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The University of Manchester

Safety Services Guidance

Guidance on the Use and Control of Chemical Carcinogens, Mutagens and Reproductive Toxins (CMRs)

Key word(s) :	Carcinogen, mutagen, reproductive toxin, COSHH, risk assessment?
Target audience :	Research Staff and students using CMRs, PIs, Safety Advisors

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Introduction

1. This document is intended to provide day to day operational and practical guidance for users of Carcinogens, Mutagens and Reproductive toxins (CMRs) to comply with the principles outlined in the University Arrangements Chapter 22.

2. In view of the serious and often irreversible effects of exposure to CMRs, prevention of exposure is the first priority. CMRs must not be used, or processes involving them be carried out, if there is a suitable non-hazardous or less hazardous substance that can be used instead. When working with CMRs, the control of exposure is to as low a level as reasonably practicable as the concept of a "safe limit" is not normally applicable[1]. There is a significant risk of death associated with many forms of cancer, and the level of exposure affects only the probability of cancers occurring in those exposed, and not the severity of the resultant disease.

3. When considering the use of alternative substances, users should take into account the potential health effects and physical properties of these alternatives.

4. Undergraduate students are not generally expected to work with CMRs but there are some instances, for sound academic reasons, where undergraduates will need to use them. In these instances, the risk assessments must take into account that undergraduates are relatively inexperienced and ensure that there is sufficient information, instruction, training and supervision in place before and during the activity.

5. Control of CMRs is achieved through working according to protocols derived from suitable risk assessments which have been prepared under the Control of Substances Hazardous to Health Regulations (COSHH) and the supporting Approved Code of Practice (ACOP)[2].

Identification of CMRs

[1] EH40: Workplace Exposure Limits http://www.hse.gov.uk/pUbns/priced/eh40.pdf , (free downloadable copy available).

[2] Control of Substances Hazardous to Health Regulations 2002 (as amended) Approved Code of Practice http://www.hse.gov.uk/pubns/books/l5.htm

6. There is no definitive list of CMRs. The best information will be the suppliers Safety Data Sheet (SDS) or Material Safety Data Sheet (MSDS). There is, however, a list of Carcinogens supplied in Schedule 1 of the COSHH Regulations[2].

7. The legal requirements for the classification, labelling and packaging of all chemicals, including mixtures, have changed due to the implementation, in the EU, of the Classification, Labelling and Packaging of Substances and Mixtures (CLP) Regulation[3]. The full implementation of the CLP Regulation (June 2015) will lead to the repeal of the Classification (Hazard Information and Packaging) Regulations (CHIP) 2009[4].

8. The change ensures a higher standard of labelling and more consistent identification of the hazards of a specific chemical and thus mainly affects manufacturers and suppliers of chemicals. However, the CLP Regulation alters the definitions of CMRs which affect their classification and labelling.

9. The CLP Regulation identifies 3 classes of CMRs; 1A, 1B, and 2, which correlate loosely (but not exactly) with classes 1, 2, and 3 respectively, under the CHIP Regulations. Class 2 chemicals under the CLP Regulation have hazard statements 'suspected of causing' or 'suspected of damaging' or 'may cause harm' whereas under CHIP, the Category 3 CMRs had risk phrases 'limited evidence' or 'possible risk' of an effect.

10. The University has decided that it would be reasonably practicable, and in line with the precautionary principle, to consider and treat CLP categories 1A, 1B and 2 of CMRs with the same degree of caution and as outlined in this guidance.

11. The following table summarises and compares the CLP and CHIP classification of CMRs.

[3] European Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation), http://www.hse.gov.uk/chemical-classification/legal/clp-regulation.htm
[4] The Chemicals (Hazard Information for Package and Supply) Regulations 2009 (CHIP), http://www.hse.gov.uk/chemical-classification/legal/chip-regulations.htm

Hazard Class and Category (CLP)	Pictogram/Signal word (CLP)	Hazard Statements (CLP)	Hazard Class and Category (CHIP)	Pictogram/Hazard Warning (CHIP)	Risk Phrases (CHIP)
Carcinogen Category 1A: Known to have carcinogenic potential in humans	 Danger	**Carcinogen** H350 – may cause cancer H350i – may cause cancer by inhalation	**Carcinogen** Category 1: Substances known to be carcinogenic to humans	 T+ very toxic T toxic	**Carcinogen** R45 – may cause cancer R49 – may cause cancer by inhalation
Carcinogen Category 1B: Presumed to have carcinogenic potential in humans	As above	**Carcinogen** H350 – may cause cancer H350i – may cause cancer by inhalation	**Carcinogen** Category 2: Substances that should be regarded as carcinogenic to humans	As above	**Carcinogen** R45 – may cause cancer R49 – may cause cancer by inhalation
Carcinogen Category 2: Suspected human carcinogen	 Warning	**Carcinogen** H351 – suspected of causing cancer H351i – suspected of causing cancer by inhalation	**Carcinogen** Category 3: Substances that may cause concern owing to possible carcinogenic effects	 Harmful	**Carcinogen** R40 – limited evidence of carcinogenic effect

Hazard Class and Category (CLP)	Pictogram/Signal word (CLP)	Hazard Statements (CLP)	Hazard Class and Category (CHIP)	Pictogram/Hazard Warning (CHIP)	Risk Phrases (CHIP)
Germ Cell Mutagenicity Category 1A	 Danger	**Germ Cell Mutagenicity** H340 – may cause genetic defects	**Mutagen** Category 1: Substances known to be mutagenic to humans, i.e. induce heritable genetic defects or increase their incidence	 T+ very toxic T toxic	**Mutagen** R46 – may cause heritable genetic damage
Germ Cell Mutagenicity Category 1B	As above	**Germ Cell Mutagenicity** H340 – may cause genetic defects	**Mutagen** Category 2: Substances that should be regarded as mutagenic to humans.	As above	**Mutagen** R46 – may cause heritable genetic damage
Germ Cell Mutagenicity Category 2	 Warning	**Germ Cell Mutagenicity** H341 – suspected of causing genetic defects	**Mutagen** Category 3: Substances that may cause concern owing to possible mutagenic effects	 Harmful	**Mutagen** R68 – possible risk of irreversible effects

Hazard Class and Category (CLP)	Pictogram/Signal word (CLP)	Hazard Statements (CLP)	Hazard Class and Category (CHIP)	Pictogram/Hazard Warning (CHIP)	Risk Phrases (CHIP)
Reproductive toxin Category 1A	 Danger	**Reproductive toxin** H360 – may damage fertility or the unborn child	**Reproductive toxin** Category 1: Substances that induce heritable genetic defects or increase their incidence	 T+ very toxic T toxic	**Reproductive toxin** R60 – may impair fertility R61 – may cause harm to the unborn child
Reproductive Toxin Category 1B	As above	**Reproductive Toxin** H360 – may damage fertility or the unborn child	**Reproductive Toxin** Category 2: Substances that induce heritable genetic defects or increase their incidence	As above	**Reproductive Toxin** R60 – may impair fertility R61 – may cause harm to the unborn child
Reproductive Toxin Category 2	 Warning	**Reproductive Toxin** H361 – suspected of damaging fertility or the unborn child	**Reproductive Toxin** Category 3: Substances that may cause concern owing to possible mutagenic effects	 Harmful	**Reproductive Toxin** R62 – possible risk of impaired fertility R63 – possible risk of harm to the unborn child

Hazard Class and Category (CLP)	Pictogram/Signal word (CLP)	Hazard Statements (CLP)	Hazard Class and Category (CHIP)	Pictogram/Hazard Warning (CHIP)	Risk Phrases (CHIP)
Additional category Reproductive Toxicity effects on or via lactation	No pictogram	H362 – may cause harm to breastfed children	**Additional category**	No pictogram	R64 – may cause harm to breastfed babies

Control of exposure to CMRs

12. Those planning to use or produce known or suspected CMRs must carry out a COSHH assessment before work commences. The assessment for potential exposure to any CMR should follow the basic principles of good practice for COSHH assessment.

13. When planning the use of the CMR, consider:

a) the physical state of the CMR:
- gas (or other airborne state, e.g. fume, mist, fog, aerosol, etc.)
- liquid (low boiling point liquids being potentially more likely to lead to exposure than high boiling point liquids) or
- solid (fine, powdery solids being more likely to lead to exposure than large crystalline or pelleted material).

b) The likely route of exposure – commonly either inhalation or skin absorption - less commonly direct entry *via* e.g. needlestick injury or open wound, and the level of exposure.

c) All staff and students using or affected by the use of CMRs, with particular attention given to the identification of those users or other people falling into a vulnerable group and who may be at particular risk (e.g. young[5], old, pregnant[6], breastfeeding, immumo-compromised), must sign and print their names on the risk assessment.

d) The control measures to be used to prevent or reduce exposure, including any instruction for not allowing workers at particular risk (see c) in areas where they may be exposed to CMRs.

e) Operating instructions and maintenance regimes, where relevant, must ensure that exposure is reduced to as low as reasonably practicable.

f) Cleaning staff working in CMR designated areas and maintenance staff working on equipment that may have been contaminated with CMRs must only proceed with their tasks once a permit to work or clearance certificate has been obtained.

g) Precautions that must be taken when conditions are not routine, e.g. emergencies and maintenance activities

h) Use of personal protective equipment

[5] HSE Guidance on Young People at Work
[6] HSE Guidance on New and Expectant Mothers at Work

i) Relevant monitoring procedures

j) Relevant health surveillance procedures

k) Details of essential information and training requirements and the procedure for reporting any accidental release or potential exposure, defects in equipment or procedures.

NB Everyone working with CMRs in a research laboratory or workshop must have a valid “fitness to work” certificate. Undergraduates handling CMRs in practical classes who are well and closely supervised do not need a “fitness to work” certificate unless they are either pregnant or immune-compromised or otherwise ‘vulnerable.’

14. When completing the COSHH assessment, the ‘hierarchy of control’ should be followed. This means that measure a) should be implemented as far as reasonably practicable, before measure b) is considered, and so on.

    a) Eliminate the use of the CMR if possible

    b) Substitute the CMR with a non-CMR e.g. benzene with cyclohexane, or work with soft woods rather than hard woods if possible. If the use of a safer alternative substance or process is not reasonably practicable, then adequate control of exposure must be achieved and maintained. Where Workplace Exposure Limits (WELs) are set, these levels must not be exceeded.

    c) Modify the process and or workplace to reduce exposure, for example if a researcher is going to use a CMR but their fume hood is by the door of a laboratory, investigate doing the work in a fume hood in an area of the laboratory where passing footfall is potentially much lower.

    d) Enclose the process (e.g. use a glove box) or use partial enclosure such as local exhaust ventilation (LEV) (e.g. a fume hood, microbiological safety cabinet).

    e) Develop and adopt safe systems of work. Never purchase or make up more material than is needed. Purchase of pre-weighed material is recommended. If this is not available, for example, weigh a stoppered container first and then add the CMR in a fume hood or under LEV, re-stopper the container and reweigh it (do not handle the opened CMR over the balance). Repeat until sufficient material has been weighed, but adjust the proportions of the other chemicals to suit if possible to reduce the handling of the CMR. Clean up any spills immediately and put the soiled cleaning materials and chemical residues – e.g. blue roll, tissues etc. into a labelled and sealed container for disposal by specialist contractor.

f) Use appropriate personal protective equipment – labcoat, gloves, eye protection etc. PPE should be disposable where possible. Laboratory coats should be fastened – consider also the use of a disposable polythene apron. Gloves should be selected bearing in mind the manufacturers performance data and any recommendations given in the SDS (MSDS). Experimental procedures should be designed to minimise splashing and aerosol formation, visors should be available if appropriate. If the use of close fitting respiratory protection is necessary, face fit testing must be carried out before it is used. Contaminated items should either be decontaminated by experienced personnel before being removed from the designated area or be disposed of in appropriately labelled containers by a licensed contractor.

g) Confirm that sufficient information, instruction, training and supervision has been received and understood to ensure that the work can be carried out safely. This is particularly important for users from overseas who do not speak English as a first language. NB Where personal protective equipment is a control, the level of supervision should be sufficient to note improper use or fit, or users not wearing it, and to take steps to ensure it used and worn correctly.

15. In addition, the following measures must be adopted:

a) Prohibit eating (including chewing gum), drinking, application of cosmetics, smoking and mouth pipetting in areas where CMRs are present.

b) Clearly designate areas and equipment for CMR use; display suitable warning signs and restrict access to the minimum number of people. The laboratory door should be closed when work is in progress. The work area needs to be suitably sized to ensure people can work safely without physical obstruction.

c) Do not contaminate equipment that others might use – e.g. by rigorously removing gloves when touching items that are not directly associated with the experiment or procedure, such as PCs, door and drawer handles etc.

d) CMRs must be stored, handled and disposed of safely, using closed and clearly labelled containers.

e) Ensure good hygiene measures are in place, including cleaning procedures to remove any contamination from walls, doors, tools, equipment (e.g. balances), clothing, PPE, other surfaces (e.g. internal linings of fume hoods)

f) Ensure there are adequate washing facilities so that employees can maintain a high standard of personal hygiene, which will reduce exposure and avoid the spread of CMRs.

Recording the COSHH Assessment

16. Where CMR use is identified a written record of the COSHH assessment must be made. This should include the names and signatures of everyone carrying out the work activities and should be reviewed at regular intervals, e.g. annually; when the activity has significantly changed; as new information becomes available; or when new workers become involved or the health status of an existing worker has changed etc.

17. A copy of the assessment must be kept according to local arrangements for the storage of risk assessments. Please contact your local Safety Advisor for these details.

Monitoring

18. Where the COSHH assessment concludes that the control measures may not be adequate to control exposure by inhalation, air monitoring will be necessary. In laboratories where the control measures are working efficiently (i.e. fume hood face velocity is as per the original specification) usage is low, duration of the experiment is short, quantitative monitoring should not be necessary.

19. In certain circumstances, e.g. following a spillage, qualitative monitoring using a UV lamp to detect fluorescent substances can be useful in determining the location of surface contamination. Contact Safety Services for further advice on monitoring.

Health Surveillance

20. A comprehensive COSHH assessment seeks to eliminate or reduce exposure to harmful substances to insignificant levels due to the implementation of control measures. If there is either a failure of the control measures so that exposure to a CMR has occurred, or that residual exposures after controls are in place are significant, the PI or affected individual must contact the University Occupational Health Service to discuss health surveillance requirements. They should also complete the Exposure to CMR Health Surveillance Form.

21. If a member of staff or a student reports symptoms of exposure then the PI/Supervisor must notify Safety Services using the Event Notification Form.

22. The purpose of the Event notification is twofold:

a) Safety Services staff will assist the School in checking the COSHH assessment, the effectiveness of the existing control measures and the validity of the

conclusion about exposure and ensure that records are archived for the legally required time period.

b) Safety Services staff will liaise with Occupational Health to ensure that health surveillance is initiated if appropriate.

Good Working Practice when using CMRs

23. The use of substances known to be CMRs can only be justified by careful consideration of the alternatives and the importance of the work. Work on a small scale rather than a large scale. Any novel compound with a molecular structure closely related to that of a known CMR should be treated, in the absence of any information to the contrary, with the same degree of caution that would be used with a known CMR. Use substances in the least harmful physical form, for example pellets rather than dusts, high boiling point liquids rather than low boiling point liquids etc.

24. Before starting work assemble all the materials and equipment which will be required in order to avoid cross contamination (touching of doors, cupboards etc.) with potentially contaminated gloves.

25. Work with CMRs should only be undertaken by people who:

a) Are aware of the hazardous properties of the substance(s)

b) Are suitably experienced

c) Have been instructed in the appropriate techniques

d) Have read all the relevant safety documentation e.g. local arrangements, standard operating procedures and are aware of and have implemented the necessary controls

e) Have read and signed that they have understood the appropriate risk assessment(s) and where appropriate are directly supervised during the work until competent

f) Are medically fit for work with CMRs following health screening unless they are being directly and closely supervised as stated in Chapter 22 of the University Arrangements on working with CMRs.

g) CMRs should be stored in unbreakable plastic containers (or be doubly contained if originally in glass), labelled with the appropriate hazard warnings. When not in use they should be kept in a locked storage unit bearing the names

and contact details of responsible people who may be contacted 'out of hours' in the event of an emergency. CMRs that are too volatile to be stored as above should be kept in a suitably ventilated unit with restricted access and only be opened in a fume hood or under LEV to avoid possible exposure to a build-up of vapour.

26. Pregnant women, women likely to become pregnant or those breast feeding must not work with reproductive toxins where a risk assessment has indicated significant uptake by the workers involved. Strict controls must be observed to ensure that women likely to come into contact with known or suspect reproductive toxins are warned of the risk. (See also Guidance on New and Expectant Mothers at Work)

27. Care must still be taken to avoid exposure to reproductive toxins by men as well as women not of child-bearing age.

28. New or unfamiliar techniques should be practised using a non CMR before commencing work with the real thing. This is especially important when working with animals due to the additional hazard of unpredictable behaviour when substances are being administered and special care is required in their handling and restraint.

29. Where small samples of CMRs need to be taken into non-designated areas, e.g. for specialised analysis, the same stringent precautions should be observed in respect of labelling, handling, containment, decontamination and waste disposal as are required in designated areas.

30. If local exhaust ventilation (LEV) is used as a means of control, e.g. a fume cupboard the airflow must be sufficient to reduce exposure to below the WEL prescribed in EH40, Workplace Exposure Limits, an HSE publication and the COSHH Approved Code of Practice and guidance.

31. Use of a fume cupboard must not place at risk those who might be affected by the emissions to atmosphere. COSHH also requires that all control measures are properly maintained. Further information is available from either the School Safety Advisor or University Safety Coordinator.

Accidental spillage or loss of containment

32. Any accidental spillage or uncontrolled release of a CMR which could have caused someone to be exposed to it must be reported to Safety Services on an Incident Form. Please also include an estimation of the amount of CMR released and any physical properties e.g. solid, liquid (boiling point), gas etc. which can be used to assess the likely exposure. Safety Services will then initiate an investigation into

the incident and ensure that the appropriate records are retained in accordance with the legal requirements.

33. Other documents that will be required in the investigation include any associated chemical and general risk assessments relating to the incident.

Additional precautions for animal work

34. Work with laboratory animals should only be conducted after discussion and agreement with the manager of the Biological Services Facility.

35. Metabolism may inactivate CMRs *in vivo* in animals or may convert them to other toxic substances. Problems associated with the exhalation or excretion of hazardous materials should be considered for each individual experiment, as dosage and other factors may affect the degree and duration of the hazard.

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