

Safe Use and Control of Substances that are Carcinogenic, Mutagenic or Toxic to Reproduction

Reviews and Revisions

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INTRODUCTION

Carcinogens, Mutagens and Reproductive toxins (CMRs) are chronically toxic and pose a serious threat to human health so exposures to them must be prevented or reduced to a minimum. Cancer is a disease characterised by uncontrolled growth of altered cells and their ability to move from the original site and spread to different parts of the body. **Carcinogens** are substances or mixtures which cause cancer or increase its incidence. A mutation means a permanent change in the amount or structure of the genetic material in a cell. **Mutagens** are agents that increasing the occurrence of mutations. **Reproductive toxins** are agents which cause adverse effects on sexual function and fertility in males and females, developmental toxicity in the offspring and effects through or via lactation.

Exposure to substances that are Carcinogens, Mutagens and Reproductive toxins (CMRs) must be prevented or adequately controlled.

This Procedure provides details of what is required to satisfy the requirements of the Control of Substances Hazardous to Health Regulations 2002 (as amended) Approved Code of Practice. It applies to:

- **categories 1A, 1B and 2** CMRs (as classified by suppliers under the Classification, Labelling and Packaging of Substances and Mixtures Regulation (CLP Regulation) and
- **categories 1 and 2** CMRs (as currently defined in COSHH and classed by suppliers under the Chemicals (Hazard Information and Packaging Regulations)) 2009.

GENERAL PRINCIPLES

This Procedure gives practical advice to enable users to minimise the risk to health from CMR's (including suspected CMR's).

CMR substances may be encountered across the university in a variety of locations, e.g. workshops and studios, not just chemical laboratories. This Procedure provides practical instruction to Faculty Deans/Heads of Service and others responsible for ensuring the safe handling and use of known and presumed CMR substances. Furthermore, users of known or presumed CMR substances should be directed to this Procedure as essential reading prior to commencing work.

Guidance contained within this document should be complied with as a minimum and it is expected that, where appropriate, Faculty policies, COSHH Risk Assessments, General Risk Assessments and Safe Working Procedures will make reference to it.


Whilst procedural guidance contained within this document refers to carcinogens, it is expected that the same procedures/practices will be applied when using Category 1a and 1b mutagens and reproductive toxins. Consequently, the term carcinogen is taken to include mutagens or

substances toxic to reproduction. Recommendations contained within this Procedure should be complied with as a minimum wherever practicable.

Please note that exposure to Category 2 CMRs and substances and mixtures that have effects on or via lactation can be prevented or adequately controlled by following the University's COSHH Guidance '[Link goes here](#)'. Information regarding their classification and hazard communication is included in this document for reference only.

DEFINITIONS

Classification of CMR substances and mixtures according to EU legislation and IARC criteria

EU classification of CMR substances			
Category	Criteria		
Cat. 1 A	known to have CMR potential for humans, based largely on human evidence		
Cat. 1 B	presumed to have CMR potential for humans, based largely on experimental animal data		
Cat. 2	suspected to have CMR potential for humans		
effects on or via lactation	evidence of adverse effects in the offspring due to transfer in the milk and/or on the quality of the milk and/or the substance is present in potentially toxic levels in breast milk		
EU classification of CMR mixtures based on hazards of components (if not specified otherwise)			
Category	Criteria		
Cat. 1 A or B	carcinogen/mutagen (CM): contains $\geq 0,1\%$ carcinogen or mutagen cat. 1 (A or B); reprotoxic (R): contains $\geq 0,3\%$ reprotoxic cat 1 (A or B)		
Cat. 2	CM: contains $\geq 1\%$ carcinogen or mutagen cat. 2; R: contains $\geq 0,3\%$ reprotoxic cat. 2		
effects on or via lactation	R: contains $\geq 0,3\%$ reprotoxic with effects on or via lactation		
Hazard statements for CMR categories			
Hazard statements	Category 1A or 1B	Category 2	Effects on or via lactation
Carcinogens	H340: May cause genetic defects	H341: Suspected of causing genetic defects	
Mutagens	H350: May cause cancer	H351: Suspected of causing cancer	
Reprotoxics	H360: May damage fertility or the unborn child	H361: Suspected of damaging fertility or the unborn child	H362: May cause harm to breast-fed children
Hazard symbol for CMR	 <div style="border: 1px solid black; padding: 2px; display: inline-block; margin-left: 20px;">308</div>		

Note the absence of the GHS08 pictogram for substances and mixtures that have effects on or via lactation. Hazards caused by reproductive toxins with effects on or via lactation are only communicated by the H362 hazard statement.

A substance can have one or more of the CMR hazards. When it has more it is classified according to the evidence for each type of hazard, for example:

- CM: benzene is carc. 1A, muta. 1B;
- CR: lead (II) chromate is carc. 1B, repr. 1A;

COSHH 2002 (as amended) Schedule 1: Other substances and processes to which the definition of “carcinogen” relates

- Aflatoxins
- Arsenic
- Auramine manufacture
- Calcining, sintering or smelting of nickel copper matte or acid leaching or electrorefining of roasted matte
- Coal soots, coal tar, pitch and coal tar fumes
- Hardwood dusts
- Isopropyl alcohol manufacture (strong acid process)
- Leather dust in boot and shoe manufacture, arising during preparation and finishing
- Magenta manufacture
- Mustard gas (β, β' -dichlorodiethyl sulphide)
- Rubber manufacturing and processing giving rise to rubber process dust and rubber fume
- Used engine oils

The following polychlorodibenzodioxins:

- 2, 3, 7, 8 –TCDD
- 1,2,3,7,8-PeCDD
- 1,2,3,4,7,8-HxCDD
- 1,2,3,6,7,8-HxCDD
- 1,2,3,7,8,9-HxCDD
- 1,2,3,4,6,7,8-HpCDD
- OCDD

The following polychlorodibenzofurans:

- 2,3,7,8-TCDF
- 2,3,4,7,8-PeCDF
- 1.2.3.7.8- PeCDF
- 1,2,3,4,7,8-HxCDF
- 1,2,3,7,8,9-HxCDF
- 1,2,3,6,7,8-HxCDF
- 2,3,4,6,7,8-HxCDF
- 1,2,3,4,6,7,8-HpCDF
- 1,2,3,4,7,8,9-HpCDF
- OCDF

Where T=Tetra, Pe=Penta,Hx=Hexa and O=Octa

RESPONSIBILITIES

The Head of faculty must ensure that these arrangements are implemented and adhered to within their areas of responsibility. In particular, they must ensure that:

- a) There is a system in place to provide assurance that staff and PG students are trained to work with CMR's.
- b) All work with CMRs must be justified by a comprehensive COSHH assessment and may only be undertaken by suitably experienced personnel (or others supervised by such people).
- c) COSHH assessments are carried out competently and copies kept locally so they are available for reference and inspection. The use of CMR's in undergraduate teaching must be avoided where possible. In circumstances where it is necessary that CMR's are used, the need and conditions of use should be justified and approved on a case by case basis.
- d) Where COSHH assessments identify a risk of significant exposure, or where there has been an exposure incident, Health & Safety will assist faculties check and validate the assessment and/or exposure levels.
- e) COSHH/risk assessments and standard operating procedures must be communicated to, and signed by, everyone working on the materials and must be kept up to date when new people are recruited.
- f) COSHH assessment must be in place and ensure that these are reviewed at least annually or when the University documents are updated.

The Head of Faculty may nominate an individual e.g. the Technical manager or other competent person to act on their behalf and to give advice on the safe handling of CMR's.

The Academic and Class supervisor must ensure that:

- a) Protocols are reviewed at least annually by the academic responsible for the practical class and work must not go ahead without an adequate degree of supervision, which is detailed in the COSHH assessment. The Academic /class supervisor must ensure, so far as is reasonably practicable, that any students required to use CMR's are not immunocompromised or knowingly pregnant.
- b) approve the use of each CMR in their work activities (Technical Manager for research projects, academic module leads for teaching classes). This will be reflected in the COSHH assessment.
- c) COSHH assessments and/or standard operating procedures are communicated to, and signed by, all individuals working on the project and are available locally for reference and inspection.
- d) Occupational Health and H&S are notified (using the IR1 form), if a COSHH assessment identifies the need for health surveillance or if an exposure to CMR's has occurred
- e) The use of CMR's by any person who is:

- under 18 years of age;
- immunocompromised;
- knowingly pregnant or a nursing mother etc.

is **prohibited** unless until a specific risk assessment is carried out that indicates that it would be safe for them to carry out the work. For access to the assessment click [here](#)

- f) Staff and students are competent for the work in which they are involved. Training records (local on-the-job training or formal courses) are kept locally and are available for inspection.
- g) Records are archived if required.
- h) Internal monitoring/inspections are carried out to ensure that these arrangements and any local instructions are being followed.

The Technical Manager must ensure that:

- a) A CMR inventory is compiled for class 1a and class 1b
- b) CMR's must not be used where a safer alternative can be substituted.
- c) The usage of CMR agents is logged for class 1a and class 1b and reported on at least an annual basis
- d) Records are stored or archived for the appropriate length of time and there is a procedure in place when students and staff relocate or leave.
- e) There is effective communication with the line manager(s) of staff not reporting directly to them, resulting in comparable control of exposure.

Individual users of CMR's must ensure that:

- a) They protect themselves and others by following the safe working procedures and using the control measures identified in the COSHH assessment.
- b) Ensure that they have read and signed the relevant COSHH assessments/ standard operating procedures
- c) Inform their line manager / supervisor if their personal health circumstances change, e.g. new medical condition / medication which may affect their immune status, pregnancy etc.
- d) Fulfil their legal obligation to comply with a health surveillance programme if and when required by the risk assessment or as a result of an exposure.

EXPOSURE RISK AND HAZARDOUS PROPERTIES OF CMR's

Prevention of Exposure

In the first instance, as with all hazardous substances, exposure to a carcinogen should be prevented by using a safer alternative where one is available, and its use is reasonably practicable. Carcinogenic, toxic and other properties of chemical substitutes should be established and taken into account when considering alternatives.

When undertaking any synthetic research, synthetic routes should be chosen to avoid the use of carcinogenic starting materials and to avoid, as far as possible, the formation of by-products, intermediates, wastes or residual contaminants consisting of or containing carcinogenic substances.

Control of Exposure

Where the use of a safer alternative substance is not practicable, or one does not exist, then exposure **must** be adequately controlled to as low a level as is reasonably practicable. This is particularly relevant as the level of exposure affects only the probability of cancers occurring and not the severity of the disease. However, the precautions required to be taken will be determined by the extent of risk and the scope for minimising that risk.

It should be noted that many substances that are known to be carcinogenic are also likely to present additional hazards, such as acute toxicity, which will also need to be controlled. Measures adequate to control toxicity however, may not provide adequate control against cancer.

In addition to the principles of safe chemical practice, all the following **must** be applied:

- a) Carcinogenic materials must be stored in closed containers that are clearly labelled and marked with visible hazard warning signs. All containers must be kept segregated from other chemicals where possible in a lockable, preferably ventilated, cupboard fitted with trays to contain spillage and clearly labelled 'CMR's'. Access to these must be restricted to designated members of staff, and the amounts of CMR material kept to a minimum.
- b) A register of the use and location of CMR class 1a and class 1b within Faculties should also be maintained and updated regularly (annually, it may be prudent to use the general laboratory inventory process).
- c) Eating, drinking and smoking are not permitted where there is a risk of contamination from a CMR substance, and in any case, the consumption of food and drink is forbidden in laboratories.
- d) CMR materials that are stored in glass containers may only be transported within robust, secondary containers large enough to contain any spills arising from breakage.
- e) Prior to commencing work with a CMR material, as with any hazardous material, a thorough risk assessment must be undertaken. Consideration must be given to:
 - whether the substance can be eliminated i.e., whether the work can be done in some other way
 - whether the substance can be substituted by a non- or less hazardous substance
 - the type of hazard (gas, fume, dust etc.)

- the route by which the particular substance(s) can enter the body, be it by inhalation, ingestion or penetration of the skin, mucosal surfaces or eyes
 - level of exposure
 - operating and maintenance instructions and procedures (where applicable)
 - maintenance and emergency procedures
- f) Exposure to a CMR substance should be controlled by total containment of the substance or process. Whilst this is unlikely to be possible in a research environment, the use of glove boxes etc. must be employed if reasonably practicable, particularly where a CMR substance presents a dust or vapour inhalation hazard.
- g) Where total containment of a CMR substance or process is not possible, CMR substances should be used within a fume cupboard of good quality and high efficiency where practicable.
- h) Where it is not possible to totally or partially enclose a process which presents a CMR dust or vapour inhalation hazard (e.g. wood dust in a work shop), then local exhaust ventilation (LEV) must be used as a minimum and respiratory protective equipment (RPE) worn. **A recirculating fume hood must NOT be used for CMR materials.**
- i) Glove boxes and fume cupboards where work involving carcinogenic substances is undertaken must be clearly designated with a 'CMR Hazard' warning sign.
- j) Walls, floors and other surfaces in areas where CMR substances are used must be cleaned i.e. washed down at regular intervals and whenever necessary.
- k) Only the minimum amount of CMR substance necessary may be used, and the number of people likely to be exposed and the duration of their exposure must be kept to a minimum. It is essential that all work involving CMR substances be thoroughly planned in advance.
- l) The appropriate protective clothing **must** be worn when manipulating/working with carcinogenic substances. This includes the wearing of gloves made of a suitable material to provide protection against accidental skin contact; wearing clean, if necessary disposable, protective clothing in addition to a laboratory coat and eye protection. It should be noted that laboratory gloves provide only very limited protection and should be discarded appropriately and immediately following contamination.
- m) In order to avoid spreading contamination from the site of use of a carcinogenic substance, the following precautions **must** be taken:
- Weighing of materials and preparation of solutions must only take place within an adequate fume cupboard or other well-ventilated enclosure
 - Care must be taken to avoid contaminating the exterior of containers. Any such contamination must be cleaned off in the fume cupboard or ventilated enclosure prior to returning to store
 - Manipulations involving solutions of carcinogenic substance should be performed over, or in a chemically resistant tray lined with absorbent material (e.g. bench-kote)
 - Care must be taken to avoid the formation of airborne dust or processes that may give rise to aerosols

- Apparatus and glassware contaminated with carcinogens are the responsibility of the person who used it. The contaminated apparatus and glassware must not be placed in communal washing-up containers nor washed up by non-technical staff but must be cleaned within a fume cupboard and any washings, including solvent, carefully stored as waste
 - Spills within the fume cupboard must be cleared up carefully and any materials used disposed of as carcinogenic waste
 - Users must never touch door handles, light switches or telephones with gloves (assumed contaminated) or wear gloves outside the laboratory. Gloves should be removed using the proper 'surgical' procedure to avoid skin contamination
 - Contaminated tissues, filter-papers, absorbent tray liners, disposable laboratory wear including laboratory gloves, ion-exchange materials and other solid waste must be sealed in clearly labelled plastic bags for disposal as carcinogenic chemical waste. Contaminated material must not be allowed to accumulate in the laboratory
 - Users must practice careful hygiene and wash and dry hands thoroughly before leaving the laboratory
- n) The use of sharps in procedures involving carcinogenic substances should be avoided where possible. Disposable sharps including broken glass **must** be decontaminated before disposal and the washings treated as carcinogenic chemical waste.

ACCIDENT/INCIDENT REPORTING

Where an incident occurs, that results in the potential or actual exposure of any individual to CMR's even if there is no apparent health effect, it must be recorded on the [University Accident/Incident reporting system](#). The Central Health & Safety Section must be immediately informed as such an occurrence may be reportable to the HSE.

A copy of the incident report will be forwarded to Occupational Health who will review the circumstances of the exposure and ensure an appropriate entry is made on the individual's health record, and if deemed necessary invite the individual to attend for an appointment.

- a) The above records must be kept for **40 years** and be available for inspection. All accidents and incidents, especially those involving a loss of containment (e.g. failure of fume cupboards or microbiological safety cabinets, spillages, splashes) must be reported to H&S on IR1 form without delay.
- b) Any loss of containment incident or complaint of symptoms must be investigated. The investigation report and all associated documentation must be provided by the Principal Investigator (PI), or the Director of the practical class if undergraduates are affected, to the health and Safety Office. H&S will arrange for the long-term retention of the documentation, and for its ultimate destruction.
- c) Health surveillance records and Occupational Health attendances in connection with verified exposure to CMRs will be retained by Occupational Health.

- d) If there has been no exposure to CMR's, the COSHH assessments etc. can be destroyed by Faculty or other operational groups 5 years after last use, in accordance with the University's records retention schedule.

UNIVERSITY PROCEDURES

Ordering from Approved Suppliers

The requestor prepares the purchase requisition and a suitable COSHH assessment and will obtain authorization to purchase from the department Technical Manager. The user must identify the material is a CMR agent and added to the laboratory / workshop inventory. The Department Technical manager will approve the purchase and will stipulate the delivery address.

Receipt of Materials

No consignment bearing the CMR hazard symbol will be opened, but taken directly to the addressee. CMR agents should be opened in a fume hood.

The addressee, will check the contents and documentation on receipt of the goods. The receipt of the material is recorded in the addressee's department stock records.

Storage of Materials

The CMR agents will be stored in a labelled locked COSHH cabinet

TRAINING

Every employee who undertakes work with CMR's must receive suitable and sufficient information, instruction and training to enable him/her to conduct that work in accordance with the current legislation. The standard of training is that recommended and approved by the University. This includes sufficient detail to fulfil the objectives:

- To be familiar with the types and properties of CMR's
- To be familiar with the terminology used in CMR handling
- To be aware of the legal requirements associated with the use of CMR's
- To understand the risks associated with CMR's and the steps which are taken to keep these to a minimum
- "Know what to do in an emergency"

Retraining will take place at periods no longer than five years after the previous training

The following information is taken from the Occupational Safety and Health Administration (OSHA) Wiki for CMR substances and provides background information as to the health impacts of CMR substances and mixtures.

Carcinogens and mutagens

Carcinogenesis and mutagenesis processes and the relation between them are not completely understood but at present two mechanisms are considered: one inducing cancer by involving

mutations (caused by genotoxic substances) and one that induces or promotes it by other means (caused by non-genotoxic substances).

Genotoxic agents or their metabolites induce direct changes in the genetic material (DNA) while the non-genotoxic agents are considered to be involved in other types of mechanisms, for example acting as tumor promoters. Genotoxic and non-genotoxic substances may interact at the different stages of carcinogenicity.

The body is normally programmed (by encoded genetic information) to control cell growth in order to insure development, functionality and repair of tissues. A variety of factors (including exposure to CMR's) may disturb these mechanisms and transform normal cells into malignant ones. Malignant cells do not have the same functions, nor do they multiply or die as the cells from which they are derived. They tend to proliferate fast and invade the neighboring tissues or enter the bloodstream or lymphatic system and spread in distant parts of the body (metastasis).

Mutagens can damage the genetic material of the cells (DNA and/or chromosomes). This can lead to permanent changes: mutations. Numerous mutations occur in a lifetime. Many of them are neutral, but some can negatively affect the cells in which they occurred. When mutations occur in germ cells (male or female reproductive cells) the changes they cause are heritable. Germ cell mutagenicity can act over several generations and cause problems like reduction of fertility, malformations, genetic diseases, embryonic death or genetically determined phenotypic alterations. Because of their mechanism of action germ cell mutagens are likely to have carcinogenic effects. Mutations that occur in somatic cells (non-reproductive cells) can increase the likelihood of cancer, but somatic mutations are not passed along to the next generation.

Non-genotoxic carcinogens are assumed to participate in the carcinogenesis process by a mechanism not related directly to the genetic material. They have been shown to act as tumor promoters, endocrine modifiers, immuno-suppressants or inducers of tissue-specific toxicity.

There are differences in how each human individual responds to chemicals (metabolic fingerprint). Tissue specificity has also been noticed. Data show that certain CMRs can be associated to target organs (organs that are most affected), like nasal cancer to exposure to chromium(VI) compounds, pleural mesothelioma to asbestos exposure, scrotal cancer from polycyclic aromatic hydrocarbons like benzo[a]pyrene from soot.

Reprotoxic substances

Reproductive toxicity refers to direct and specific effects on sexual function and fertility. This includes alterations to the reproductive system (e.g. direct injury to the female and male reproductive cells), adverse effects on onset of puberty, production and transport of gamete (i.e. sperm and egg or 'ovum'), reproductive cycle normality, sexual behavior, fertility, parturition (childbirth), pregnancy outcomes, premature reproductive senescence (ageing) or modifications in other functions that are dependent on the integrity of the reproductive systems. Effects transmissible via lactation to breastfed babies are also included.

Health effects of reprotoxicants for pregnant women depend on when they are exposed. Exposure during the first three months of pregnancy might cause induction of metabolic disorders in the mother body, abnormal embryogenesis, birth defects or miscarriage. During the last six months, exposure could slow foetus growth, affect the development of its brain or cause premature labour.

Not only women can be affected by reprotoxic substances, men are also at risk. Reprotoxics can affect e.g. the male steroid hormone system and have an impact on sperm quality and concentration. The development of the foetus may also be disturbed through heritable changes (epigenetic mechanisms) in egg or semen cells, causing no change in the underlying DNA sequence of the organism; instead, non-genetic factors cause the organism's genes to behave (or "express themselves") differently. There is some evidence of epigenetic effects or transgenerational effects of paternal exposure that can impact on the pregnancy outcome, e.g. increased risks of childhood cancers.

Developmental toxicity has a broader meaning but for pragmatic purposes of EU classification (CLP Regulation), it essentially means adverse effects induced during pregnancy, or as a result of parental exposure. These effects can be manifested at any point in the lifetime of the organism. The major manifestations of developmental toxicity include death of the developing organism, structural malformations, altered growth and functional deficiency.

CONTINGENCY PLANNING

Accidents and Emergencies

In the case of a CMR accident or emergency the four main priorities are:

- The protection of human life.
- The protection of employee health and safety by immediately removing any CMR contamination on their persons.
- Containment and/or prevention of the spread of any free CMR material
- The removal of any resultant CMR contamination from the building and equipment.

The four main incidents to which these principles apply are envisaged to be: -

- Accidental intake of CMR material via inhalation, ingestion or through a wound or from the escape of gaseous CMR
- Accidental spillage of CMR material.
- Fire in a designated CMR area.
- Loss of CMR material.

The Accidental Intake of CMR Material

Where such intake is through a wound, immediately irrigate the area with water from the nearest sink. Seek medical attention as soon as possible. Medical staff must be told that CMR material has been/may have been in contact with the wound. Where intake is through the escape of gaseous materials the employee must evacuate and seal off the area ensuring that no other employees may enter.

The Accidental Spillage of CMR Material

In the case of spillage of CMR material, steps should be taken immediately to restrict the further dispersal of the material in such a way that it does not affect any individual's health and safety. Skin

and clothing should be checked for contamination followed by decontamination as necessary using soap and water, taking care not to break the skin.

Fire in a CMR Area

Should the fire alarm sound whilst work is proceeding in a CMR area, containers should be closed, except where this could cause undue delay, and the building should then be evacuated immediately in the normal way. If a fire is observed in a CMR area, the alarm should be raised immediately. The Incident Controller should be informed as to the state of the area vacated. If an individual is found to have been trapped or incapacitated in a CMR area during a fire, their rescue by the fire service rescue team must be effected irrespective of any likely chemical hazard.

Loss of CMR Material

Should there be any loss or suspected loss of CMR material (including waste) from any area, the Technical Manager (s) must be informed immediately.

Appendix 1

