European Biosafety Network

Presentation by Ian Lindsley, Secretary of the European Biosafety Network, on the prevention of occupational exposure to hazardous drugs, including cytotoxic substances
ETUI, Brussels, 4 December 2018



About the EBN

European Biosafety Network

- Established in 2009 by the founding partners, the Spanish General Council of Nursing and the British public services union UNISON.

UNISON
the public service union

Spanish General Council of Nursing

- The Network is an inclusive organisation made up of national and European professional institutions, representative associations, unions and other interested parties committed to biological and occupational safety in healthcare throughout the European Union.

The European Biosafety Network - Activity

European Biosafety Network

Engaging with and bringing together:

- Healthcare and non-healthcare workers and their representatives at the European and national level, healthcare management, leading academics and experts, national governments and coalitions of stakeholders, the European Commission, the European Parliament, Social Partners, the European Agency for Safety and Health at Work, government agencies and other important stakeholders.

- Raising awareness, providing information, guidance on implementation, risk assessment and prevention, education and training, reporting and monitoring and public policy work.

The 2nd European Biosafety Summit
1 June 2011, Dublin

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Women, work and cancer

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- 12.7 million health workers in Europe, including 7.3 million nurses.
- Women doctors made up 49% of the healthcare workforce in 2016 and the percentage is increasing, up from 29% in 1990, with women making up 46.1% of the total workforce.
- Nursing and caring professionals are made up of 90% women and 10% men across Europe.
- Number of elderly persons (aged 65 or over) in the EU is forecast to increase by 57 % between 2015 and 2080 and the share of the elderly in the total population is projected to increase from 18.9 % in 2015 to 29.1 % by 2080.
- An aging population and falling birth rate means not only greater pressure on the healthcare system but also an increase in the number of people contracting cancer and leaving employment in healthcare.
- Growing concerns about a shortage of healthcare professionals in the EU.

Background on Hazardous Drugs

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- The European Commission said that in 2012 up to 106,500 cancer deaths were attributed to occupational exposure to carcinogenic substances, making cancer the first cause of work-related deaths in the EU.

- Every year more than 12.7 million health workers, mostly women, in Europe are potentially exposed to carcinogenic, mutagenic and reprotoxic hazardous drugs, including cytotoxic or antineoplastic drugs.

- The health hazard for handling these drugs is well documented, a major concern as they are not only classified as carcinogenic, but also mutagenic (mutating genetic material) and reprotoxic (interfering with reproduction).

- Cytotoxic drugs used to treat cancer in patients are generally nonselective and are therefore likely to damage normal cells too for patients and exposed workers.

- The EBN is arguing for protection for all workers and patients from occupational exposure to hazardous drugs but most of the research and data relates specifically to healthcare workers, who are mostly women.

Background on Hazardous Drugs

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- Studies show that nurses exposed to cytotoxic drugs are twice as likely to miscarry and that hospital workers who handle cytotoxic drugs are three times more likely to develop malignancy.

- Increased genetic damage has been demonstrated in nurses, particularly in day hospital nurses, the group handling the highest amount of drugs during the administration process.

- As cancer often takes decades to emerge, a case of leukaemia diagnosed in a nurse or in a pharmacist today might be the product of workplace exposures in the 1970s or the 1980s.

- Threshold levels of exposure cannot be predicted and therefore contact with genotoxic (gene destroying) carcinogens should be avoided at all levels.

Risk of occupational exposure to Hazardous Drugs

From the NIOSH Alert 2004-165 - www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf

"Several reports have addressed the relationship of cancer occurrence to health care workers' exposures to antineoplastic drugs. A significantly increased risk of leukemia has been reported among oncology nurses identified in the Danish cancer registry for the period 1943−1987 [Skov et al. 1992]. The same group [Skov et al. 1990] found an increased, but not significant, risk of leukemia in physicians employed for at least 6 months in a department where patients were treated with antineoplastic drugs."

Skov T, Maarup B, Olsen J, Rørth M, Winthereik H, Lynge E [1992]. Leukaemia and reproductive outcome among nurses handling antineoplastic drugs. Br J Ind Med 49: 855–861.
Skov T, Lynge E, Maarup B, Olsen J, Rørth M, Winthereik H [1990]. Risk for physicians handling antineoplastic drugs [letter to the editor]. The Lancet 336:1446

Risk of occupational exposure to Hazardous Drugs

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A Dutch study (Fransman 2014) that shows a model of an increase of 154 deaths from leukemia per million nurses working with the cytotoxic drug cyclophosphamide.

Another study, Ratner 2010 shows increased incidence of breast cancer (RR = 1.83; 95% CI = 1.03 - 3.23, 12 cases) and rectal cancer (RR = 1.87, 95% CI = 1.07 - 3.29, 14 cases) in nurses working in a cancer centre.

Fransman W, Kager H, Meijster T, Heederik D, Kromhout H, Portengen L and Blaauboer BJ. Leukemia from dermal exposure to cyclophosphamide among nurses in the Netherlands: quantitative assessment of the risk. Ann Occup Hyg. 2014; 58:271-282.
Ratner PA, Spinelli JJ, Beking K, Lorenzi M, Chow Y, Teschke K, Le ND, Gallagher RP, Dimich-Ward H. Cancer incidence and adverse pregnancy outcome in registered nurses potentially exposed to antineoplastic drugs. BMC Nurs. 2010; 9:15.

Observatory on Hazardous Drugs

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- The EBN has developed a European Observatory on occupational exposure in the preparation, administration and disposal of hazardous drugs in healthcare.

- The Observatory study conducted from September 2018 by Ipsos MORI into the current state of the protocol and procedure surrounding hazardous drugs, including cytotoxic drugs, in European Oncology.

- The final report will cover 14 EU countries drawn from across the EU – Spain, Portugal, France, Italy, Denmark, Latvia, Estonia, Netherlands, UK, Belgium, Ireland, Poland, Germany, Sweden.

- So far, the interim data is drawn from a partial sample with the responses of 147 heads of hospital pharmacies and 142 oncology outpatient unit supervisors/managers.

- **Preliminary findings for preparation in pharmacies include:**

- Most pharmacists had a list of hazardous drugs but information was not updated or used to prevent exposure.
- Most countries had cleaning protocols in place but were not often used for the decontamination of biological safety cabinets (BSCs) and aseptic isolators (AIs).
- In 9% of pharmacies sterile rooms were not equipped with either BSCs or AIs.
- Regular training and medical testing did not exist for most workers exposed to hazardous drugs.
- Only 79% of IV hazardous drugs are prepared in pharmacies thus putting oncology nurses and other workers on wards at huge risk.
- The level of regular monitoring in pharmacy offices is very low (55%).
- Regular monitoring of surface contamination is low outside pharmacies and wards, eg ventilation of storage areas (e.g. Spain 38%, France 65%), which suggests that minor breakages, spills etc. may cause sustained airborne contamination.

- **Preliminary findings for administration on oncology wards include:**

- 39% of spiking was reported to take place in administration areas, a risky procedure which drives spills and leakage that increase the risk of exposure for nurses and technicians, patients and accompanying carers/family members.
- The most basic forms of PPE are not used, and where used often the more minimal forms of protection, e.g. single instead of double gloves.
- Regular monitoring in the wards is low (55%) and the frequency of monitoring when it is taking place is also often low .
- Administration systems are outdated and unsafe, particularly the practice of “un-spiking” bags, putting the safety of both workers and patients at risk.
- Standard cleaning procedures in oncology wards are not enough to remove medication contamination.
- There is a lack of regular training and medical testing for workers exposed to hazardous drugs in both pharmacies and on oncology wards.

Madrid Regional Law

- Earlier this year the Madrid regional government passed a law to protect the health and safety of healthcare workers, which states that the handling of hazardous drugs is important in the prevention of occupational hazards.

- The most relevant group of hazardous drugs consists of antineoplastic drugs, but other drugs have been included that are widely used in the health sector.

- The Ministry of Health will standardise the use of hazardous drugs and minimise the occurrence of exposure through the establishment of guidelines and a unified record and monitoring system for exposure, as well as requiring PPE and closed system transfer devices to be used in the preparation and administration of hazardous drugs.

Hazardous drugs are classified in the regional law according to the following groups:

Group 1: Antineoplastic medicines.
Group 2: Non-antineoplastic medicines that comply with at least one of the following criteria: carcinogenicity, teratogenicity or another toxicity for development, reproductive toxicity, toxicity in organs at low doses, genotoxicity or new medicines with structure and toxicity profiles similar to existing medicines that are determined to be hazardous according to the criteria above.
Group 3: Medicines that pose a risk to the reproductive process and that can affect men and women who are actively trying to conceive and women who are pregnant or currently breastfeeding.

Carcinogens and Mutagens Directive
Directive 2004/37/EC

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- The Carcinogens and Mutagens Directive of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens or mutagens at work has been subject to two revisions and a third batch of amendments will be concluded probably early next year.

- **Provisions of the CMD include:**

- The employer shall assess and manage the risk of exposure to carcinogens or mutagens
- Workers' exposure must be prevented.
- The employer shall reduce the use of carcinogens or mutagens by replacing them with a substance that is not dangerous or less dangerous.
- If replacement is not possible, the employer shall use a closed technological system.

- **Further provisions:**

- Where a closed system is not technically possible, the employer shall reduce exposure to the minimum.
- The employer shall also provide appropriate training on potential risks to health, precautions to prevent exposure, hygiene requirements, protective equipment, clothing and incidents handlings.
- The Member States shall establish arrangements for health surveillance of workers if there is a risk to their health and safety.

ANNEX I: List of substances, mixtures and processes
ANNEX II: Practical recommendations for the health surveillance of workers
ANNEX III: Limit values and other directly related provisions (in 2017 binding limit values and skin notations were reviewed/set for new agents)

Carcinogens and Mutagens Directive 2

- **A compromise amendment to the Carcinogens and Mutagens Directive (CMD) during the second batch of amendments was passed unanimously by the European Parliament Employment Committee on 27 March 2018:**

- *(3a) This new revision of the Directive 2004/37/EC, establishing limit values and skin notations with regard to XXX additional carcinogens, is a new step in a longer process to update that Directive. Directive 2004/37/EC should be reviewed on an ongoing basis and revised when necessary in the light of available information, including scientific and technical data progressively acquired, including residual risk data, after consulting the SCOEL and the ACSH for the purpose of achieving better workers' protection. Further revisions to that Directive should address the issue of workers exposed to carcinogenic or mutagenic substances resulting from the preparation, administration or disposal of hazardous drugs, including cytotoxic drugs, and work involving exposure to carcinogenic or mutagenic substances in cleaning, transport, laundry and waste disposal of hazardous drugs of materials contaminated by hazardous drugs and in personal care for patients under treatment of hazardous drugs.*

Carcinogens and Mutagens Directive 2

- **The compromise amendment to the Carcinogens and Mutagens Directive (CMD) was provisionally amended further during the trialogue process of the European Council, Parliament and Commission as follows:**

(3b new) Amendments to Annex I and Annex III to Directive 2004/37/EC provided for in this Directive are a further step in a longer term process to update it. As the next step in that process, the Commission has submitted a proposal for the establishment of limit values and skin notations with regard to five additional carcinogens. Moreover, the Commission stated in its Communication of 10 January 2017, 'Safer and Healthier Work for All — Modernisation of the EU Occupational Safety and Health Legislation and Policy', that there should be further amendments to Directive 2004/37/EC. The Commission should, on an ongoing basis, continue its work on updates of Annex I and Annex III to Directive 2004/37/EC, in line with Article 16 thereof and established practice, and amend ~~it~~ them when necessary in the light of available information, including progressively acquired scientific and technical data such as residual risk data. That work should result, where appropriate, in proposals for future revisions of the limit values set out in Directive 2004/37/EC and in this Directive, as well as proposals for additional substances, mixtures and processes in Annex I and additional limit values in Annex III.

Carcinogens and Mutagens Directive 2

- **The compromise amendment to the Carcinogens and Mutagens Directive (CMD) was amended further during the trialogue process of the European Council, Parliament and Commission as follows:**

(3c new recital) It is important to protect workers exposed to carcinogenic or mutagenic substances resulting from the preparation, administration or disposal of hazardous drugs, including cytostatic/cytotoxic drugs, and work involving exposure to carcinogenic or mutagenic substances in cleaning, transport, laundry and waste disposal of hazardous drugs of materials contaminated by hazardous drugs and in personal care for patients under treatment of hazardous drugs. As a first step, the Commission has issued guidance to reduce occupational health and safety risks in the healthcare sector, including on the risk related to the exposure to cytostatic/cytotoxic drugs, in a dedicated guide to prevention and good practice. This guidance is without prejudice to possible further legislative or other initiatives.

Carcinogens and Mutagens Directive 3

- **Compromise amendments to the Carcinogens and Mutagens Directive (CMD) were passed by the Employment Committee of the European Parliament on 20 November as follows:**

- (3a) In pharmacology, hazardous drugs are drugs that are known to cause harm, because of their genotoxicity, carcinogenicity, teratogenicity, reprotoxicity and other forms of toxicity at low doses1a. Those drugs include cytotoxic agents, which inhibit or prevent the rapid growth and division of cancer cells, and are primarily used to treat cancer, frequently as part of a chemotherapy regime. However, the cytotoxic drugs available for current use are generally non-selective and are therefore likely to damage normal (non-tumour) cells too. Thus, many cytotoxic drugs are known to be genotoxic, carcinogenetic or mutagenic.
- _____
- 1a IARC monographs on the evaluation of carcinogenic risks to humans, volumes 1-121 http://monographs.iarc.fr/ENG/Classification/index.php.

Carcinogens and Mutagens Directive 3

- (3b) It is therefore important to protect workers exposed to carcinogenic or mutagenic substances resulting from the preparation, administration or disposal of hazardous drugs, including cytotoxic drugs, and work involving exposure to carcinogenic or mutagenic substances in the context of providing services relating to cleaning, transport, laundry, waste disposal of hazardous drugs or of materials contaminated by hazardous drugs, and personal care for patients treated with hazardous drugs. As a first step, the Commission has issued dedicated guidance to reduce occupational health and safety risks in the healthcare sector, including on the risks related to exposure to cytotoxic drugs, in a dedicated guide to prevention and good practices.

- (3c) As a second step, the Commission should, taking into account the latest developments in scientific knowledge, assess the possibility of extending the scope of Directive 2004/73/EC to include hazardous drugs, including cytotoxic drugs, which are carcinogenic or mutagenic, or to propose a more appropriate legal instrument, in order to ensure the occupational safety of workers handling those drugs. Accordingly, the Commission should present, if appropriate, and after consulting the social partners, an appropriate legislative proposal. In doing so, it is imperative, however, that, in accordance with Article 168(1) TFEU, access to the best available treatments for patients should not be questioned or jeopardised.

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Article 18b

- By the fourth quarter of 2019, the Commission shall, on the basis of scientific data and appropriate consultation, assess the possibility to amending the scope of this Directive to include a list of hazardous drugs, including cytotoxic drugs, which are carcinogenic or mutagenic, or to propose a more appropriate legal instrument in order to ensure occupational safety of workers handling such drugs. On that basis, the Commission shall present, if appropriate, and after consulting management and labour, a legislative proposal.

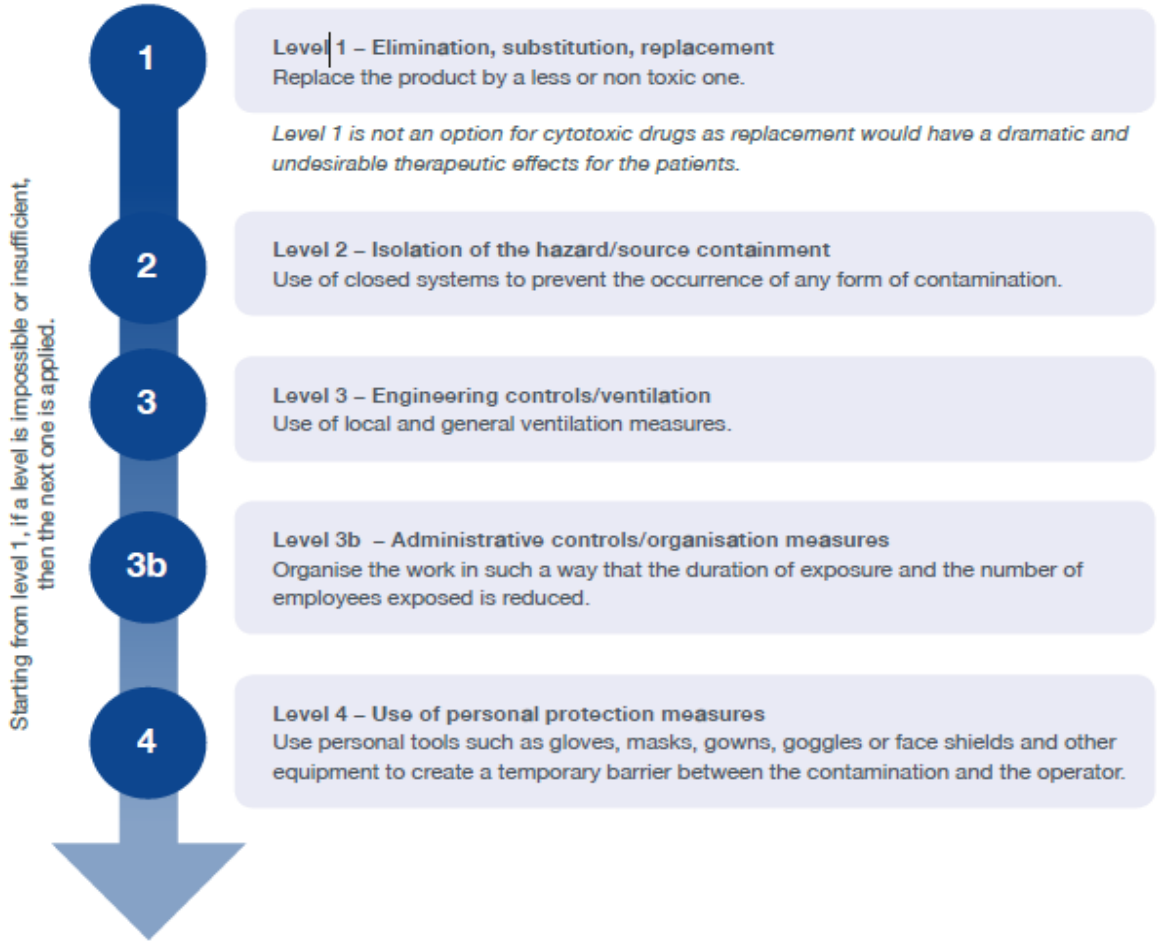
ISOPP guidance

The International Society of Oncology Pharmacy Practitioners (ISOPP) has produced the best and most detailed guidance under the title *'ISOPP Standards of Practice Safe Handling of Cytotoxics*, covering all possible items related to the safe handling of hazardous cytotoxic drugs which are used to treat cancer.

www.oncosystems.com.tr/dosyalar/_ISOPP_Standards_of_Practice_-_Safe_Handling_of_Cytotoxics.pdf

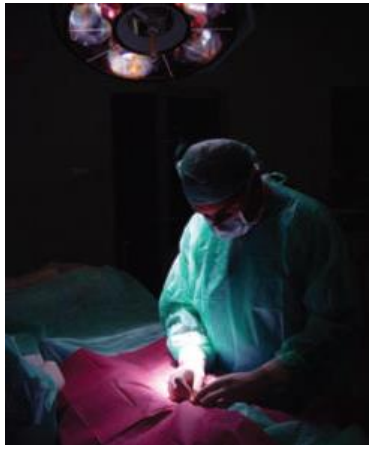
The ISOPP guidance is due to updated and recommends that actions are taken in a hierarchical order of prevention, similar to the controls in the CMD (*Directive 2004/37/EC) on the protection of workers from the risks related to exposure to carcinogens or mutagens at work*.

ISOPP hierarchy of prevention



In Europe, levels 3 and 4 predominantly apply, with some hospitals applying level 2.

Occupational health and safety risks in the healthcare sector



European Commission

Directorate-General for Employment, Social Affairs and Inclusion

Unit B.3

Manuscript completed in December 2010

European Commission guidance

- The European Commission existing guidance includes a relatively small section on cytostatic/cytotoxic drugs.

- It identifies that the greatest exposure to cytotoxic drugs occurs when they are delivered, during the preparation of infusions, in-house transport, the application/administration of cytotoxic drugs on the wards, when handling patients and during cleaning activities.

- Protective measures include:
  - centralisation and separation of the cytotoxic drug preparation and the application/administration work areas and easy to clean surface areas;
  - use of Personal Protective Equipment, waste/disposal and cleaning;
  - pressure relief systems and transfer systems help to prevent the release of cytostatic drugs in the individual work steps of the preparation process;
  - use of closed infusion and instillation systems with safe connection and transfer units in the application/administration of cytotoxic drugs.

Guidance and legislation

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- The EBN supports the application and implementation of the existing guidance but it dates from 2010, is not particularly detailed and needs to be updated to take account of new information, new technology and best practice.

- The Commission has said it will consider revising the section of the guidance on cytotoxic/cytostatic hazardous drugs.

- Guidance must also be underpinned by legislation and further amendments to the CMD passed by Parliament in the third batch which will now proceed to the trialogue process and a final Council decision by mid February 2019.

- The Commission will undertake a study in 2019 and bring back a proposal to include a list of hazardous drugs in the CMD by end of 2019.

- It can be difficult to transpose existing European legislation into national action, guidance and legislation but does not mean that we do not need to update European legislation and guidance.

Further EBN asks

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- Revised guidance on hazardous drugs by the Commission should include detailed, suitable and updated information on the risks, personal protective equipment (PPE), as well as suitable decontamination, cleaning and disinfection guidelines based on surface contamination levels and type of drugs and regular monitoring of surface contamination needs to be mandatory.

- Engineering controls, PPE, closed system transfer devices and information and training of workers exposed to contamination from hazardous drugs should be mandatory.

- On 13 December the main political parties in Spain will meet with unions colleagues and other stakeholders to commit to a national law on preventing occupational exposure to hazardous drugs.

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www.europeanbiosafetynetwork.eu