

Policy and guidelines for the use of chemical carcinogens, mutagens and substances toxic to reproduction (CMR)

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1. Introduction

This document describes the control measures appropriate for meeting legal requirements and promoting best practice for work involving the use of carcinogens, mutagens, and substances toxic to reproduction (STR) often referred to as CMR (Carcinogens, Mutagens and Substances Toxic to Reproduction). It aims to provide Heads of Schools/ Departments and others responsible for the use of known **or suspected** CMR's with information on the steps they need to take to ensure compliance with current legislation. These guidelines should, where appropriate, be incorporated into School/ departmental policies and specific experimental procedures.

2. Scope

The Control of Substances Hazardous to Health [COSHH] Regulations 2002 (as amended) place specific legal duties on employers, relating to the use of carcinogens [Agents which cause cancer]. These statutory requirements relate specifically to those agents which must be labelled Carcinogen Category 1A or Carcinogen Category 1B under the Classification, Labelling and Packaging [CLP] of Substances & Mixtures Regulations. In June 2015 the CLP regulations fully replaced Chemicals (Hazard Information and Packaging) Regulations 2002 [CHIP] and introduced changes to hazard pictograms, and introduced Hazard and Precautionary Statements in place of Risk and Safety Phrases. Tables 1 & 2 show both new classifications under CLP and how these relate to the previous CHIP classification.

Mutagens [agents that cause heritable genetic changes] and substances toxic to reproduction [agents that impair fertility or cause harm to a developing foetus], are not subject to the same specific legislative requirements as carcinogens.

For the purpose of this Policy and associated guidelines no further distinction is drawn between these categories and the procedural requirements must be applied to all. The term CMR has been used throughout the document as a generic term to cover all categories.

3. Responsibilities

The following responsibilities are in addition to the general responsibility for safety as laid down in the University Safety Policy.

3.1. Heads of School must ensure that arrangements are in place to:

- Identify those procedures carried out within the School that involve the use of substances which fall into the category of CMR [see Section 4 for definitions and classification]
- Ensure safe storage, labelling and transport of any such agents
- Ensure risk assessments are undertaken
- Ensure that employees/students/visitors who may work with these agents are authorised and suitably trained in the standards required and ensure these are conformed to.
- In order to assist him/her in discharging these responsibilities the Head of School may nominate a suitably qualified and competent individual to act on their behalf and to give advice on the safe use of these agents.

3.2. **Principal Investigators and Scientific Supervisors.**

In addition to the requirement for ensuring suitable risk assessments are undertaken, the PI must also ensure that:

- workers within their group are informed of the nature of the hazard,
- workers are authorised and suitably trained in the control measures to be applied to remove or reduce risks to a minimum and are competent to carry out the work,
- training records must be kept,
- an appropriate level of supervision is maintained at all times
- Further information on training and supervision can be found here;
<http://www.nottingham.ac.uk/safety/safety-management/supervision/supervision.aspx>

3.3. Individual workers have a duty to protect themselves and others from any hazards arising out of their work and therefore must comply with the requirements of this code.

4. Definitions

Under CLP each hazard, is categorised depending on the degree of the severity of the hazard with category 1 being the most hazardous / harmful.

4.1. Carcinogens are agents that cause cancer and fall into two categories. **Table 1** shows the definitions of the categories, the CLP hazard pictograms, hazard statement and classification under the new CLP regime. More detailed information is contained in Appendix I.

4.2. Mutagens are substances that cause heritable genetic changes (mutations). Most mutations are harmful and most mutagens are carcinogens and vice versa. See Table 2.

4.3. Substances toxic to reproduction (STR) are substances known to impair fertility or to cause developmental toxicity in humans. This definition covers a broader range of health effects than the earlier "teratogenic" which applied only to substances that adversely affected the developing foetus.

Mutagens and STRs are classified similarly to carcinogens in Categories 1 to 2. See **Table 2**.

4.4. **Oncogenes**

An oncogene is a gene that causes the transformation of normal cells into cancerous tumour cells, especially a viral gene that transforms a host cell into a tumour cell. Guidance on the control measures to be adopted when working with oncogenic sequences and naked oncogenic DNA can be found in the *University Code of Practice for Work with Biological Agents and Genetically Modified Organisms*.

5. Sources of information on categorisation

Appendix I contains the following information




- List of substances detailed in Schedule 1 of COSHH Regs 2002 (As amended)
- List of Cat 1 & 2 carcinogens as previously classified under CHIP 2002 in the Approved Supply List [ASL]. This list is no longer updated as the CHIP regulations were revoked on 1st June 2015 but is left in for reference.
- List of Mutagens and STR as previously classified under CHIP [ASL]. This list is no longer updated as the CHIP regulations were revoked on 1st June 2015 but is left in for reference.

The International Agency for Cancer Research [IARC]. The IARC is part of the World Health Organisation. Its' 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. Over the years it has published a series of Monographs on a variety of chemicals and classes of substance and has classified them according to severity of carcinogenic hazard.

The IARC have a [searchable database](#) which lists the classification of a large number of substances lists. This also details the Monograph volumes that also provide useful information on deactivation and disposal regimes.

TABLE 1 CATEGORISATION OF CARCINOGENS





Note – CHIP Risk Phrases and Categorisation are no longer valid and are provided as historic contextual information

Category	CLP Category & Definition	CLP Hazard Statement	Previous CHIP Risk Phrase	CHIP classification	Example
	Category 1A Chemicals known to have a carcinogenic potential for humans based largely on human evidence.	H350 – may cause cancer. H350i – may cause cancer by inhalation	R 45 may cause cancer or R49 may cause cancer by inhalation	Category 1	Arsenic, Asbestos, Benzene For more detailed list see App I
	Category 1B chemicals – presumed to have a carcinogenic potential for humans based largely on animal evidence	H350 – may cause cancer. H350i – may cause cancer by inhalation	R 45 may cause cancer or R49 may cause cancer by inhalation Toxic (T) symbol	Category 2	Acrylamide Diazomethane For more detailed list see App I
	Category 2 Suspected human carcinogens – based on human and animal evidence but which is not sufficiently convincing to place chemical in Cat 1	H351 – suspected of causing cancer	R40 (Limited evidence of carcinogenic effect). Harmful (Xn) symbol	Category 3	These would include novel compounds of undetermined carcinogenicity that may be synthesised in house, but have yet to be fully tested.

Categories 1A & 1B [formerly Cat 1 and 2 under CHIP] are subject to specific control under COSHH.

Category 2 [formerly Cat 3 under CHIP] are not included in the COSHH definition of a carcinogen but are subject to the general requirements of COSHH.

Table 2 - Categorisation of mutagens and STRs

Category	CLP Category & Definition	CLP Hazard statement	Risk phrase CHIP
Mutagens 	Category 1A chemicals known to induce heritable mutations in germ cells of humans. Category 1B chemicals which should be regarded as if they induce heritable mutations in germ cells of humans	H340 May cause genetic defects	R46 May cause heritable genetic damage
Mutagens 	Category 2 – chemicals which cause concern for man owing to the possibility that they may induce heritable mutations in germ cells of humans	H341 Suspected of causing genetic defects	R68 Possible risk of irreversible effects
STR 	Category 1A – chemicals known to be human reproductive toxicant. Category 1B – chemicals presumed to be human reproductive toxicant.	H360 May damage the unborn child/impair fertility	R60 May impair fertility or R61 May cause harm to the unborn child
STR 	Category 2 - chemicals suspected to be human reproductive toxicant [where evidence not sufficiently convincing to place in Cat 1]	H361 Suspected of damaging fertility / the unborn child	R62 Possible risk of impaired fertility R63 Possible risk of harm to the unborn child.

Note: Cat 1 substances, unlike carcinogens, are not specifically prescribed in COSHH but should be subject to the same requirements as carcinogens.

6. Risk Assessment

As with any other chemical, a **risk assessment** must be carried out for the procedure involving the use of a CMR. The assessment should take account of the following:

- identification of the substance to be used and justification for its use
- the nature and severity of the hazard i.e. is it a CMR?
- whether substitution by a less hazardous substance is reasonably practicable.
- evaluation of the risk of exposure. Are there any workers who may be at particular risk including possible risks to pregnant women?
- identify the control measures by which exposure can be **prevented** or if not *reasonably practicable* **controlled**. [**See Table 3**]
- precautions under non-routine conditions e.g. emergencies
- use of personal protective equipment
- waste disposal and deactivation protocol [**See App IV**]
- monitoring procedures, where necessary [e.g. testing for contamination]
- health surveillance procedures
- information/training and supervisory requirements

The assessment must be reviewed:

- if there is any indication that control measures may not be working such as following an accident or incident or if indicated by monitoring activities.
- if there is any change to the process
- in the event of neither of the above, at least annually.

7. Control of exposure

7.1. Physical and procedural controls

The COSHH Regulations set out strict statutory and legal obligations in relation to the control of exposure to carcinogens to prevent exposure. **Table 3** specifies the principles and hierarchy of measures that are legally required and must be adhered to and offers some practical advice on how these can be implemented.

TABLE 3**PHYSICAL & PROCEDURAL CONTROLS**

Control measure	Practical advice for implementation (these should be considered and documented in your risk assessment)
Prevent exposure	Investigators must consider: <ul style="list-style-type: none">• Substitution – replacing either the substance or the process with a safer alternative• Avoiding the formation of carcinogenic by-products or intermediates.
<i>If prevention is not possible, control exposure to as low as reasonably practicable by the use of:</i> Total Enclosure of the process or parts of the process that could result in exposure (<i>unless not reasonably practicable</i>)	<ul style="list-style-type: none">• Use a glove box or isolator

<p>Use of plant, processes and systems of work which minimise the generation of, or suppress and contain spills, leaks, fumes and vapours</p>	<ul style="list-style-type: none"> • A risk assessment and SOP MUST be produced for the task / protocol using the CMR. • Make sure that safe storage, handling, labelling, decontamination and disposal methods are available. • Use a fume cupboard or powder weighing cabinet specifically designed for use with CMR/highly toxic compounds (Not a weigh-safe). Make sure it is working and be aware of air turbulence as this can spread fine powders within the fume cupboard. An example of a safe weighing protocol is included in Appendix III. • Handling must be confined to dedicated areas that are clearly identified with appropriate hazard signs. • Obtain agents in pre-weighed vials or 'isovac' containers to remove need for dispensing [even if this is more expensive]. • Purchase CMR in the smallest amounts available for practical use. • Minimise frequency and duration of use. If the compound is stable in solution then weigh out enough for several experiments and divide into suitable aliquots for future use. • Where possible, work over a tray to contain spills. • Ensure effective spillage and emergency procedures are in place. • Minimise the number of people exposed. Exclude non-essential personnel. • Good occupational hygiene, wash hands after handling compound. No eating drinking /smoking/application of cosmetics.
<p>Training & Supervision</p>	<ul style="list-style-type: none"> • Ensure those carrying out the dispensing process are skilled, experienced and fully trained in the safe use of these compounds. PIs are asked to nominate one or two people in the group who are authorised to do this on behalf of less experience workers. • Training must be recorded.
<p>Maintenance of controls</p>	<ul style="list-style-type: none"> • Ensure that all controls are maintained and working for example annual checks on LEV by a competent person and monthly face velocity checks by a trained user. • Testing for contamination where necessary and physically possible
<p>Personal protective equipment may be used as secondary protection but must never be the primary means of controlling exposure.</p>	<ul style="list-style-type: none"> • Lab coat should be double fronted, side fastening with cuffs. • Gloves should be of the correct type depending on the nature of the compound and any associated solvent that may be involved. Check glove manufacturers' charts or seek advice. Gloves MUST be of a minimum of UoN Class C. Information on UoN Glove Standards. • Respiratory protection [RPE] such as face masks may only be worn as a secondary means of protection in addition to working in a fume cupboard or in the event of a spill outside primary containment. RPE must be of the correct type and, depending on type, may require face fit testing. The wearer must have received suitable training in the correct use of the RPE. A regime of checks should be in place for RPE.

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| | <ul style="list-style-type: none">• Protective clothing must not be worn outside the area designated for work with CMR. |
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7.1.1. Storage

The substances listed in **Appendix I** must be kept in securely closed containers except when in use and must be stored in secured areas.

Storage of CMR substances must be kept to a minimum. Containers and storage areas must be clearly identified and labelled with appropriate hazard signs [see table 2]

7.1.2. Decontamination & Disposal

The procedure for safe disposal of CMR and materials contaminated by them, must be determined as part of the risk assessment process, before the agent is put into use.

Many CMR can be rendered harmless by the addition of an appropriate chemical solution – often strong acid or alkali.

If the compound cannot be deactivated it will be subject to the requirements of Hazardous Waste Regulations and will require disposal by specialist contractor. Seek advice from the Environmental Manager in the Estate Office about disposal.

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

7.1.3. Emergency procedures

Safety data sheets [SDS] will give details of first aid and spill procedures for specific compounds. These should be referred to before commencing the work as part of the risk assessment process. Specific first aid and spill information should be included in the assessment and incorporated into the safe operating procedure.

Appendix V gives general first aid guidance which should be followed in addition to any specific actions identified by the risk assessment.

7.1.4. Transport

Ideally work should be organised in such a way as to avoid the transport of CMR outside the room where they are stored. Where transport to another lab or area within the University is unavoidable, secondary containers must be used to reduce the risk of any spillage.

Transport outside of the University on public highway is subject to the requirements of the Carriage of Dangerous Goods Regulations. A courier service licensed to transport such substances may be warranted in certain circumstances. Refer to the [University Code of Practice for the Transport of Dangerous Goods](#) or contact the Safety Office for advice.

7.2. Administrative controls

7.2.1. Approval for work

All new procedures involving the use of known/suspected carcinogens must be covered by a suitable and sufficient risk assessment which has been approved and validated in accordance with the School's procedures. The person approving the assessment must be satisfied that

- the use is essential,
- the proposed scale of the work is justified
- that adequate facilities exist to allow its safe use, storage and disposal
- the investigator undertaking the work is trained and competent

The person approving the work must sign to that effect on the process risk assessment and SOP.

7.2.2. Work procedures

All work involving known or suspected CMR must be carried out in accordance with specific written standard safe operating procedures [SOP]. These must be drawn up in light of the risk assessment findings and in accordance with the principles outlined in Table 3 above.

7.2.3. Authorised Users

Providing the control measures detailed in Table 3 are adopted and adhered to, individuals' exposure will be effectively zero. Additionally, as there is no known safe level of exposure, there is little value in recording every time a powdered carcinogen is dispensed; however Schools/Departments must ensure that processes involving CMR are appropriately risk assessed, users trained and training records kept.

This can best be achieved by recording the training in section 4 of the [training record template](#) or equivalent local process and ensuring that a list of authorised users is appended to the risk assessment for the procedure in which the CMR is used. The procedural risk assessment must include the following information:

- Title of project/ procedure,
- The full chemical name of the CMR along with any trade name or short name by which it is commonly referred to,
- Quantity normally used in the procedure,
- The form [liquid, gas, powder],
- Name of responsible scientist /PI,
- A list of authorised users involved in the work including the date they started on the project and the date they finished.

Any accidental exposure to a CMR such as might occur as result of spillage must be recorded – see 8.2 below.

8. Monitoring

8.1. Proactive monitoring of the workplace

Because exposure to CMR can result in serious health effects, consideration must be given to appropriate monitoring procedures in the form of:

8.1.1 Local Exhaust Ventilation (LEV) Inspection and Monitoring

- LEV includes fumehoods, MSC's, extract hoods and other ventilated enclosures provided to protect health.
- Regular checks at pre-determined intervals that engineering controls are operating effectively and that procedures are being followed.
- All LEV should be subject to an annual maintenance inspection and monthly user checks.
- Fume cupboards annual maintenance checks are arranged by Estates, other LEV is arranged by the school / user.

8.1.2 Environmental Monitoring

- Environmental monitoring of the work area outside of the primary containment facility. E.g. monitoring for surface contamination or airborne contamination to demonstrate control or to detect significant unplanned releases.
- Environmental monitoring is mandatory by law for any procedure involving the use of vinyl chloride monomer and spray given off from vessels at which an electrolytic chromium process is carried on, except trivalent chromium.
- The results of environmental monitoring must be compared with any prescribed standards [e.g. Workplace exposure limits] where available. Where these levels are shown to have been exceeded this must be recorded and the record must be retained for 40 years. In order to ensure the integrity of any such record, the [University's on-line Accident/Incident](#) recording system should be used.

8.2. Reactive monitoring - Accident/incident recording

Where an incident occurs, that results in the potential or actual exposure of any individual to a CMR, even if there is no apparent health effect, it must be recorded on the University Accident/Incident reporting system. The Safety Office must be immediately informed as such an occurrence may be reportable to the HSE.

The individual should be referred to Occupational Health who will ensure an appropriate entry is made on the individual's health record.

All accident / incidents reports, logged on the university system and all health records are maintained by the University for 40 years as required under COSHH.

9. Training and supervision

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

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

10. Use of carcinogens for teaching

The use of powdered or highly concentrated solution of CMR, particularly those regulated by law, for teaching is prohibited. Use of aqueous solutions which contain CMR in low concentration for teaching is permitted subject to risk assessment and authorisation by an individual nominated by the Head of School/Department and the ongoing need and conditions of use reviewed annually, see Appendix VI for details on concentrations.

11. Health Surveillance

Health surveillance has its limitations in identifying people at risk or in detecting signs of cancer early enough for effective medical intervention.

Health surveillance will be required where the work will entail sufficient exposure that there is a reasonable likelihood of an adverse health effect arising. Health surveillance is mandatory for work entailing exposure to the following carcinogenic substances:

Column 1	Column 2
<i>Substances for which medical surveillance is appropriate</i>	<i>Process</i>
<i>Vinyl chloride monomer (VCM).</i>	<i>In manufacture, production, reclamation, storage, discharge, transport, use or polymerisation.</i>
<i>Nitro or amino derivatives of phenol and of benzene or its homologues.</i>	<i>In the manufacture of nitro or amino derivatives of phenol and of benzene or its homologues and the making of explosives with the use of any of these substances.</i>
<i>Potassium or sodium chromate or dichromate.</i>	<i>In manufacture.</i>
<i>Ortho-tolidine and its salts. Dianisidine and its salts. Dichlorobenzidine and its salts.</i>	<i>In manufacture, formation or use of these substances.</i>
<i>Auramine. Magenta.</i>	<i>In manufacture.</i>
<i>Carbon disulphide. Disulphur dichloride. Benzene, including benzol. Carbon tetrachloride. Trichlorethylene.</i>	<i>Processes in which these substances are used, or given off as vapour, in the manufacture of indiarubber or of articles or goods made wholly or partially of indiarubber.</i>
<i>Pitch.</i>	<i>In manufacture of blocks of fuel consisting of coal, coal dust, coke or slurry with pitch as a binding substance.</i>

Otherwise careful application of the hierarchy of control described in Table 3 should ensure there is no reasonable likelihood of an identifiable disease or adverse health effect occurring, therefore health surveillance is not required.

Further clarification as to whether health surveillance may be required should be sought from Occupational Health.

12. New and expectant mothers

Whilst the use of the control measures outlined above should be sufficient to prevent exposure to all workers, pregnant women and their unborn child may be particularly vulnerable to the effects of these substances. When a female worker becomes pregnant she must immediately inform her line manager and/or the School Safety Officer so that an additional risk assessment can be undertaken before carrying out any further work with these substances.

Female workers who work with CMR and who are contemplating becoming pregnant should seek advice from their GP or from Occupational Health.



Appendix I

Schedule 1 – COSHH Regulations.

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 (ft, fi'-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, Hp=hepta and O=Octa.

Indicative List of Carcinogens

List of Cat 1 & 2 carcinogens as previously classified under CHIP 2002 in the Approved Supply List [ASL]. This list is no longer updated as the CHIP regulations were revoked on 1st June 2015 but is left in for reference.

Carcinogens

Substances assigned the risk phrases R45 (May cause cancer) and R49 (May cause cancer by inhalation) under CHIP

Category 1- R45

CAS Numbers

4-Aminobiphenyl and its salts	92-67-1
Arsenic acid and its salts	
Arsenic pentoxide	1303-28-2
Arsenic trioxide	1327-53-3
Asbestos	132207-33-1
Benzene	132207-33-1
Benzidine and its salts	92-87-5
Bis(chloromethyl)ether	542-88-1
Chloromethyl methyl ether (chlorodimethyl ether)	
Chromium trioxide	1333-82-0
Dinickel trioxide	1314-06-3
Erionite	12510-42-8
2-Naphthylamine and its salts	91-59-8
Nickel dioxide	12035-36-8
Nickel monoxide	1313-99-1
Nickel subsulphide	12035-72-2
Nickel sulphide	16812-54-7
Vinyl chloride (Chloroethylene)	75-01-4
Zinc chromates including zinc potassium chromate	

Category 2 [R49]

Acrylamide CAS:	79-06-1
Acrylonitrile	107-13-1
4-Aminoazobenzene	60-09-3
<i>o</i> -Aminoazotoluene	
4-Amino-3-fluorophenol	399-95-1
Benzo-[a]-anthracene	56-55-3
Benzo-[a]-pyrene	50-32-8
Benzo-[b]-fluoranthene	205-99-2
Benzo-[j]-fluoranthene	205-82-3
Benzo-[k]-fluoranthene	207-08-9
Benzotrichloride (<i>alpha, alpha, alpha</i> -trichlorotoluene)	98-07-7

Beryllium	7440-41-7
Beryllium compounds except aluminium beryllium silicates	
1,3-Butadiene	106-99-0
Cadmium chloride	10108-64-2
Cadmium oxide	1306-19-0
Cadmium sulphate	10124-36-4
Calcium chromate	13765-19-0
Captafol (ISO)	2425-06-1
Carbadox (INN)	6804-07-5
1-Chloro-2,3-epoxypropane (Epichlorohydrin)	106-89-8
Chromium(III) chromate	24613-89-6
Chromium (VI) compounds	
4,4'-Diaminodiphenylmethane	101-77-9
Diazomethane	334-88-3
Dibenz[a,h]anthracene	53-70-3
1,2-Dibromo-3-chloropropane	96-12-8
1,2-Dibromoethane (Ethylene dibromide)	106-93-4
3,3'-Dichlorobenzidine and its salts	91-94-1
1,4-Dichlorobut-2-ene	764-41-0
1,2-Dichloroethane (Ethylene dichloride)	107-06-2
2,2'-Dichloro-4,4'-methylenedianiline (MbOCA) and its salts	101-14-4
1,3-Dichloro-2-propanol	96-23-1
Diethyl sulphate	64-67-5
3,3'-Dimethoxybenzidine (o-dianisidine) and its salts	119-90-4
3,3'-Dimethylbenzidine and its salts	119-93-7
1,2-Dimethylhydrazine	540-73-8
N,N-Dimethylhydrazine	57-14-7
Dimethylcarbamoyl chloride	79-44-7
Dimethylsulphamoyl chloride	13360-57-1
Dimethyl sulphate	77-78-1
Disodium{5-[4'-((2,6-hydroxy-3-((2-hydroxy-5-sulphophenyl)azo)phenyl)azo)(1,1'-biphenyl)-4-yl)azo]salicylato(4-)} cuprate(2-) (C.I. Direct Brown 95)	16071-86-6
1,2-Epoxypropane (propylene oxide)	75-56-9
Ethyleneimine (aziridine)	151-56-4
Ethylene oxide (oxirane)	75-21-8
Hexachlorobenzene	118-74-1
Hexamethylphosphoric triamide (HMPA)	680-31-9
Hydrazine and its salts	302-01-2
Hydrazobenzene (1,2-diphenylhydrazine)	122-66-7
Hydrocarbons C26-55, arom. rich	97722-04-8
2-Methoxyaniline (o-anisidine)	90-04-0
Methyl acrylamidomethoxyacetate (containing at least 0.1% acrylamide)	77402-03-0

2-Methylaziridine (Propyleneimine)	75-55-8
Methyl-ONN-azoxymethyl acetate	592-62-1
4,4'-Methylenedi- <i>o</i> -toluidine	838-88-0
1-Methyl-3-nitro-1-nitrosoguanidine	70-25-7
4-Methyl- <i>m</i> -phenylenediamine	95-80-7
5-Nitroacenaphthene	602-87-9
4-Nitrobiphenyl	92-93-3
Nitrofen (ISO)	1836-75-5
2-Nitronaphthalene	581-89-5
2-Nitropropane	79-46-9
N-nitrosodimethylamine	
N-nitrosodipropylamine	
2,2'-(Nitrosoimino)bisethanol	1116-54-7
Petroleum, Petroleum products	
Potassium bromate	7758-01-2
Potassium dichromate	7778-50-9
1,3-Propanesultone	1120-71-4
3-Propanolide (1,3-propiolactone)	57-57-8
Strontium chromate	7789-06-2
Styrene oxide	96-09-3
Sulfallate (ISO)	95-06-7
Thioacetamide	62-55-5
<i>o</i> -Toluidine and its salts	95-53-4
4- <i>o</i> -Tolylazo- <i>o</i> -toluidine (Fast Garnet)	97-56-3
Trichloroethylene	79-01-6
Urethane (INN) (ethyl carbamate)	

Mutagens

List of Mutagens and STR as previously classified under CHIP [ASL]. This list is no longer updated as the CHIP regulations were revoked on 1st June 2015 but is left in for reference.

Substances assigned the risk phrase R46, "May cause heritable genetic damage":

Acrylamide	79-06-1
Benzo[a]pyrene	50-32-8
1,2-Dibromo-3-chloropropane	96-12-8
Diethyl sulphate	64-67-5
Ethyleneimine	151-56-4
Ethylene oxide	75-21-8
Hexamethylphosphoric triamide	680-31-9
Methyl acrylamidomethoxyacetate	
(containing at least 0.1% acrylamide)	77402-03-0

Reproductive Toxins.

Substances assigned risk phrases R60 "May impair fertility" or R61 "May cause harm to the unborn child":

Category 1

Lead compounds

Warfarin (4-hydroxy-3-(3-oxo-1-phenylbutyl)coumarin) 81-81-2

Category 2

Benzo[a]pyrene	50-32-8
Binapacryl (ISO)	485-31-4
Dimethylformamide (DMF)	68-12-2
Dinoseb, its salts and esters	88-85-7
Dinoterb, its salts and esters	1420-07-1
2-Ethoxyethanol	110-80-5
2-Ethoxyethyl acetate	111-15-9
Ethylene thiourea	96-45-7
2-Ethylhexyl 3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl -	
methyl thioacetate	80387-97-9
2-Methoxyethanol	109-86-4
2-Methoxyethyl acetate	110-49-6
Methyl-ONN-azoxymethyl acetate	592-62-1
Nickel tetracarbonyl	13463-39-3
Nitrofen (ISO)	1836-75-5

Appendix II - Background information on Cancer & Carcinogens

Cancer is a disorder of cells in the body. It begins with a group of cells that fail to respond to the normal control mechanism and continue to divide without need. The new growths are called tumours or neoplasia and may be either "benign" or "malignant". A "benign" tumour is one that remains localised whereas "malignant" tumours invade neighbouring tissues, enter blood vessels, lymphatic vessels and other spaces and can be carried to other areas of the body to form new tumours called "secondaries" or "metastases".

Cancer may arise from various causes, one of which is the adverse effects of certain substances on the cells of the body either directly or via their metabolites. Other important known factors associated with an increased risk of cancer in humans include smoking, sexual promiscuity and low fibre diet.

The following factors have a bearing on the risk of cancer developing:

Dose Some carcinogens are extremely potent and can induce cancer at very low dose levels in a susceptible species. There is often no knowledge available about the lower threshold of dose below which cancer will not occur. The probability that cancer will result is usually proportional to the dose, except that very high doses may have more immediate toxic effects.

Duration of Exposure Unlike radiation protection control, there is no simple way of monitoring individual exposure to chemical carcinogens. A single exposure to a carcinogen may be sufficient to induce cancer.

Latency With carcinogens, there is no immediate indication that harm has resulted from exposure, unless the agent has some other toxic effect. Long intervals generally elapse between exposure to carcinogens and the appearance of tumours resulting from the exposure. Intervals of two or three decades are not unusual.

Co-factors Some carcinogenic agents are unable to produce cancer alone. Subsequent exposure to another agent is necessary to amplify or promote the initial carcinogenic injury.

Routes of Entry Carcinogens can enter the human body by the following routes:

- by mouth into the gut
- by inhalation into the lungs
- by skin contact

The resulting cancers do not necessarily appear at the site of entry, because carcinogens require chemical transformation in the body into their active form.



Appendix III - Model procedure for weighing solid CMR and other toxic compounds

Considerations before handling:

- Has the process in which the compound is to be used, been subject to a suitable and sufficient COSHH Risk assessment? **If not, do not proceed – consult your supervisor.**
- Could you substitute a less harmful compound? **If yes do so.**
- Is the compound available in pre-weighed iso-vac containers? **If yes, order it in that form.**
- Have you been trained in how to carry out the procedure safely and assessed as being competent? **If not, do not proceed – consult your supervisor.**
- Decontamination, spillage and disposal procedures must have been determined by the risk assessment. **Ensure you are aware of these and have appropriate materials in hand before you start the procedure.**

Choice of equipment:

- Precision balances are sensitive to air movement and therefore will not perform optimally if placed in a fume cupboard (FC). In schools/departments where there is a need weigh carcinogens regularly, a balance should be sited adjacent to the FC, preferably just to one side of the sash opening.
- Very fine lyophilised powders may fly about within the FC if the fans are on. In this case it would be wise to consider a totally enclosed system such as an isolator
- Glass screw cap vials should be used in preference to plastic as the latter are more prone to static charge.

Procedure:

- Rehearse procedures by practicing with a non hazardous compound if similar form and make sure you know what to do in the event of a spillage.
- Ensure you are wearing a lab coat [fastened] and PPE Category 3; UoN Cat C nitrile gloves. Reduce static charge on gloves by rinsing hands in water and patting dry.
- Ensure the fume cupboard is operating efficiently and there is a good draw of air through the front aperture. Position the sash as low as possible.
- Place all items, including the substance, on a shallow tray within the fume cupboard, at least 150mm back from the opening.
- Switch on balance adjacent to the FC. When it has stabilised, zero the display and place empty, capped weighing vessel onto to pan, close doors and when reading has stabilised 'tare' to set display to zero.
- Return vessel to tray in FC, remove cap and dispense powder into vessel, recap and wipe exterior with damp tissue soaked in deactivation fluid.

- Re weigh vial and repeat until approximately the desired weight of compound is achieved. Calculate amount of diluent required to give desired concentration and add this within the fume cupboard and recap the vial.
- Ensure that the spatula is placed in decontamination solution. Wipe down the tray and all surfaces with deactivation fluid.
- Comply with any local recording procedures that are in place.



Appendix IV - Disposal guidance and common procedures

Carcinogens, mutagens and substances toxic to reproduction are considered hazardous waste under the Hazardous Waste Regulations 2005 where the total concentration exceeds the threshold limits shown in the table below.

Category	Hazard statement	Hazard code	Threshold limit
Carcinogen Cat 1A & 1B	H 350/350i	H7 Carcinogen	≥ 0.1%
Carcinogen Cat 2	H 351	H7 Carcinogen	≥ 1%
Mutagens Cat 1A & 1B	H340	H11 Mutagen	≥ 0.1%
Mutagens Cat 2	H341	H11 Mutagen	≥ 1%
STR Cat 1A & 1B	H360	H10 Toxic for reproduction	≥ 0.5%
STR Cat 3	H361	H10	≥ 5%

Disposal of Hazardous Waste must be organised with an approved licensed contractor. Further information can be obtained from the Environmental Manager in the Estate Office or from the University Safety Office.

Waste treatments in the laboratory

The following treatment regimes can be adopted:

- **Solid/liquid material** must be treated as Hazardous Waste [see above].
- **Spatulas and other none disposal items** which may be contaminated with small amounts of carcinogen /toxic substance should be decontaminated by suitable means.
- **Disposable items** such as weighing boats, pipettes, plastic tubes/vials, plates and wipes should be discarded into a yellow bag and sent for incineration. If the concentration in the container is estimated to be in excess of the threshold values shown above then this must be treated as Hazardous Waste.
- **Glassware** must be decontaminated and rendered safe before sending for washing.
- **Sharps** contaminated with carcinogens, such as needles and syringes must be disposed of directly into sharps bin. Do not re-sheath needle.



Appendix V - **First Aid Procedures**

The following general guidance should be followed in addition to any specific actions identified by the risk assessment.

Ingestion

The likelihood of ingestion is remote. In the event of this occurring, seek immediate medical advice.

Inhalation

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

Eye splash/mucous membrane contamination

Irrigate with sterile water for 15 minutes. Seek medical advice.

Skin spillage

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

Refer the individual to Occupational Health who will ensure an appropriate entry is made on the individual's health record.

Ensure the incident is recorded on the University Accident/Incident reporting system.

Inform the Safety Office immediately as such an occurrence may be reportable to the HSE.



Appendix VI - Using diluted hazardous CMR substances.

There may be occasions when CMR substances are required for use in diluted form and risk assessment indicates that some CMR controls are not required. The guidance below helps identify the concentration when a CMR substance is diluted enough to no longer be classified as CMR.

Under CLP there are specified concentration limits used when classifying mixtures, these are of relevance when doing a COSHH assessment of mixtures and diluted solutions.

- **Concentration limit:** Threshold concentration above which classification will be triggered for a specific hazard class;
- **Specific concentration limit:** a concentration limit that is specific to a substance and takes precedence over generic concentration limit.

The following generic concentration limits are specified for CMR substances in CLP.

Hazard Class	Generic Concentration Limit %
Carcinogen 1A (H350)	≥0.1
Carcinogen 1B (H350)	≥0.1
Carcinogen 2 (H351)	≥1.0
Mutagen 1A (H340)	≥0.1
Mutagen 1B (H340)	≥0.1
Mutagen 2 (H341)	≥1.0
Reproductive Toxicant 1A (H360)	≥0.3
Reproductive Toxicant 1B (H360)	≥0.3
Reproductive Toxicant 2 (H361)	≥3.0
Reproductive Toxicant (effects on or via lactation) (H362)	≥0.3

Note 1: The concentration limits in the table apply to solids and liquids (w/w units) and gases (v/v units)

Note 2: Test data takes precedence over concentration limits. If there is test data to show that the mixture is hazardous at levels lower than the concentration limit then the mixture must be classified in accordance with the data.

Note 3: Whilst the above concentration limits can be considered when categorising CMR mixtures, it should be remembered that under COSHH exposure to carcinogens should be prevented so far as is reasonably practicable.

Specific Concentration Limits

Specific concentration limits can be found in the CLP regulations; <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02008R1272-20160101&from=EN> and also on the SDS sheet. An example is shown below for phenolphthalein which has hazard code of H350 but a concentration limit of $\geq 1\%$ which is higher than the generic concentration limit.

Information from CLP regs;

604-076-00-1	phenolphthalein	201-004-7	77-09-8	Carc. 1B Muta. 2 Repr. 2	H350 H341 H361f***	GHS08 Dgr	H350 H341 H361f***	Carc. 1B; H350: C $\geq 1\%$
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Information from SDS;

SECTION 3: Composition/information on ingredients

3.1 Substances

Synonyms : 3,3-Bis(4-hydroxyphenyl)-1(3*H*)-isobenzofuranone

Formula : C₂₀H₁₄O₄

Molecular weight : 318.32 g/mol

CAS-No. : 77-09-8

EC-No. : 201-004-7

Index-No. : 604-076-00-1

Hazardous ingredients according to Regulation (EC) No 1272/2008

Component	Classification	Concentration
Phenolphthalein Included in the Candidate List of Substances of Very High Concern (SVHC) according to Regulation (EC) No. 1907/2006 (REACH)		
CAS-No. : 77-09-8	Muta. 2; Carc. 1B; Repr. 2; H341, H350, H361f	$\leq 100\%$
EC-No. : 201-004-7	Concentration limits:	
Index-No. : 604-076-00-1	$\geq 1\%$: Carc. 1B, H350;	

For the full text of the H-Statements mentioned in this Section, see Section 16.

Concentration limits for substances with other hazardous properties

Whilst there are concentration limits set under CLP for other hazards there are other variables which need to be considered such as cut off limits and additive hazards.

Generally the control measures specified in a risk assessment for these hazards would not change due to a dilution factor, however should this be required full details can be found under CLP; <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02008R1272-20160101&from=EN>

or contact the Safety Office for further advice.