Carcinogens, mutagens and teratogens - using them safely

Introduction

**Carcinogens, mutagens and teratogens**

**ALL** chemicals can be handled safely, some simply require more care in handling than others. Keep in mind that there are **MANY** common lab chemicals whose properties have not been fully investigated, and that lists of carcinogens, mutagens and teratogens are not necessarily inclusive of all substances and mixtures that could have undesirable effects on human cell growth, reproductive organs or reproduction.

On the other hand, the presence of any of these or other materials in your lab does not mean that you have been exposed, nor that you are likely to experience carcinogenic, teratogenic or embryotoxic effects.

Substances and preparations which, if they are inhaled or ingested or if they penetrate the skin;

- may induce cancer or increase its incidence and can affect any cells or tissues are **Carcinogens**
- may induce hereditary genetic defects or increase their incidence and affect the germ cells (gonads) are **Mutagens**
- may induce non-hereditary congenital malformations or increase their incidence and effect the growing foetus are **Teratogens**

The Department has produced separate guidance and information for workers planning families.

UCLA has produced a standard operating procedure for chemical carcinogens, reproductive toxins, acutely and extremely toxic chemicals.

The HSE has issued an 8-page information sheet on the safe handling of cytotoxic drugs, some of which are mutagens and carcinogens in their own right.

**Classification of chemicals**

A large number of chemicals are subject to EU-wide agreement on their classification and labelling. Although the resulting list does not represent a complete list of all dangerous chemicals it does cover many of the most common chemicals and their properties. The agreed list is known as Annex I to the Dangerous Substances Directive and is subject to regular updating for technical progress. The UK implementation of this is in the CHIP Regulations and they define the various categories of chemical hazard (including carcinogens, mutagens and reproductive toxins) as below. The information on many thousands of chemicals is available in the Approved Supply List (ASL).

**Chemicals that may cause cancer or increase its incidence.**

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<thead>
<tr>
<th>Cat</th>
<th>Description</th>
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<tr>
<td>1</td>
<td>category 1 carcinogens</td>
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<td>category 2 carcinogens</td>
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<td>3</td>
<td>category 3 carcinogens</td>
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**Chemicals that induce heritable genetic defects or increase their incidence.**

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<td>category 2 mutagens</td>
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<td>3</td>
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**Chemicals that produce or increase the incidence of non-heritable effects in progeny and/or an impairment in reproductive functions or capacity.**

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In the future the CHIP will be replaced by the Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation), adopting in the EU the Globally Harmonised System (GHS)
Carcinogens

A carcinogen is a substance that causes cancer (or is believed to cause cancer).

A carcinogenic material is one that is known to cause cancer. The process of forming cancer cells from normal cells or carcinomas is called carcinogenesis.

A known human carcinogen means there is sufficient evidence of a cause and effect relationship between exposure to the material and cancer in humans. Such determination requires evidence from epidemiology, clinical, or tissue/cell studies involving humans who were exposed to the substance in question. Obviously, it is unethical to deliberately test potential carcinogens on humans, so "proving" something (in the rigorous scientific sense) to be a carcinogen in humans is a difficult, demanding and lengthy task!

Substances that are reasonably anticipated to be human carcinogens meet any of the following descriptions:

- There is limited evidence of carcinogenicity from studies in humans. A cause and effect interpretation is credible, but that alternative explanations such as chance, bias, other variables etc. cannot be ruled out. Again, science can never prove a hypothesis, only disprove one. Scientific "facts" are established only when a preponderance of the evidence supports a hypothesis and there is 1) no evidence to disprove it and 2) no equally viable alternative hypotheses.
- There is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumours (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumour, or age at onset.
- There is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the substance is structurally related to other materials that are either human carcinogens or reasonably anticipated to be human carcinogens.
- There is convincing relevant information that the material acts through mechanisms that are likely to cause cancer in humans.

A wide variety of information is required to assess carcinogenicity and risks to humans. For example, a substance may cause cancer in laboratory animals, but the mechanism by which this occurs may not occur in humans.

Cancer is a disorder in which the mechanisms which control proliferation of cells no longer function adequately. Because of the implications of this 'biomagnifier' effect leading to irreversible life-threatening changes, it is an emotive subject and chemical carcinogenicity has commonly been perceived to be different from other forms of chemical toxicity.

The International Agency for Research on Cancer (IARC) is part of the World Health Organization. IARC's mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. The Agency is involved in both epidemiological and laboratory research and disseminates scientific information through publications, meetings, courses, and fellowships. Their 'Summaries & Evaluations' page at http://www.inchem.org/pages/iarc.html provides a list of chemical reviews (via the 'Chemical Safety Information from Intergovernmental Organizations' (IPCS INCHEM) site based in Canada.).

NIOSH have produced a list of carcinogens at http://www.cdc.gov/niosh/topics/cancer/npotocca.html.

The US National Toxicology Program (NTP) have produced their 11th Report on carcinogens (2011) which lists compounds as either:
- Chemicals that are Known To Be Human Carcinogens or
- Chemicals that are Reasonably Anticipated To Be Human Carcinogens (both of these documents are in pdf format).

The Royal Society of Chemistry has produced a Note on Potency of Chemical Carcinogens (December 2010) including sections on:
- How are chemical carcinogens identified?
- Is there a threshold dose? and
- How should animal data be extrapolated to man?
**Mutagens**

A **mutagen** is a substance or agent that causes an increase in the rate of change in genes (subsections of the DNA of the body's cells). These **mutations** (changes) can be passed along as the cell reproduces, sometimes leading to defective cells or cancer.

Examples of mutagens include certain biological and chemical agents as well exposure to ultraviolet light or ionizing radiation.

**Mutagenesis** is the formation of mutations.

There are many types of mutations, some of which are harmful and others which have little or no effect on the body's function.

Mutagens can be identified using the Ames test and other biochemical testing methods.

Do not confuse a mutagen with a carcinogen (a substance that causes cancer). Mutagens may cause cancer, but not always.

Do not confuse a mutagen with a teratogen (a substance that causes change or harm to a foetus or embryo).

Avoid working with mutagens whenever possible. If you must work with a mutagen be sure to wear personal protective equipment (PPE) and utilize workplace controls such as a fume cupboards to minimize your exposure.

Ethidium bromide is a mutagen.

The Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences (IEPhB) has produced a 'Partial List of Mutagens' at http://www.iephb.nw.ru/~spirov/hazard/mutagen_lst.html

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**Teratogens** (and embryotoxins or fetotoxins)

A **teratogen** is an agent that can cause malformations of an embryo or unborn child (foetus). This can be a chemical substance, a virus or ionizing radiation.

This is closely related to an **embryotoxin**, an agent that causes poisoning effects on a developing foetus.

Both embryotoxins and teratogens are reproductive toxins, substances which cause damage to a pregnant women's reproductive and/or endocrine system and/or a developing foetus.

**Pregnant women should avoid all contact with teratogens, particularly during the first three months of pregnancy**, as this can result in damage to the developing child. For example, alcohol is a teratogen and drinking during pregnancy can lead to a child born with foetal alcohol syndrome.

Many drugs can also have an adverse effect on developing foetuses, the most infamous example being thalidomide. This drug was used to control morning sickness, but was withdrawn from the market after it was discovered to cause limb and other developmental deformities.

There are few examples of transplacental carcinogens, substances which can cause foetuses exposed during pregnancy to eventually develop cancer. The best-known example is DES, diethylstilbestrol, a compound formerly used to prevent miscarriages before its trans-generational carcinogenic activity was known.

Always minimize the use and release of teratogens (or believed teratogens) in the workplace. Women who are of child-bearing age should pay particular attention to teratogenic materials because they could be pregnant without knowing it and expose their foetus. Teratogens typically cause their most severe damage during the first 3 months of pregnancy when many pregnancies are not yet known. Many teratogens cause effects at very low exposure levels.

**Embryotoxins** are substances that act during pregnancy to cause adverse effects on the developing foetus. These effects may include embryolethality (death of the fertilized egg, the embryo, or the foetus), malformations (teratogenic effects), retarded growth, and postnatal function deficits. A few substances have been demonstrated to be embryotoxic in humans.

Texas Tech University has produced a 'Partial List of Teratogens' at www.ttuhs.edu/admin/safety/lab/Teratogens.pdf.

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