Guidelines for working safely with carcinogens

Introduction

The aim of this guideline is to create an awareness of the hazards associated with the handling of chemical carcinogens and how their exposure can be safely managed in the workplace. These guidelines should be adopted by Schools, Centres, Institutes and Divisions across the University who use carcinogens, and incorporated into staff development training programs. These guidelines can also be applied to the use of other materials with high toxicity, such as mutagens, teratogens or cytotoxic drugs.

The management of carcinogens at The University of Queensland is overseen by the university OH&S Unit. These procedures have been approved by the university OH&S Council and should be used in conjunction with the Australian Standards for Laboratories (AS2243:1-10) and other documents identified within these guidelines.

Legislative Requirements

The following legislation applies to persons who handle carcinogenic substances.

- Part 16 of the *Queensland Workplace Health and Safety Regulation 1997* *http://www.legislation.qld.gov.au/LEGISLTN/CURRENT/W/WorkplHSaR08.pdf* prescribes requirements for the usage of hazardous substances in the workplace. These regulations must be complied with within Queensland workplaces.
- Australian Standard AS 2243 (Parts 1-10) - Safety in Laboratories;
- National Occupational Health and Safety Council – Exposure Standards for atmospheric contaminants in the occupational environment (1995) - http://www.safeworkaustralia.gov.au/NR/rdonlyres/317D25BA-E837-4F5B-AC65-24FE588888CA/0/ExposureStandards4AtmosphericContaminants_Nov06version.pdf ;
- International Agency for Research on Cancer (IARC) Evaluation of carcinogenic risk of chemicals to humans - http://monographs.iarc.fr/ENG/Classification/index.php
- Queensland Division of Workplace Health and Safety – Guidelines for handling cytotoxic drugs and related waste - http://www.deir.qld.gov.au/workplace/resources/pdfs/cytotoxicdrugs_guide2006.pdf ;
- Australian Standard 2567 – Laminar flow cytotoxic drug cabinets;
- Australia Standard 2639 – Laminar flow cytotoxic drug safety cabinets – installation and use.

Responsibilities within the University

This section details the job responsibilities for individuals who use chemical carcinogens at The University of Queensland.

Supervisor

The supervisor has responsibility for overseeing the health and safety of people in the workplace by ensuring that health and safety information is conveyed and that procedures for safe usage of carcinogens are in place. The responsibilities for supervisors in relation to carcinogens are as follows:

- Ensure that employees and students in work areas are familiar with and follow safe working procedures when using carcinogens;
- Ensure protective equipment is available and functional;
- Identify carcinogens on purchase requisitions;
- Maintain an inventory of all carcinogens in the work area and ensure MSDS's are available;
- Review risk assessments to determine whether workers are following procedures and recommended work practices;
- Ensure information on carcinogen usage is provided to all users via information, training and supervision.

Individual User

Individual users of hazardous chemicals are required to comply with occupational health and safety legislation and ensure that their own health and safety and others is not placed at risk. The following responsibilities are inherent requirements of working with carcinogenic materials:

- Conduct an assessment of the risks associated with the use of the carcinogen(s) with consideration given to the type of carcinogen, it's physical and chemical properties, potential route(s) of exposure, duration of exposure, quantities handled and the specific process involved;
- Prior to commencing work with the carcinogen(s), plan activities, including waste disposal, storage, decontamination;
- Attend required health and safety training;
- Participate in medical surveillance when required;
- Use protective equipment where risk assessment requires;
- Report any occupational health and safety problems to the supervisor or Occupational Health and Safety Unit.

Handling of carcinogens

Where possible, every effort must be made to use non-carcinogenic (or less toxic) chemicals in preference to carcinogenic (or highly toxic) substances. When using carcinogens, the ALARA principle, As Low As Reasonably Achievable, should be adopted.

Exposure to carcinogenic or other highly toxic chemicals can occur by:

- Inhalation of dust or vapour;
- Absorption through the skin from contaminated clothing, spillage on benches, floors or from apparatus; and
- Ingestion from contaminated hands or food, or smoking.

The following work practices should be followed:

- No food, drink or tobacco shall be taken into, prepared or consumed where carcinogenic or highly toxic chemicals are used or stored;
- Hands must be washed immediately upon completing a procedure where a chemical carcinogen has been used and when leaving the work area. Immediately after skin contact or emergency exposure to a carcinogen, wash or, if appropriate, shower the affected area;
- Pipetting by mouth is strictly forbidden. Mechanical pipetting aids or disposable pipetting tips should be used;
- Do not attempt to recap or cut used needles. Dispose the entire needle and syringe in a sharps container for disposal as hazardous waste;
- Warning signs should be located on the door of the work area where carcinogens are used (e.g. Caution – Limited access. Carcinogenic chemicals in use);
- Carcinogenic chemicals should be dispensed from the location at which they are stored. The amount taken should be no more than is required immediately and the aliquots should be labelled with a carcinogen warning and the name of the substance;
- Working surfaces should be covered with an absorbent material backed with plastic and should be replaced at regular intervals or when a spillage occurs;
- All experiments involving dust, vapour or aerosols of a carcinogenic nature should be carried out in a high efficiency fume cupboard. Laminar flow cabinets do not protect the worker from exposure to the carcinogen and should not be used for this purpose;
- Regular housekeeping of bench areas should be performed to prevent contamination from spreading to other areas within the workplace. Special clean-up procedures for spilled carcinogens are described further in the document and should be considered prior to using a chemical.

Material Safety Data Sheets

Material Safety Data Sheets are required to be kept for all hazardous substances used at the workplace, in accordance with the *Queensland Workplace Health and Safety Regulation 2008*. Chemwatch should be accessed to obtain a copy of the MSDS for the substance – located at: http://hazsafety.pf.uq.edu.au/chemwatch/default.htm . Access to the MSDS should be readily available for perusal for the purposes of risk assessment, manufacturer and product identification, health effects, precautions for use, correct storage, emergency and first aid procedures. If the MSDS for the carcinogen is not available from Chemwatch, a copy should be obtained from the manufacturer prior to commencing work with the substance.

If the person using the carcinogen has an adverse exposure to the substance, a copy of the MSDS should be taken with them to the University Health Service to facilitate the administration of first aid.

Storage and Labelling

Designated areas (e.g. an entire laboratory, an area of a laboratory, or a device such as a fume-cupboard) should be identified where carcinogens are used or are to be used. Doors into areas where carcinogenic chemicals are used should be marked to identify the nature of the hazard (e.g. Caution – Limited access. Carcinogenic chemicals in use).

All carcinogenic, suspected carcinogenic or highly toxic chemicals should be stored in screw-cap containers or ampoules at the appropriate temperature and labelled clearly, indicating the chemical composition, date of preparation and the nature of the hazard (ie. Carcinogen – Handle with care). Carcinogens should be packaged to withstand shocks, pressure changes, and any other conditions that may cause leakage of contents.

These materials should be stored in designated areas, cabinets, or refrigerators within the primary work or storage area, with consideration given to incompatibilities with other substances. The MSDS provides information on incompatibilities of classes of chemicals. Precautions should be taken to protect from rodents, weather, incompatible chemicals, and spillage. Additional storage requirements (e.g. use of double containers) may be necessary for certain highly potent carcinogens with physical properties that enhance spontaneous release and exposure (e.g. highly dispersible powders or volatile solids).

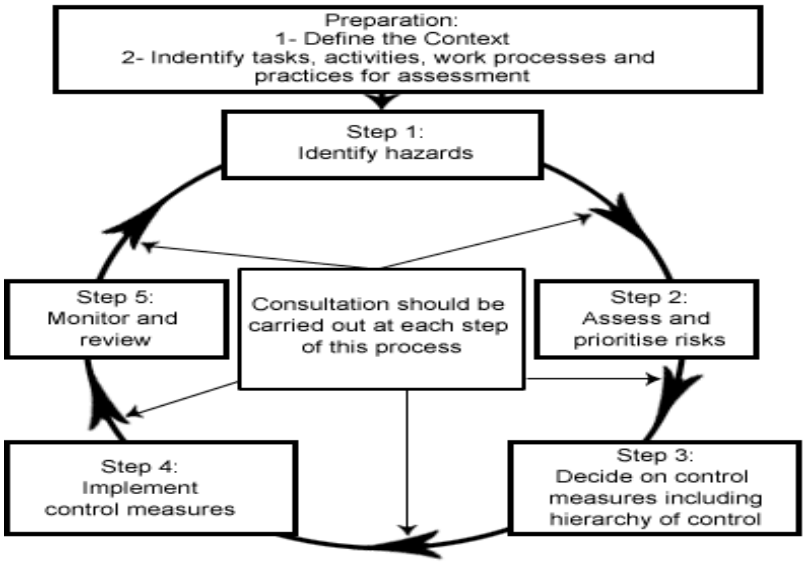
If it is necessary to transport such chemicals within the laboratory, the sealed container should be placed in a second unbreakable container to minimise the risk of accidental breakage or spillage.

An inventory of chemicals should be maintained where they are stored in the workplace

Risk Assessment

Once the proposed use of a carcinogen has been identified, a risk assessment of the overall operation shall be performed to determine the appropriate safety requirements. The *Workplace Health and Safety Regulation 2008* requires that prior to a hazardous substance being used, a risk assessment must be conducted.

The process of risk management for chemicals involves the five steps shown in the following diagram – the five steps are undertaken in a cyclic until an acceptable level of risk is achieved.



An evaluation of the risk associated with the hazard is necessary to determine if the risk is significant, in which case additional or improved measures will be required to control (prevent or minimise) exposure to the hazard. In addition to determining the level of significance of the risk, the risk assessment process serves to facilitate the decisions required for appropriate controls, training, monitoring and health surveillance.

Factors such as the type of carcinogen, its innate carcinogenic potency, physical and chemical properties, potential route(s) of exposure, duration of exposure, quantities handled, controls currently in place and their efficiency, and the specific process involved needs to be assessed. All risk assessments should be conducted and recorded using the University risk management database, located at http://www.uq.edu.au/ohs/

Disposal

Before beginning a laboratory activity that involves a chemical carcinogen, plans should be developed for the handling and disposal of contaminated wastes and surplus carcinogens. Users should properly segregate, package and label all solid and liquid wastes contaminated with carcinogens. Under no circumstance should carcinogenic or highly toxic chemicals be disposed of down drains or into the atmosphere.

Disposal containers can be obtained from the University Chemical Store on extension 51418 or email chemwaste@uq.edu.au .When requesting containers, details of the carcinogens which will be disposed of should be identified so that appropriate labels can be made for the container. All containers which hold carcinogen waste should have a label which states the type of hazard e.g. carcinogenic waste –contains (name of carcinogen).

Cytotoxic waste should be disposed of using the purple cytotoxic bins in accordance with www.pf.uq.edu.au/Ems/Generic/pro_cytxcWste.pdf

Emergency Procedures

Before commencing an activity that involves a chemical carcinogen, plans should be developed for emergency response to spills, exposures or accidents. General guidance for emergency planning includes developing procedures for:

- Evacuating the area and contacting fire department;
- Restricting access to the area;
- Providing care to injured or exposed personnel;
- Showering or washing;
- Obtaining medical attention immediately. Contact University Health Service;
- Decontaminating the area.

Suitable protective clothing should be worn and, if necessary, self-contained breathing apparatus equipment used. The latter should only be worn by people trained in its use.

Personal or significant laboratory contamination should be reported to the laboratory supervisor immediately. An accident/incident report form should be completed on the online reporting database http://www.risk.admin.uq.edu.au/uq-injury/forms/default_content.asp . The supervisor and head of school are both required to sight and sign off on the incident report. A record of all spillages should be kept including the date of spillage, names of persons exposed, carcinogen spilt, quantity and clean-up procedures employed. The incident or injury should be investigated fully by the supervisor and/or workplace health and safety officer and laboratory safety procedures reviewed in light of the findings.

Decontamination

The following decontamination procedures should be followed to prevent spreading of carcinogens within the workplace.

- After using any carcinogenic or highly toxic chemical, users should always rinse their hands well in cold water then wash them thoroughly with soap and hot water;
- Contaminated glassware or equipment should be neutralised with chemicals or washed separately with solvents appropriate for the chemical. The glassware or equipment should then be rinsed in cold running water and washed and brushed in hot water and detergent before being assigned to any routine washing procedure;
- Contaminated benches should be wiped down with cold water followed by hot water and detergent. Similarly, all benches where a carcinogenic or highly toxic chemical has been used should be cleaned regularly, irrespective of known contamination;
- It is essential that an effective system is in operation for the cleaning of protective equipment and for the laundering of laboratory coats;
- Prior to maintenance work being conducted in the area or upon any piece of equipment, all work should cease and the area and equipment be decontaminated. Particular care should be taken to avoid contamination of drains and ventilation ducts;
- Cytotoxic drug cabinet decontamination and the removal and disposal of HEPA filters should be carried out only by specially trained personnel.

Procedures for the chemical destruction of carcinogens are in Appendix I.

Ventilation requirements

Ventilation for controlling exposure to carcinogens may include a combination of the facility features and engineering controls listed below:

- Negative pressure of the workplace relative to common areas (e.g. corridors);
- Filters, traps and scrubbers on air, vacuum and ventilation piping;
- Chemical fume hoods, glove boxes, closed systems and other isolation devices;
- Non permeable work surfaces;
- Secondary containment trays.

Laboratory fume hoods (excluding laminar flow cabinets) are designed to provide protection for the user from chemical and radiological contaminants which are used inside the hood. Use of carcinogenic or highly toxic chemicals should occur in the fume cupboard, not on an open bench. It should be noted that though fume cupboards are designed to protect the user from the hazardous substances being used, fume cupboards do not eliminate exposure 100% even under ideal conditions. Careless work practices can cause considerable exposure to a user who may believe they are protected. To optimise the performance of the fume hood, the following work practices should be adhered to:

- Ensure that the fume hood has a current inspection sticker (dated within the last year). If the face velocity of the fume-hood has failed the inspection, work involving carcinogens should not

commence until the fume hood exhaust system is repaired.

- Utilise the hood with the sash positioned as low as possible (usually 45cm in height). This will ensure adequate face velocity and allow the sash to act as a protective shield. Keep hood sashes down to an opening of about 15cm when the hood is not in use to conserve energy in variable air volume systems.
- The fume hood is not a storage cabinet. Do not store significant quantities of chemicals within the hood as these materials can obstruct the air flow or exacerbate an incident or emergency in the hood. However, minor quantities of waste or highly toxic chemicals may be stored within the hood, as this may be safer than storing on the open bench. Highly hazardous chemicals should not be stored in fume hoods in which high hazard processes are being undertaken (e.g. heating, pressurised equipment etc).
- The degree to which these controls should be applied depends on the safety level of the operation.
- Use of solid materials may not require a ventilated enclosure, but highly volatile chemicals or those that generate aerosols or dusts should be conducted in a ventilated enclosure or with a local exhaust system above the process.
- Analytical instruments that produce vapours or aerosols should be connected to a mechanical exhaust system when used with carcinogens. 'Ductless' hoods should not be used for carcinogens.

Glove boxes are used for handling highly toxic substances, unsealed radioactive materials and for carrying out operations with extremely high emission rates. Glove boxes are operated under negative pressure using a pump or exhaust fan arrangement. The exit gases should be trapped or filtered through a HEPA filter and then released into the hood exhaust.

A cytotoxic drug safety cabinet is used where a sterile environment is required for the product being worked with, but personal protective equipment (PPE) is also required. A typical example of when these cabinets are used is during the weighing out of cytotoxic drugs in a hospital pharmacy. Cytotoxic Drug Safety Cabinets should be installed and used in accordance with AS 2639 – 1994.

Personal Protective Equipment

A risk assessment of the process and a review of the material safety data sheet will indicate which control measures are required to control the workers exposure. When controlling exposure to occupational hazards the Workplace Health and Safety Act requires that the hierarchy of controls is followed, (i.e. controls ranging from elimination and substitution of the hazard, to ventilation, through to personal protective equipment).

Personal Protective equipment is considered the least effective control measure and should only be considered to complement another control measures.

Personal protective equipment should be chosen for its suitability to the task (e.g. comfort, enables dexterity of movement) as well as to the chemical and physical properties of the substance to be used, its volatility, stability, flammability, solubility and miscibility.

When working with hazardous chemicals, the minimum laboratory attire which must be worn is laboratory coat, safety glasses and closed footwear. Additional protective equipment such as face shields, gloves and respiratory protection (where ventilation is ineffective) may be required in certain cases.

When handling carcinogenic chemicals, chemically resistant gloves must be worn. A chemical resistance

guide for glove materials should be used to determine the best type of glove for the carcinogen being handled. For example, Ansell produces a chart which lists glove materials and the permeation and degradation ratings for use with particular chemicals. This chart, in conjunction with the material safety data sheet should be referenced prior to commencing work with carcinogenic chemicals. Gloves should be inspected before each use, cleaned and replaced periodically.

Protective equipment should be stored adjacent to the work area and should not be taken to other areas of the laboratory. Laboratory coats, in particular, should be removed and stored before leaving the laboratory and should not be worn in rooms designated for eating and drinking.

Protective clothing (e.g. labcoats) should be cleaned by an industrial laundry rather than being taken home by the wearer. In situations where significant contamination has occurred, equipment should be disposed of or decontaminated prior to cleaning. For the purposes of cleaning and maintaining personal protective equipment, there should be a training program in place, especially if such equipment is re-useable. If possible, protective equipment should be designed and used for operations involving carcinogen handling alone.

Animal facilities

Working with animals which have been administered with carcinogenic chemicals can present a high risk to the person handling the animal or the animal's excreta. The following work practices are recommended for the use of carcinogens in animal experiments:

- **Compliance with legislation and Code of Practices:** All experiments involving animals must be carried out in accordance with the NH&MRC publication, *Australian code of practice for the care and use of animals for scientific purposes – 7th edition 2004* http://www.nhmrc.gov.au/publications/synopses/ea16syn.htm . In addition, investigators must ensure compliance with relevant federal or state legislation regarding the use of experimental animals. Such compliance at the University of Queensland will include written approval of the University Animal Experimentation Ethics Committee and may also be conditional upon approval by the University Biosafety Committee.
- **Isolation of animal(s):** Animals treated with carcinogenic or other highly toxic chemicals (e.g. cytotoxic drugs) should be isolated and housed in such a manner that other experimental animals will not be contaminated. The species may govern the appropriate means of containment. For large animals (e.g. sheep or other livestock), this may best be achieved by keeping animals in a separate room.
- **Cages**: These should be clearly labelled indicating the ethical clearance number, a carcinogen hazard warning label and the carcinogen in use.
- **Biological activity of substance**: Special consideration should be given to the method of administering such chemicals or compounds of unknown biological activity. Volatile chemicals represent the greatest risk through inhalation and should be administered by injection of a solution.
- **Topical application**: Administration by topical application, gavage or intra-traceal instillation should be performed in a fume cupboard. This will only be appropriate for small to medium sized animals. Where the size of the animal makes the use of a fume cupboard impractical, the area must be adequately ventilated and protective clothing worn. If the chemical used is likely to be exhaled, the animal should be kept under the fume cupboard during this period. Ideally, purpose built exposure

chambers with known tolerances should be used.

- Such tolerances should principally include the resistance of the chamber to chemicals (solvents, etc.) and the maximum tolerated pressure. Exposure chambers not within this category should be set up inside a fume cupboard.
- **Food and water**: Administration of volatile chemicals to animals in their food and water is very difficult to perform without contaminating cages and other equipment. Therefore, unless specifically required, methods or administration other than in diet should be used. Mixing of carcinogenic or highly toxic chemicals in diet should be carried out in sealed mixers in a fume cupboard. Special protective clothing and respiratory protection may be required when mixing diets.
- **Animal waste**: The risk from excreta-contaminated animal bedding or residual food can be reduced by either:

(a) using heavy adsorbent paper rather than sawdust in cages of open-tray bedding; or
(b) housing the animals in cages of completely closed design (solid base and walls, with metal roof grille).

- **Waste disposal:** Carcasses of laboratory animals, cage litter and miscellaneous solid wastes that are known to be contaminated or which could be contaminated should be double bagged, labelled clearly and stored whilst awaiting disposal. This includes disposable protective clothing, gloves, shoe covers, plastic-backed absorbent paper, residues from the clean-up of carcinogenic chemical spills, and exhaust air filters.
- Autoclaving of waste material will not disperse or neutralise carcinogens and can present a hazard to staff operating the autoclave. Carcinogenic substances will need to be removed from the surface of cages before autoclaving.
- **Information and education:** All staff who are likely to work near or in the area holding the animal(s) used in the experiments using carcinogens must be informed of the experiment, potential hazards and safety precautions to be implemented in the handling of the animals, disposal of waste, action to be taken in the event of an accidental spill of carcinogen or exposure to the substance. If appropriate, staff must be informed of the different hazards associated with the substance (e.g. atmospheric contaminant such as formaldehyde or an anti neoplastic agent such as procarbazine).
- Those responsible for the daily management of an animal facility are to be advised of the experimental substance so appropriate precautions can be implemented.
- **Personal protection:** When staff or students are performing any task involving carcinogenic substances (preparation of substance, feeding or watering animals, cleaning of cages and disposing of animal waste), they should wear as a minimum:
    - A long sleeved gown with closed front and elasticised cuffs or overalls;
    - Safety spectacles with side shields, goggles or full face shield; and
    - Gloves which are specific to the chemical being handled.

For further information on working safely with cytotoxic drugs and animals, refer to the OH&S guideline for cytotoxic compounds and related waste http://www.uq.edu.au/ohs/pdfs/cytotoxic-guideline.pdf .

Carcinogen Clearance requirements

Carcinogen clearance is a requirement of research grant application for the Australian Research Council (ARC) and National Health and Medical Research Council (NHMRC) granting bodies if research falls within IARC category 1, category 2A and category 2B carcinogens. Refer to the following link for classifications http://monographs.iarc.fr/ENG/Classification/index.php

Prior to receiving a grant, the granting body requires that the Institutional Biosafety Committee evaluate the risks associated with the use of the proposed carcinogens to be used within the experiment, and ensure that adequate precautions for use have been determined.

This is not a new requirement at the University; however, more stringent control will be exercised by the Institutional Biosafety Committee to ensure that the clearance applications are received. The Occupational Health and Safety Unit is responsible for reviewing the carcinogen clearance form, and ensuring that the controls to be implemented will control the user's exposure to carcinogens.

The process requires that any researcher applying for an ARC or NHMRC grant, should complete the carcinogen clearance form at the following web address: http://www.uq.edu.au/ohs/pdfs/carcinogenform.pdf This should be sent to the Occupational Health and Safety Unit for approval. As much information relating to precautions for use should be included on the form, to ensure the clearance is provided as quickly as possible. Once the Occupational Hygiene Adviser is satisfied with the procedures to be employed during the project, a letter advising of approval for carcinogen work will be sent to the individual researcher and the University Biosafety Adviser. The approval will then be forwarded to the granting body with the application.

APPENDIX I
Laboratory decontamination and destruction of carcinogens in laboratory wastes.

The following methods of decontamination and destruction of carcinogens in laboratory wastes are based on procedures published by the International Agency for Research on Cancer (IARC).

Organic compounds, including carcinogens, can be destroyed by sodium dichromate in a strong solution of sulphuric acid. One to two days is generally considered sufficient time for the destruction of chemicals when a freshly prepared reagent is used. By then all material should have dissolved in the reagent and can be rinsed away with water.

Carcinogens that oxidise readily can be destroyed with milder agents such as saturated solution of potassium permanganate in acetone. This solution is suitable for the destruction of hydrazines or compounds containing isolated carbon-carbon double bonds. Concentrated or 50 per cent aqueous sodium hypochlorite can also be used as an oxiding agent.

Carcinogens that are alkylating, arylating or acrylating agents can be destroyed by reaction with nucleophiles such as water, hydroxyl ions, ammonia, thiols and thiosulfate. The reaction of alkylating agents varies greatly, however, and is influenced by the solubility in the reaction medium. The complete reaction can be facilitated by dissolving the agents in ethanol or similar solvents.

Methyl methanesulfonate and ethyl methanesulfonate are moderately soluble in water and can be destroyed in 10% thiosulfate solution. Special care should be taken, however, when gram or greater quantities of these compounds and other highly reactive reagents have to be destroyed. Large volumes of aqueous bicarbonate solutions are recommended in preference to 10% thiosulfate solutions which may cause violent reactions.

Ethyleneimine and its derivatives can be destroyed by acid-catalysed hydrolysis or by thiosulfate buffered to PH 5.

Cyclophosphamide can be destroyed by potassium hydroxide in methanol.
N-Methyl-N'-nitro-N-nitrosoguanidine (MNNG) is slowly hydrolysed in water but is rapidly destroyed by 10% thiosulfate solution. The treatment of MMNG and related nitrosamides, such as N-nitrosomethyl-and N-nitrosoethylurea, with alkali should be avoided or carried out with extreme care because of the toxic gaseous diazomethane produced.

N-Nitrosodimethylamine can be destroyed by dichromate-sulphuric acid; it may also be reduced by e.g. zinc powder and acetic acid or by caustic soda and aluminium to the carcinogen, demethylhydrazine, which in turn has to be oxidised (e.g. using a permanganate solution). Nitrosamines also can be split into nitrites and amines by hydrobromic acid and acetic acid. Effective destruction of N-nitrosamines at levels below 500ppm may be achieved by hydrochloric acid and hydrobromic acid.

Polycyclic aromatic hydrocarbons (PAH's), such as benz[*a*]pyrene, can be oxidised readily by a dichromate-sulphuric acid mixture.

Aflatoxins can be degraded by adding hypochlorite solution to the material to be decontaminated, followed by acetone to destroy any 2,3-dichloro aflatoxin B1 which may have been formed.

Aromatic amines can only be destroyed by high temperature incineration. Refer to the University waste disposal procedures available at www.pf.uq.edu.au/Ems/Generic/pro_ChmWste.pdf .