ABSTRACT:
Public opinion considers cancer to be an increasingly threatening disease, affecting people of all ages. After cardiovascular diseases, it is the second cause of death amongst the global population. Pharmaceutical industry is the industry which discovers, develops, produce products/medicines for the use of medication by using various chemicals by using different procedures. Chemicals are classified into various hazard classifications in accordance with their physiochemical properties and health hazards. While handling of such hazard chemicals lead to different health hazards to the workers in industry. Hazardous chemicals class such as Explosives, Oxidizing agents, Flammable chemicals, Corrosive chemicals, Toxic chemical, Carcinogens, Teratogen/reproductive toxin and Mutagens. To know the health hazards and its remedial measures those who are handling various types of chemicals in pharmaceuticals industry. The information reveals that health hazards and its remedial measures inside the pharmaceutical industry during the handling of carcinogen chemicals.

KEYWORDS: IARC (International Agency for Research on Cancer), Neoplasia, Exogenous Endogenous, Mutagens, Carcinogen chemicals, Health Hazards, Remedial measures.

1. INTRODUCTION
Population/ Peoples are being exposed to a number of chemicals every day in both indoor and outdoor environments. Epidemiological studies of cancer incidence demonstrated that the risk of developing cancer varies between population groups and these differences are associated with lifestyle factors and habits. Population migration has resulted in the development of types of cancer typical of particular geographical areas. The factors responsible for cancer development are classified as exogenous and endogenous. The first group includes nutritional habits (food preservation and preparation), socio-economic status, lifestyle, physical agents (ionising and non-ionising radiation), chemical compounds (natural and synthetic) and biological agents. Unhealthy lifestyle habits such as: excess alcohol consumption; inhalation of tobacco and related products; the ingestion of certain foods and their contamination by mycotoxins; are responsible for higher incidences of certain types of neoplasias in a number of population groups. Endogenous factors include immune system damage and inflammation caused by uncertain aetiology (e.g. ulcerative colitis, pancreatitis, etc.), genetic makeup, age, endocrine balance and physiological condition. Chemical carcinogens are agents that are capable of inducing cancer in humans or animals. Researchers suspect genetic predisposition and environmental factors play an important role in development of cancer. A relatively small number are occupational carcinogens, having been found to cause cancer in persons exposed to them in the workplace. Many epidemiologic studies have reported excess deaths from bladder, stomach, lung, hematopoietic, and other cancers products workers. Most of these excess deaths cannot be attributed to a specific chemical because (1) workplace exposures involve many individual chemicals and combinations, and (2) changes occur in chemical industries have not been tested for carcinogenicity or toxicity.

2. History & Background
Cancer was described for the first time by Hippocrates as ‘karkinos’. Galeno introduced the word neoplasia only in the II century; he defined it as the growth of a body area adverse to nature. According to Hayes (1995), it was the English surgeon Percivall Pott who first recognized in 1775 the casual relationship between exposure to environmental substances and neoplastic development. Cells divide and Multiply as the body needs them. When these cells continue multiplying when the body doesn’t need them, the result is a mass of growth, also called a tumor. These growths are considered either benign or malignant. Each type of cancer chemical is unique with its own causes, symptoms and methods of treatment. A carcinogen chemicals is any agent that causes cancer. This may be because of the capability of the carcinogen to damage the genome or to disrupt the metabolic processes of the cell. Chemical carcinogenesis is considered to be a multi-stage process that initiates with the exposure of an individual to complex mixtures of chemicals. Cancer is one of the most common diseases in the world. Every day many of the people smoke and how its effects our internal parts and slowly converts to lung cancer. Lung cancer is one of the most common cancer in men and Breast cancer is one of the most common cancer in women. Many of the people/workers in the industry are being exposed to many of the chemicals due to lack of knowledge on the chemicals, not following the operating procedure, mishandling and sudden release due to equipment failure (break of glass ware, gasket failure etc) leads to many health problems. There are over 100 different forms of cancer.

IARC (International Agency for Research on Cancer)
The International Agency for Research on Cancer is an intergovernmental agency forming part of the World Health Organization of the United Nations. Its role is to conduct and coordinate research into the causes of cancer. It also collects and publishes surveillance data regarding the occurrence of cancer worldwide. It maintains a series of monographs on the carcinogenic risks to humans posed by a variety of agents, mixtures and exposures. Following its inception, IARC received numerous requests for lists of known and suspected human carcinogens. In 1970, the IARC Advisory Committee recommended that expert groups prepare a compendium on carcinogenic chemicals, and it began publishing its monographs series with this aim in mind.

STAGES OF CARCINOGENESIS

Studies conducted using animal models, "in vitro" studies and epidemiologic assays enabled investigators to conclude that neoplastic pathogenesis is a complex process which can be divided into three distinct stages, from an operational point of view. These are: initiation, promotion and progression. Changes in the genome’s structure occur across the three stages of neoplastic development. Changes in gene expression also take place during the promotion stage, with selective proliferation of initiated cells and the development of pre-neoplastic cells. During initiation and promotion, apoptosis and cell proliferation can occur at different rates, while remaining balanced. During progression, this balance is modified and from there malignancy arises.

Human life is led under very different conditions from these experimental procedures. Although the process of carcinogenesis is similar for man and experimental animals, the different chemical compounds to which humans are exposed throughout their lives alter the speed of the process and the frequency of mutation, the speed of cell growth and the phenotypical expression of the changed genes. On the other hand, the individual's susceptibility and their defence mechanisms have their own interaction, which modifies each of the neoplastic stages. In studies of chemical carcinogenesis with prolonged exposure and using high doses almost all of the promoter agents induce neoplasias without initiation. Exposure to phenobarbital, benzene, asbestos, and arsenic even without the previous application of initiator agents leads to neoplastic development. This contradiction has two possible explanations: either the genotoxic effect was not identified by mutagenicity and genotoxicity assays, or the initiated cells emerged spontaneously.
Exposure to chemicals at the work place

Some chemicals are directly associated with development of cancer, while some may be responsible when body is exposed to them for a prolonged period of time.

Exposure to chemical carcinogens may be environmental, occupational, living certain type of life style or drugs. Alfatoxin, which is present in foodstuff infected by fungus aspergillus is the most widespread environmental carcinogen.

Indoor Exposure:
Formaldehyde, perchloroethylene, paradichlorobenzene, cigarette smoke, trisodium nitroliotriacetate, asbestos are some of the compounds present in indoor environment in the form of various products or accessories are carcinogenic in nature.

Outdoor Exposure:
Regular exposure to compounds like Arsenic, benzene, beryllium, cadmium, hexavalent chromium (VI), nickel, ethylene oxide in work places causes cancer.

List of Carcinogen chemicals classified by International Agency for Research on Cancer (IARC)

Few of them are as below.
A-alpha-C (2-Amino-9H-pyrido[2,3-b]indole)
Acrylic acid, 2-Amino-4-nitrophenol
1,4-Dioxane, Dulcin, 5-Aminoacenaphthene
2-Aminoanthraquinone, Aminobiphenyl
1-Amino-2,4-dibromoaanthraquinone

Identification of cancerogenic chemicals

Few of the chemicals which are being used in one of the pharmaceutical plant are as below:
Acetone, Benzene, Methyl Chloro Formate, Isopropyl Alcohol, Aceto nitrile, Trans-4-hydroxy-L-proline, Benzyl Chloroformate, Thionyl chloride, 1,4 – Dioxabicyclo {2.2.2} octane, Toluene-4-sulfonyl chloride Propanol, Methyl tertiary Butyl ether, 3-Isobutyl pentane dioic acid dimethyl ester, Lypozyme CALBL, Bromine, Tetralone, Methanolic MMA, R(-) Mandelic acid, Poly ally amine hydrochloride, Cyclohexane, Epichlorohydrin, Valeryl Chloride, O-Xylene, Tri butyl tin chloride, Potassium hydroxide, Sodium Sulphate, Thiophenol, Dioxalane Diacetae, Dimethylamine, Methanol, Toluene, Triethylamine, 1,4 -Dioxane, Chlorosulphonic acid, Para toluene sulphonic acid, Methylene Dichloride, Sodium Azide, Sodium Borohydride, Ammonium Chloride, Caustic Soda flakes/ Caustic Soda Lye solution, Activated Carbon, Hyflow, Ethyl Acetate, Hydrochloric acid, Nitrogen, Dimethyl sulfoxide, Etc………..

Identified chemicals which are being used and comes under the carcinogen chemicals according to IARC

<table>
<thead>
<tr>
<th>S.No</th>
<th>Name of the Chemical</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,4 Dioxane</td>
<td>2B</td>
</tr>
<tr>
<td>2</td>
<td>Epichlorohydrin</td>
<td>2A</td>
</tr>
<tr>
<td>3</td>
<td>Ethanol</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Formaldehyde</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>Carbon</td>
<td>2B</td>
</tr>
<tr>
<td>6</td>
<td>Hydrazine</td>
<td>2B</td>
</tr>
<tr>
<td>7</td>
<td>IsoPropyl Alcohol</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>Toluene</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>Zidovudine</td>
<td>2B</td>
</tr>
<tr>
<td>10</td>
<td>Chloroform</td>
<td>2B</td>
</tr>
<tr>
<td>11</td>
<td>Dichloromethane</td>
<td>2A</td>
</tr>
<tr>
<td>12</td>
<td>DDT (4,4-Dichlorodiphenyltrichloroethane)</td>
<td>2B</td>
</tr>
</tbody>
</table>

Practices in the industries

1) Before any worker enters inside the plant
   - Fulfill the legal requirements
   - Preliminary medical health checkup will be done to know condition of the health.
   - Induction training will be given
   - Job specific trainings will be given
2) Follow the operating procedures while handling the chemicals
3) Information known about the chemicals through

<table>
<thead>
<tr>
<th>IARC Group</th>
<th>Description of group Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP – 1</td>
<td>The agent (mixture) is definitely carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans.</td>
</tr>
<tr>
<td>GROUP – 2A</td>
<td>The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans.</td>
</tr>
<tr>
<td>GROUP – 2B</td>
<td>The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans.</td>
</tr>
<tr>
<td>GROUP – 3</td>
<td>The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.</td>
</tr>
<tr>
<td>GROUP – 4</td>
<td>The agent (mixture) is probably not carcinogenic to humans.</td>
</tr>
</tbody>
</table>

Group – 1 Cartcinogenic to humans
Group – 2A Possibly carcinogenic to humans.
Group – 2B Not classifiable as to its carcinogenicity to humans.
Group – 3 Not classifiable as to its carcinogenicity to humans.
4) Check the storage facility
5) Identify the process hazards
6) Before startup of the new process, training will be given on that particular process chemicals involved and its process hazards.
7) Awareness will be given on emergency safety equipment’s
8) Medical health checkup will be done once in half year.
9) Training will be given on disposal of waste generated from the process.
10) Importance of housekeeping.
11) Workplace monitoring.

Emergency Procedure
Material safety Data Sheets (MSDS) will give details of first aid and spill procedure for specific compounds. These should be referred to before commencing the work as part of the risk assessment process. Specific first aid and spill information should be included in the assessment and incorporated into the safe operating procedure. The following general guidance should be followed in addition to any specific action identified

Ingestion: The likelihood of ingestion is remote. In the event of occurring seek immediate medical advice.

Inhalation: The likelihood is low, as work with volatile carcinogens/toxic compounds should be carried out in a fume cupboard. In the event of exposure remove the person from the area/room and into fresh air. Seek medical advice.

Eye splash/mucous membrane contamination: Irrigate with sterile water for 15 minutes. Seek medical advice.

Skin Spillage: Immediately wash off the skin with large amounts of water. If the substance/solution is aqueous or water based it is unlikely that anything will have been absorbed. If there is any likelihood of absorption through the skin, seek medical advice.

Decontamination & disposal
The procedure for the safe disposal of carcinogens and material contaminated by them must be determined as part of the risk assessment process, before the agents is put into use.

Many carcinogens can be rendered harmless by the addition of an appropriate chemical solution – often strong acid or alkali. If the compound cannot be deactivated it will be subject to the requirement of hazardous waste regulation and will require disposal by specialist contractor. Seek advice from the environmental manager in the estate office about disposal.

It should be noted that the disposal of toxic waste is a costly exercise and appropriate budgetary arrangements must be made during the planning stages of any procedure

Training & Supervision: Individuals required to work with carcinogens must be fully trained in how to handle carcinogens safely and be assessed as fully competent by their supervisor before handling the carcinogen. This training and attainment of competence must be recorded, with both trainer and trainee signing to that effect.

A very high level of supervision should also be maintained to ensure that workplace standards and working practices are maintained.

Ensure those carrying out the dispensing process are skilled, experienced and fully trained in the safe use of those chemicals

Remedial Measures and its Controls
First of all identify the chemical nature and its hazards

Risk assessment shall be done for the chemical handling

Develop safe handling procedure and instruction about the chemical

Reduce the stress and take balance diet

Avoid smoking

Engineering controls and Personnel Protective Equipment’s (PPE) to be provided while handling of carcinogen chemicals

<table>
<thead>
<tr>
<th>IARC Group</th>
<th>Engineering Controls for weighing &amp; Subdivision to be provided</th>
<th>Personnel Protective Equipment (PPE) to be provided</th>
<th>Additional Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Engineering Controls for weighing &amp; Subdivision: Glove box, down flow booth or other high containment equipment required. Solids Charging or Transfer: Closed system transfer strongly recommended. Liquid Charging or Transfer: Closed system transfer recommended.</td>
<td>Personal Protective Equipment: Lab coat/ Apron, coverall or work uniform required. Consider using dedicated work clothing. Dedicated work clothing should be removed at end of shift. Gloves: Appropriate impermeable double gloves required. Footwear: Appropriate foot protection required. Footwear dedicated to work operations recommended. Eye Protection: Safety glasses/goggles required. Respiratory Protection: Supplied air respirator required.</td>
<td></td>
</tr>
<tr>
<td>2A</td>
<td>Engineering Controls for weighing &amp; Subdivision</td>
<td>Personal Protective Equipment: Lab coat/ Apron, coverall or work uniform required.</td>
<td></td>
</tr>
</tbody>
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<tr>
<td>3</td>
<td>Engineering Controls for weighing &amp; Subdivision: Laminar flow booth recommended. Solids charging or Transfer: Closed system transfer strongly recommended. Liquid Charging or Transfer: Closed system transfer recommended.</td>
<td>Personal Protective Equipment: Lab coat/ Apron, coverall or work uniform required. Consider using dedicated work clothing. Dedicated work clothing should be removed at end of shift. Gloves: Appropriate impermeable double gloves required. Footwear: Appropriate foot protection required. Footwear dedicated to work operations recommended. Eye Protection: Safety glasses/goggles required. Respiratory Protection: Supplied air respirator required.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Engineering Controls for weighing &amp; Subdivision: At a minimum, effective local exhaust ventilation is required. Solids charging or Transfer: Closed system transfer recommended. Liquid Charging or Transfer: Closed system transfer recommended.</td>
<td>Personal Protective Equipment: Lab coat, coverall or work uniform required. Gloves: Appropriate impermeable gloves required. Footwear: Appropriate foot protection required. Footwear dedicated to work operations recommended. Eye Protection: Safety glasses/goggles required. Respiratory Protection: Consider disposable dust mask (Protection factor = 10)</td>
<td></td>
</tr>
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Conclusion:
In the one of the pharmaceutical industry the chemicals which are studied to find out the carcinogen chemicals and its effects
There are two carcinogen chemicals which are being used i.e. 1,4-dioxane and methylene dichloride in large volumes at present. These two chemicals are being used by following the engineering controls. Observed the medical surveillance report for all employees and conclude that, no identify of carcinogen effects for those handling the chemicals for the past two years. It is clear that reducing or eliminating exposures to carcinogenic chemicals in the environment could prevent a large number of cancers

Reference: