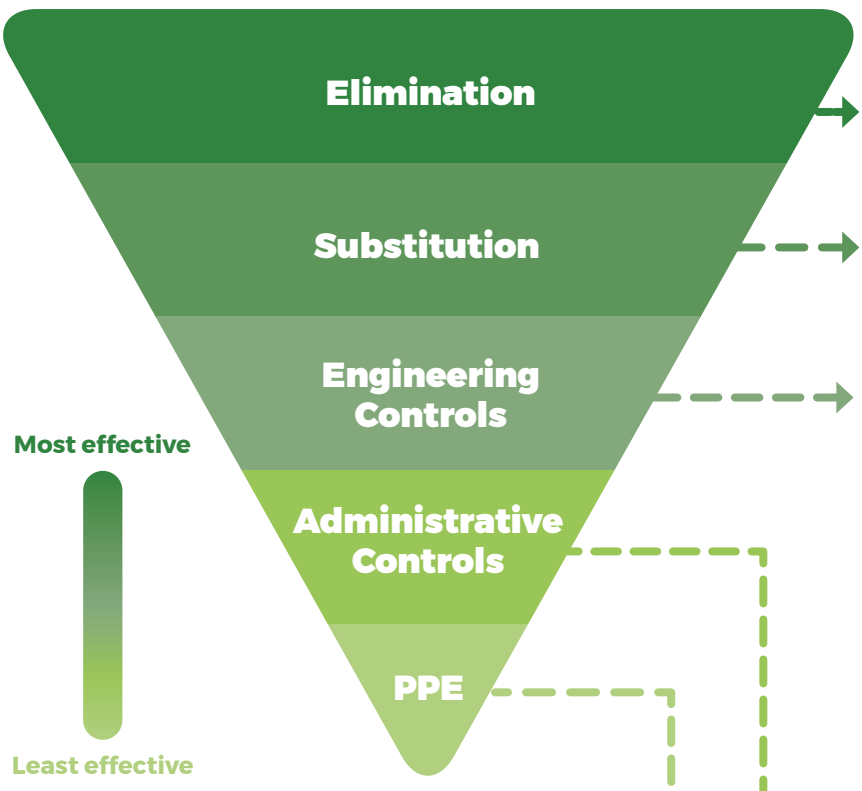

Image adapted from CDC Centers for Disease Control and Prevention[2]

Physically remove the hazard

Replace the hazard

Isolate people from the hazard

Environment
- Preparation areas centralised within the hospital pharmacy, where possible
- Access through a filter zone
- Effective air exchanges must occur and outgoing air should be treated with filter systems

Hoods/biosafety cabinets[1]
- Should be used for CMDs
- Require both regular and extraordinary maintenance, especially when replacing filters
- Hoods with pre-treatment systems for filters placed under the work surface are available to prevent contamination (EN 14175-3)

Robotic systems
- Can be employed to assist healthcare workers with intensive workloads during drug preparation activities
- Open systems are often used for dilution and transfer during preparation
- Even with recent technological advancements these systems still involve interaction with the operator and the external environment

Isolators
- Should be certified as compliant with the technical standard ISO EN 14644-7:2004, ensuring the correct functionality of the "closed system"

CSTDs
- Should be barrier-type, and their efficacy evaluated according to NIOSH Docket Number 288, CDC-2015-0075

PPE - protect the worker

Gloves
- Classified as Category III PPE or protection class 5 for intensive preparation
- 0.65 AQL for chemical permeability

Protective clothing
- Classified as Category III PPE with CE marking
- Sterile suits in clean rooms with hoods or robotic systems

Respiratory protection devices
- Half-mask with P3 dust filter
- FFP3 half-mask with appropriate performance characteristics

Goggles
- Must have CE marking as PPE and provide protection against drops and splashes of liquid
- A personal device for each user is required if devices are not single use and must be cleaned and disinfected

Administrative controls - change the way people work

- The EU must produce a list of HDs

Emergency spill procedures must be in place
- Emergency kits must be available and include PPEs

Disposal containers
- Must have an irreversible final closure
- Should be resistant to vertical fall impacts, spill damage or spillage losses

Abbreviations
PPE personal protective equipment
AQL acceptable quality rating
CMDs carcinogenic and mutagenic chemicals
HDs hazardous drugs
CE Conformité Européenne
CSTDs closed-system drug-transfer devices
FFP3 filtering facepiece protection level 3

Regulatory references

- Directive 2004/37/EC. Available at: https://bit.ly/3N7ykHJ [Accessed Jan 2024].
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1 ISPESL - National Institute for Prevention and Safety at Work. 2010. [Guidance for the protection of healthcare workers from the risk of exposure to antineoplastic drugs]. Available at: https://bit.ly/3vwa6kB [Accessed Jan 2024].
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