Available Online at

http://www.ijcpa.in

April-June 2016

International Journal of CHEMICAL AND PHARMACEUTICAL ANALYSIS

eISSN: 2348-0726 ; pISSN : 2395-2466

Review Article | Volume-3 | Issue-3 | Article ID: 993

COMPARATIVE REGULATORY ASPECTS OF HAZARDOUS DRUGS HANDLING IN US, EUROPE, AUSTRALIA AND INDIA

Dilip G. Maheshwari*[1], Manali R. Patel[2]

*[1]Head of Department of Quality Assurance and Pharm Regulatory Affairs, L.J Institute of Pharmacy, Ahmedabad, Gujarat, INDIA

[2]Department of Quality Assurance and Pharm Regulatory Affairs, L.J Institute of Pharmacy, Ahmedabad, Gujarat, INDIA

***Corresponding Author:** Email: bhrigu.tiwari@yahoo.com*

Received: 29 March 2016 / Revised: 19 April 2016 / Accepted: 20 June 2016 / Available online : 30 June 2016

ABSTRACT

Health care is nearly 10 years behind other industries in its efforts to reduce the errors. Medication error may be nobody's baby, but when it happens, it could well turn out to be everyone's worry and the reasons given for medication error range from silly to the downright serious. The hazardous drugs are known to be mutagenic, teratogenic and carcinogenic, so extra precaution should be taken while storing, diluting, administering the drugs and disposing the waste. The objectives of this article are to define the standards for using cancer chemotherapy in hospitals; to tackle any spillage of drug and how to dispose of the waste of anticancer drugs. It can be also helpful in determining regulatory requirements of hazardous drugs in different countries like US, Europe, Australia and India. This could be beneficial to any hospital where chemotherapy is given without any defined standard operating procedure.

Keywords *– Hazardous Drugs, Health care, Health Standards, Precautions, Regulatory Requirements*

1. INTRODUCTION

A drug is generally chemical substance which provides biological effects on humans as well as on animals. In the broadcast of pharmacology term; drug is defined as a chemical substance used for diagnosis of disease or to enhance mental or physical well-being. Drugs are producing a physiological effect when ingested or otherwise introduced into the body and when any drug exists beyond its therapeutic value, the drug harmfulness should be defined. Hazardous drugs are also one of the type of drugs which are harmful to the patient or health care workers interacting with these type of drugs. Hazardous drugs (HDs) are defined as drugs that cause genotoxicity which is an ability to cause a change or mutation in genetic material; carcinogenicity that cause cancer in animal models , humans or both and teratogenicity which cause defects on fatal development or fatal malformation. It may tend to cause risk exposure to the health care workers handling hazardous drugs. Substances hazardous to health may be defined as very toxic, toxic, corrosive, harmful or irritant. Basically antineoplastic cytotoxic drugs, anti-viral medications, anesthetic agents and other drugs have been classified under hazardous drugs. The concerns about exposure to hazardous drugs first appeared in the 1970s. Although the antineoplastic agents are termed to be most hazardous drugs, the other drugs may also be considered hazardous because even small quantities of drugs produce physiological effect. Therefore the safe handling of hazardous drugs became mandatory for protecting the health care workers. Safe

handling refers to the process in which health care workers adhere to evidence-based practice (EBP) set forth by the national organizations that have been designed to eliminate or significantly reduce occupational exposure. Earlier the regulations for safe handling of hazardous drugs were not well established, therefore it increased its harmful effect on health care workers. The safe handling of hazardous drugs is more relevant regarding their regulations, packaging and handling purposes. Starting from manufacturing, transport, administration, receipt, preparation, storage, distribution, packaging, labelling to disposal of hazardous medications; it may expose hundreds or thousands of health care workers majorly associated with pharmaceutical companies, healthcare organisations and private healthcare companies. The basic goal for safe handling of hazardous drugs is to provide better protection to human health as well as to the environment. Therefore different countries have implemented regulations and recommendations for safe handling of hazardous drugs.

2. REGULATIONS FOR HAZARDOUS DRUGS HANDLING IN US

In US, government has a few separate guidelines like ASHP, OSHA, and NIOSH describing regulatory requirements on safe handling of hazardous drugs. **ASHP (American Society of Health-System Pharmacists)** is a professional organization providing their focus on all pharmacists who serves at hospitals, health care societies, private health care organizations and the health care facilities. The guidance to reduce potential harmful effects of hazardous drugs on employees have been implemented to individuals and many groups connected tirelessly with this industry. ASHP published its technical assistance bulletin (TAB) for handling of hazardous and cytotoxic drugs in 1990. This bulletin contained the information and recommendations for hazardous drugs. Continuous reports were observed on concerns for health care worker safety and workplace contamination that led **Occupational Safety and Health Administration (OSHA)** to introduce and develop new guidelines on promoting safety of health care worker and preventing contamination in 1986. The another one is **NIOSH (National Institute for Occupational Safety And Health);** U.S. federal agency of Centers for Disease Control and Prevention (CDC) conducting research and suggesting recommendations for the prevention of work-related illness. NIOSH has an official order of helping to assure "every man and woman in the Nation safe and healthful working conditions and to preserve our human resources." The main purpose is to identify the requirements for receipt, storage, mixing, preparing, compounding, dispensing, and administration of hazardous drugs to protect the patient, healthcare personnel, and environment[1-3].

3. REGULATIONS FOR HAZARDOUS DRUGS HANDLING IN EUROPE

The EU (European Union) is a unique economic and political partnership between 28 European countries that together cover much of the continent. A European law covering dangerous substances was introduced in 1967 to protect public health, in particular the health of workers handling dangerous substances. The law, known as the Directive on Dangerous Substances introduced EU-wide provisions on the classification, packaging and labelling of dangerous substances. Since it was adopted in 1967 the directive has regularly been updated to take into account the latest scientific and technical progress so as to ensure the highest level of protection for individuals and the environment. Under the REACH regulation on chemicals, substances classified as carcinogenic, mutagenic or having reproductive toxic effects may need authorisation to be used or placed on the market. The current classification and labelling system is in the process of being replaced by a new law known as the Regulation on the Classification, Labelling and Packaging of Substances and Mixtures, which takes effect from 20 January 2009[4-8].

4. REGULATIONS FOR HAZARDOUS DRUGS HANDLING IN AUSTRALIA

South Australia is the southern, central state of mainland Australia. Government of South Australia is prescribed in its constitution since 1856. South Australia (SA) Health represents general guidelines regarding the handling of hazardous drugs including cytotoxic drugs and

related waste. SA Health is accomplished to protecting and improving the health of all South Australians by providing leadership in health reform, public health services, health and medical research, policy development and planning, with an increased focus on well-being, illness prevention, early intervention and quality care. This policy describes direction to management and staff interacting with administration, preparation, transportation, management and storage of hazardous drugs and related waste, in the industry, hospitals and private health community. Therefore, guidelines for South Australian Health Services guidance document incorporates evidence-based and best-practice standards for describing safe handling procedures[9,10].

5. REGULATIONS FOR HAZARDOUS DRUGS HANDLING IN INDIA

The Government of India, officially known as the Union Government was established by the Constitution of India. The Gazette of India, Extraordinary is a public journal and an authorised legal document of the Government of India. Ministry of Environment, Forests and Climate Change (MoEFCC) under the Gazette of India, Extraordinary specifies the rules for handling of hazardous drugs under the environment protection act (29 of 1986); the central government therefore deriving the general regulations for classification, packaging and labelling of hazardous drugs. These regulations are published for providing the information to the public likely to be exposed to the various hazardous drugs[11-12].

6. COMPARISON BETWEEN DIFFERENT REGULATORY AGENCIES ON HAZARDOUS DRUGS HANDLING

Countries	**US**	**Europe**	**Australia**	**India**
Regulatory Agencies	• The American Society of Health-System Pharmacists **(ASHP)** • occupational Safety and Health Administration **(OSHA)** • National Institute for Occupational Safety And Health **(NIOSH)**	• Law, known as the Directive on Dangerous Substances • Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures **(CLP)**	• South Australia Health (**SA**)	• Ministry of Environment, Forests and Climate Change (MoEFCC) environment protection act (29 of 1986)
Starting Year of Hazardous Drugs Regulations	1990	2009	2008	2011
Definition of Hazardous Drugs	Hazardous drugs (HDs) are drugs known or suspected to cause adverse health effects from exposures in the workplace. Hazardous drugs include those used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs and other miscellaneous drugs.	Any drug which could potentially cause harm is considered to be hazardous. Certain drugs can cause different types of harm, ranging from mild skin irritation to cancer.	Hazardous drug is defined as an agent that, due to its inherent toxicity, presents a danger to healthcare personnel. Hazardous drugs are identified as being carcinogenic, teratogenic, genotoxic or as having other developmental, reproductive or organ toxicity regardless of dose; or a similar profile to drugs already considered hazardous.	Hazardous drugs are drugs that are associated with or suspected of causing adverse health effects. Hazardous drugs may possess any one of the characteristics like Carcinogenicity, Fertility Impairment, Genotoxicity, Serious Toxicity and Teratogenicity
Regulations to be followed	ASHP, OSHA, NIOSH	REACH Regulation	SA Health	IHM (Indian Health Manual)
Type of BSC (Biological Safety Cabinet)	Class I	Not Specified	Class I and II	Not Specified
Personal Protective Equipment	Gloves, Gowns, Hair, Face, Shoe cover Eye and Face Protection Respiratory Protection	safety glasses, safety goggles, and face-shield	Coveralls and gowns, Gloves, Protective eyewear, Shoe Cover, Respiratory Protective Equipment, Head Covering	Gloves, Gowns, Eye Protection

Packaging	• Drug packages, bins, shelves, and storage areas for hazardous drugs must bear distinctive labels identifying those Drugs as requiring special handling precautions.	• It shall be so designed and constructed that its contents cannot escape, except in cases where other more specific safety devices are prescribed; • Packaging and fastenings must be strong and solid throughout to ensure that they will not loosen and will safely meet the normal stresses and strains of handling; • Containers containing a substance or a mixture sold or made available to the general public and labelled "fatal", "toxic" or "corrosive" shall have a child-resistant fastening and a tactile warning of danger;	Containers used should be: >hard walled and robust >made from moulded foam that is capable of withstanding shock >securely closed and sealed. The current safety data sheet must be supplied in the packaging, when the cytotoxic drug is being supplied for the first time to the workplace or where the safety data sheet has been updated since the last supply	• Hazardous drugs and any associated should be designed, constructed, maintained and closed so as to prevent any contents from escaping when subject to handling. • Packaging must be constructed and closed as to prevent any package from leakage that might occur the normal condition of transport • Inner packaging must be placed in an outer packaging in such a way that they are protected from breakage, puncture or leakage.
Labelling	All syringes and IV bags containing HD's should be labelled with a distinctive warning label, such as: **""SPECIAL HANDLING/ DISPOSAL PRECAUTIONS"**	According to **CLP Article 17,** a substance and mixture classified as hazardous must bear a label including the following elements: • Name, address and telephone number of supplier(s); • The nominal quantity of substance or mixture in the package where this is being made available to the general public, unless this quantity is specified elsewhere on the package; • Product identifiers; • Hazard pictograms, where applicable; • The relevant signal word, where applicable; • Hazard statements, where applicable; • Appropriate precautionary statements where applicable; • A section for supplemental information, where applicable.	The primary container label should include the wording 'cytotoxic'. The secondary packaging as well as transport containers, should have the purple label with the cell in late teleophase and the warning **'CYTOTOXIC – HANDLE WITH CARE'** prominently affixed.	**"Caution: it is dangerous to take this preparation except under medical supervision"** - Conspicuously printed, -surrounded by a line, -no other words. (Exception topical / external preparations.)
Hazardous waste Classification	• Trace-contaminated hazardous drug waste • Bulk hazardous drug waste • Hazardous drugs not listed as hazardous waste • Hazardous waste and mixed infectious–hazardous Waste	Not Specified	Unused Cytotoxic Pharmaceuticals Contaminated waste form preparation process, Packaging that has been in contact with HDs Contaminated specimens from laboratory like bandages, dressings and aids.	Not Specified

Hazardous waste Disposal	• Incineration • Hazardous management Practice • Licensed sanitary landfill • Commercial waste disposal technique • Chemical Inactivation	• Waste reduction • Re-use • Recycling • Recovery • Disposal	• Incineration at 1100º C.	Not Specified

7. CONCLUSION

A continuing rise in the rate of Hazardous drugs is no longer acceptable as hazardous drugs affect the health of millions of people and poisons large areas of our planet. In many places people live surrounded by garbage and landfills and therefore exposed to hazardous drugs. It is essential that governments and corporations face up to drugs regulations as well as to precautions, using what we know about handling procedures, PPE(Personal Protective Equipment) but also developing new technologies that reduce exposure to hazardous drugs. Therefore, a number of international and national regulations now state that producers have to be held accountable for the amount and toxicity of hazardous drugs. This includes the intelligent use of raw materials, steering production, advanced precautions to reduce exposure towards the hazardous drugs that lead to better protection of health workers.

8. ACKNOWLEDGEMENTS

The authors are thankful to Dr. K. Pundarikakshudu, Principal of L. J. Institute of Pharmacy, Ahmedabad, India for providing all the facilities to carry out work.

9. REFERENCES

1. Am J Hosp Pharm. American Society of Hospital Pharmacists. ASHP technical assistance bulletin on handling cytotoxic and hazardous drugs, **1990**. pp 95.
2. OSHA Technical Manual: Occupational Safety & Health Administration https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html
3. NIOSH Alert: CDC; Workplace safety and health http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf
4. European Commission: "The Directive on dangerous substances" http://ec.europa.eu/environment/archives/dansub/home_en.htm
5. European Chemical Agency: "REACH Regulations" http://echa.europa.eu/regulations/reach
6. European Chemical Agency: "Guidance on CLP" http://echa.europa.eu/web/guest/guidance-documents/guidance-on-clp
7. European Commission: "Explanatory Memorandum" http://ec.europa.eu/environment/chemicals/labelling/pdf/ghs_sc_volume1.pdf
8. Official Journal of the European Union: "Regulations", December 2008, http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008R1272&from=EN
9. Government of South Australia: "About SA Health", http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/about+us/about+sa+health
10. South Australia Health: "Handling of Hazardous Drugs and Related Wastes in South Australian Health Services Policy Directive", July 2015, http://www.sahealth.sa.gov.au/wps/wcm/connect/f99069004b3f738aa4ddade79043faf0/Directive_Handling+of+Hazardous+Drugs+and+Related+Wastes+in+SA+Policy_v2_Jan2016.pdf?MOD=AJPERES&CACHEID=f99069004b3f738aa4ddade79043faf0&CACHE=NONE

11. The gazette of India: Extraordinary, “Ministry of Environment and Forest Notification”, http://www.moef.nic.in/downloads/rules-and-regulations/SO523_E_new.pdf
12. The Gazette of India Extraordinary: PART II -- Section 3 -- Sub-section (ii), “Ministry of Environment and Forests Notification”, http://envfor.nic.in/legis/hsm/so763(e).pdf