AMENDMENTS TO THE CARCINOGENS AND MUTAGENS DIRECTIVE ON HAZARDOUS DRUGS AND IMPLICATIONS FOR CHANGE TO THE HEALTHCARE SYSTEM IN EUROPE TO ENSURE COMPLIANCE WITH ITS REQUIREMENTS
The European Parliament unanimously approved amendments to Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work on 19 February 2019 and these changes, requiring the Commission to consult and do the necessary scientific work to justify the inclusion of hazardous drugs, are expected to be formally approved by the European Council in March.

The amendments to the CMD in this third batch confirm that hazardous drugs, including cytotoxic drugs that are primarily used for cancer treatment, could have genotoxic, carcinogenic or mutagenic properties and it is therefore important to protect workers exposed to such drugs resulting from the preparation, administration or disposal of hazardous drugs, including cytotoxic drugs, or from work involving services related to cleaning, transport, laundry or waste disposal of (materials contaminated by) hazardous drugs, or personal care for patients treated with hazardous drugs. The amendments further confirm that the Commission shall, taking into account the latest developments in scientific knowledge and after appropriate consultation, assess whether to amend the Directive to include a list of hazardous drugs, including cytotoxic drugs, no later than the end of the second quarter of 2020.

The European Biosafety Network (EBN) is confident that the scientific evidence and consultation with employers, workers and healthcare professionals over the course of the next year will justify and confirm the European Commission’s anticipated action to include a list of hazardous drugs when it publishes its report and legislative proposal for the fourth batch of amendments to the CMD in 2020. The EBN expects that a limited number of individual hazardous drugs, including cytotoxic drugs, will be put forward by the Commission and the Parliament for inclusion in the CMD.

Thus, the Member States and healthcare system in Europe need to be prepared to transpose and meet the new requirements of the CMD in relation to how they manage these hazardous drugs now and in the future.

Amendments to the Carcinogens and Mutagens Directive (CMD)
Requirements of the Carcinogens and Mutagens Directive and implementation to prevent exposure to hazardous drugs, including cytotoxic drugs, in European healthcare

**Article 3** Risk Assessment

The employer shall assess and manage the risk of exposure to carcinogens or mutagens. This process shall be renewed regularly and data shall be supplied to the authorities upon request. The type of exposure and degree and duration of the exposure to hazardous drugs shall be determined in order to assess the risk. Exposure to hazardous drugs takes place through inhalation, skin contact, ingestion, or injection so biological and surface monitoring protocols must be in place to assess the level of risk.

**Article 4** Reduction and replacement

The employer shall reduce the use of carcinogens or mutagens by replacing them with a substance that is not dangerous or less dangerous. In the case of occupational exposure to hazardous drugs, including cytotoxic drugs used to treat cancer in patients, replacement is not normally an option.

1.-CSTD: The National Institute for Occupational safety and Health from USA (NIOSH) defines a CSTD as a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system. The International Society of Pharmacy Practitioners (ISOPP) summarizes this definition as a system that is essentially leakproof and airtight.
Exposure shall not exceed the limit value of a carcinogen, as set out in Annex III of the Directive, but threshold levels of exposure to hazardous drugs cannot be predicted and it is therefore difficult to establish limit values. Therefore, contact with genotoxic carcinogens should be avoided at all levels, in accordance with the “As Low As Reasonably Achievable” (ALARA) principle, and also that is why hazardous drugs should be included as a work category in Annex I of the CMD not Annex III.

Most of the studies performed on surface monitoring of hazardous drugs in Europe (eg, in Germany and Spain) suggest 0.1 ng/cm² as the threshold level. In one Dutch study, urine samples from healthcare professionals who worked in facilities with contamination levels < 0.1 ng/cm² were negative for one of the most widely used and carcinogenic hazardous drugs cyclophosphamide.

Wherever a carcinogen or mutagen is used, the employer shall:
• Limit the quantities of these carcinogens or mutagens at the place of work.
• Keep the number of workers exposed as low as possible.
• Design the work processes so as to minimise the substance release.
• Evacuate carcinogens or mutagens at source, also respecting the environment.
• Use appropriate measurement procedures (especially for early detection of abnormal exposures in the event of unforeseeable events or accidents).
• Apply suitable working procedures and methods.
• Use individual protection measures if collective protection measures are not enough.
• Provide the necessary hygiene measures in particular regular cleaning of floors, walls and other surfaces. In the context of hazardous drugs, this means that regular monitoring of surface contamination should be universal, more frequent and more comprehensive and that decontamination and cleaning protocols are in place for all workers and patients in the healthcare system.
• Keep workers informed about related issues.
• Demarcate risk areas and use adequate warning and safety signs (including “No smoking” signs).
• Draw up emergency plans.
• Use sealed and clearly/visibly labelled containers for storage, handling, transportation and waste disposal.
Information for the competent authority

Employers shall make certain information available to the competent authority upon request (activities, quantities, exposures, number of exposed workers, preventive measures) and inform workers if abnormal exposure has happened.

Unforeseen exposure

In cases of abnormal exposure or incident, only workers essential for repairs shall be permitted to work in the affected area, and only with appropriate protection. The exposure should not be permanent and shall be minimised.

Foreseeable exposure

If a temporary, planned, higher exposure is unavoidable, the employer/management shall consult workers/representatives on the measures which will be taken to minimise exposure, and provide appropriate prevention, together with access control.

Access to risk areas

If there is a risk to workers, specified areas shall be made accessible solely to workers who, by reason of their work or duties, are required to enter them.

Hygiene and individual protection

The employer shall take adequate measures to ensure proper hygiene (minimising the risk of contamination with carcinogens or mutagens).

Provisions and conditions must be free of charge for the workers, and will include:

- The prohibition of eating/drinking/smoking in contamination risk areas.
- Provision of appropriate protective clothing.
- Provision of separate storage places for working/protective clothing and for street clothes.
- Access to appropriate and adequate washing and toilet facilities
- Availability of cleaned, checked and maintained protective equipment, stored in a well-defined place. Specific protocols for personal protective equipment (PPE) are required to minimise the risk of exposure in each of the different phases of the manipulation of hazardous drugs. In the healthcare system, it should be an absolute priority to increase the use of all forms of PPE where appropriate as, for example, PPE is not used in 25% of oncology units in Europe.
Information and training of workers

The employer shall also provide appropriate training on potential risks to health, precautions to prevent exposure, hygiene requirements, protective equipment, clothing and incidents handlings.

In healthcare, there is a particular need to increase the provision of information and training for patients and caregivers, who are currently falling a long way behind the levels offered to healthcare workers but who are also at high risk of exposure to hazardous drugs.

Information for workers

Workers and/or any workers’ representatives in the undertaking or establishment can check that this Directive is applied or can be involved in its application, in particular with regard to: the consequences for workers’ safety and health of the selection, wearing and use of protective clothing and equipment, without prejudice to the employer’s responsibility for determining the effectiveness of protective clothing and equipment; and the measures determined by the employer which are referred to in the first subparagraph of Article 8(1) relating to foreseeable exposure, without prejudice to the employer’s responsibility for determining such measures.

Workers and/or any workers’ representatives in the undertaking or establishment must be informed as quickly as possible of abnormal exposures, of the causes thereof and of the measures taken or to be taken to rectify the situation. The employer must keep an up-to-date list of the workers at risk of exposure and the exposure to which they have been subjected. These obligations can only be implemented effectively if employers have in place biological and surface monitoring protocols for hazardous drugs. The doctor, competent authority and persons who have responsibility for health and safety at work must have access to that list. Each worker must have access to the information on the list that relates to them personally.
Article 13  Consultation and participation of workers

Employers shall make certain information available to the competent authority upon request (activities, quantities, exposures, number of exposed workers, preventive measures) and inform workers if abnormal exposure has happened.

Article 14  Health surveillance

The Member States shall carry out health surveillance of workers at risk prior to exposure and at regular intervals thereafter and may continue after the end of exposure. In the European healthcare system, medical testing of workers is only regularly carried out on average in approximately 60% of pharmacies and oncology units so health surveillance needs to be increased to ensure it is universal.

to exposure, then the subsequent health surveillance of other exposed workers may be required, and the risk shall be reassessed. Individual medical records of health surveillance shall be kept.

The doctor or authority shall propose any protective and preventive measures and workers shall have access to the results of the health surveillance. Information and advice must be given to workers regarding any health surveillance that they may undergo following the end of exposure. Workers shall have access to the results of the health surveillance that concern them. Workers concerned, or the employer, may request a review of the results of the health surveillance. All cases of occupational cancers shall be notified to the competent authority.
Amendments to the Carcinogens and Mutagens Directive

**Article 15** Record keeping

Employers will keep an up-to-date list of workers exposed, and will give specified access to data to authorized persons (doctor, authorities, workers and representatives). Records shall be kept for at least 40 years following the end of exposure, and transferred to the authority concerned if the firm ceases to exist.

**Article 16** Limit values

As mentioned in relation to Article 5, threshold levels of exposure to hazardous drugs cannot be predicted and it is therefore difficult to establish limit values. Therefore, contact with genotoxic carcinogens should be avoided at all levels, in accordance with the “As Low As Reasonably Achievable” (ALARA) principle, and also that is why hazardous drugs should be included as a work category in Annex I of the CMD not Annex III. Most of the studies performed on surface monitoring of hazardous drugs in Europe (e.g., in Germany and Spain) suggest 0.1 ng/cm² as the threshold level. In one Dutch study, urine samples from healthcare professionals who worked in facilities with contamination levels < 0.1 ng/cm² were negative for one of the most widely used carcinogenic hazardous drugs cyclophosphamide.
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