Australian Government

National Occupational
Health and Safety Commission

APPROVED CRITERIA FOR CLASSIFYING HAZARDOUS SUBSTANCES [NOHSC:1008(2004)]

3rd Edition

October 2004

The National Occupational Health and Safety Commission (NOHSC) has declared the *Approved Criteria for Classifying Hazardous Substances,* 3rd Edition.

National standards declared by NOHSC under s.38(1) of the *National Occupational Health and Safety Commission Act 1985* (Commonwealth) are documents which prescribe preventive action to avert occupational deaths, injuries and diseases. Most national standards deal with the elimination, reduction or management of specific workplace hazards.

The expectation of the Australian Government and NOHSC is that national standards will be suitable for adoption by the Australian, State and Territory governments. Such action will increase uniformity in the regulation of occupational health and safety throughout Australia and contribute to the enhanced efficiency of the Australian economy.

It should be noted that NOHSC documents are instruments of an advisory character, except where a law, other than the *National Occupational Health and Safety Commission Act 1985*, or an instrument made under such a law, makes them mandatory.

The application of any NOHSC document in any particular State or Territory is the prerogative of that State or Territory.

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FOREWORD

The National Occupational Health and Safety Commission (NOHSC) is a tripartite body established by the Australian Government to lead and coordinate national efforts to prevent or reduce the incidence and severity of occupational injury and disease by providing healthy and safe working environments.

In seeking to improve Australia's occupational health and safety (OHS) performance, NOHSC works to:

- support and add value to efforts in the jurisdictions to tailor approaches to prevention improvement;
- facilitate, through strategic alliances, the development and implementation of better approaches to achieving improved prevention outcomes; and
- integrate the needs of small business into its work.

NOHSC has developed a strategic approach to injury and disease prevention that focuses on identifying nationally significant OHS problems and providing practical solutions to these problems for workplaces.

This approach has four elements. They are:

Identifying OH&S problems - National and international data and research will identify developing and emerging OH & S problems, including major trends, gaps and issues.

Finding practical solutions - Prevention initiatives that have been successful in one State or Territory will be evaluated, adapted and made available to all jurisdictions. The focus will be on finding practical solutions and, ideally, the best combination of measures to accelerate prevention improvement in workplaces, and reduce the need for government intervention.

Facilitating improved prevention performance - Improved prevention performance will be facilitated by ensuring that workplaces have available to them information and strategies that are practical and relevant to their needs.

Measuring performance – NOHSC will measure the prevention performance of the jurisdictions and the nation as a whole, and use the findings for continuous improvement of prevention efforts.

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PREFACE

Under NOHSC's *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)][1] (National Model Regulations) and the Australian, State and Territory government regulations introduced in accordance with the National Model Regulations, *manufacturers* and *importers* of substances supplied for use at work are required to determine whether they are hazardous to health before supply.

They are also required to produce labels and Material Safety Data Sheets (MSDS) for all hazardous substances, with appropriate information about the hazards of these substances.

Determining whether a substance is hazardous to health is central to the safe management of substances used in the workplace.

To determine whether a substance is a hazardous substance, manufacturers and importers should first refer to the *List of Designated Hazardous Substances* (the List), published by NOHSC. The List comprises the more common hazardous substances that meet NOHSC's *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] (the Approved Criteria). Under the National Model Regulations if a substance is on the List then it is a hazardous substance. The List is therefore an aid to determining and classifying hazardous substances.

When a substance is not included on the List, the manufacturer or importer will need to use the Approved Criteria to determine if it is hazardous to health. If the substance is determined to be hazardous, the Approved Criteria enable the health hazard(s) to be identified so that MSDS and labels can be more easily prepared.

The classification criteria used in this publication are adopted from European Community's (EC) legislation for classifying dangerous substances. The criteria are taken from:

- EC Council Directive 67/548/EEC[3] on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (Dangerous Substances Directive, DSD); and,

- Directive 1999/45/EC[4] of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations (the Dangerous Preparations Directive, DPD).

To take into account technical progress and changes in the EC Council Directives, it is intended that the classification criteria contained in the Approved Criteria be updated from time to time.

This third edition has been updated to generally reflect the current status of:

- EC Council Directive 67/548/EEC as amended by Commission Directive 2001/59/EC[5] of 6 August 2001, and;
- Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 as amended by Commission Directive 2001/60/EC[7] of 7 August 2001.

The main changes to the European Directives include:

- the replacement of Dangerous Preparations Directive 88/379/EEC by a new Dangerous Preparations Directive 1999/45/EC in which the technical content has been moved to a number of Annexes that can be revised by Adaptations to Technical Progress;
- the introduction of three new Risk phrases – R66, R67, and R68;
- the replacement of R40 with R68, and a change of use and wording for R40;
- the inclusion of criteria for classifying substances on the basis of their physico-chemical and ecotoxicological effects;
- a list and criteria for use of safety phrases;
- the provision of both generic and specific concentration cut-off levels for mixtures containing substances classified as hazardous on the basis of their health and environmental effects;
- the inclusion of criteria for the evaluation of the health hazards of mixtures containing hazardous ingredients having sensitising, carcinogenic, mutagenic, and toxic for reproduction effects; and,
- a new appendix listing special provisions applying to certain dangerous preparations, supplied to / used by the general public and/or workplaces.

These changes are reflected in the Approved Criteria.

In the EC Directives, criteria for classifying substances or preparations on the basis of their physicochemical properties or environmental effects have been included. In the Approved Criteria, these criteria are provided as Appendices (Appendix 6, 7 respectively). They do not form a mandatory part of the Approved Criteria, but are provided for information only.

Other inclusions to the Approved Criteria comprise a listing of particular provisions concerning certain preparations, which are provided at Appendix 8. In Australia, the Approved Criteria described in Chapters 1-7 are mandatory and are given effect under the *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)] (National Model regulations) and the Australian, State and Territory regulations introduced in accordance with the National Model Regulations. The provisions described in Appendix 8 are not mandatory under current Australian workplace chemicals regulations and as such are provided here for information only.

The inclusion of appendices covering non-mandatory material in the current Approved Criteria will facilitate the gradual transition to the GHS, in line with the anticipated adoption

by the United Nations of the harmonisation system. Subsequently, the Approved Criteria will be reviewed to consider the transition to the mandatory use in Australia of physicochemical and environmental criteria.

In summary, the Approved Criteria are designed to be used by manufacturers and importers for determining whether substances are hazardous or not, and for preparing labels and MSDS. They will also be used by NOHSC to review and maintain the *List of Designated Hazardous Substances*.

It is not expected that employers and employees using substances in the workplace will need to apply these Criteria. They would normally identify hazardous substances from the supplier's label, the MSDS, or for those substances produced in the workplace, by reference to the *List of Designated Hazardous Substances*.

Manufacturers and importers are expected to use the Approved Criteria in conjunction with Australian, State and Territory government regulations and codes of practice introduced to regulate workplace hazardous substances.

This publication is one of six titles produced by NOHSC and released together as part of its workplace hazardous substances regulatory package. The six titles that comprise the set are:

- *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)];
- *National Code of Practice for the Control of Workplace Hazardous Substances* [NOHSC:2007(1994)];
- *National Code of Practice for the Preparation of Material Safety Data Sheets* 2nd Edition [NOHSC:2011(2003)];
- *National Code of Practice for the Labelling of Workplace Substances* [NOHSC:2012(1994)];
- *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]; and
- *List of Designated Hazardous Substances*.

These publications are supplemented by the following titles:

- *Guidance Note for the Assessment of Health Risks Arising from the Use of Hazardous Substances in the Workplace* [NOHSC:3017(1994)]; and
- *Guidance Note for the Control of Workplace Hazardous Substances in the Retail Sector* [NOHSC:3018(1994)].
- *National Model Regulations for the Control of Workplace Hazardous Substances Part 2 – Scheduled Carcinogenic Substances* [NOHSC:1011(1995)].

- *Exposure Standards for Atmospheric Contaminants in the Occupational Environment* [NOHSC:1003(1995)].

NOHSC maintains the regulatory package with reviews and updates of the individual titles from time to time.

Chapter 1

INTRODUCTION

1.1 The object of classification is to identify all the physicochemical, toxicological and ecotoxicological properties of substances and preparations which may constitute a risk during normal handling or use. Having identified any hazardous properties, the substance or preparation must then be labelled to indicate the hazard(s) in order to protect the user, the general public and the environment.

1.2 The *Approved Criteria for Classifying Hazardous Substances* are cited in the *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)][1]. It provides the mandatory criteria for determining whether a substance is hazardous based on its health effects, and optional criteria for determining whether a substance is hazardous based on its ecotoxicological and physicochemical properties. It is addressed to all those concerned (manufacturers, importers, national authorities) with methods of classifying and labelling substances and preparations.

1.3 The Approved Criteria also provide examples showing how to apply the classification criteria to determine whether a substance is hazardous to health, and for classifying the nature of the hazard(s).

Classification of Hazardous Substances - Manufacturers' and Importers' Duties.

1.4 The responsibility for determining whether a substance is hazardous, and for identifying its health hazards, belongs to the manufacturer or importer. If the substance or mixture cannot be classified, it cannot be supplied.

1.5 Although manufacturers and importers are responsible for determining whether substances are hazardous or not, and for their classification, they do not have to carry out this work themselves. However, they should ensure that a competent person carries out the work.

1.6 In this context, a competent person is a person who understands the Approved Criteria and who has the skills and experience to apply the criteria to the information about the substance.

1.7 When a substance that does not appear on the List is classified by an importer or manufacturer, and determined to be hazardous, the manufacturer or importer is required to notify NOHSC of that determination. Notification of a hazardous substance shall be made to NOHSC on the approved form (see Appendix 5).

1.8 The Approved Criteria focus primarily on the classification of a substance's toxicological properties. Manufacturers and importers will need to consider the physicochemical hazards defined in the *Australian Dangerous Goods Code*[6], in addition to these health effects criteria, when producing labels and MSDS.

1.9 Criteria applicable to the classification of physicochemical and ecotoxicological properties of a substance are also provided in these Approved Criteria. Where information is available that describes the physicochemical properties of a substance, these criteria may be used to identify any physicochemical hazard supplementary to those defined by the *Australian Dangerous Goods Code*. Information describing the ecotoxicological properties of a substance may be used to extend the classification of the substance to identify hazards to the environment.

1.10 This will permit a more comprehensive classification and complete labelling of the substance by identifying hazards additional to health hazards. The addition of physicochemical and ecotoxicological risk and safety phrases to product MSDS and labels will harmonize Australian classification practices with those of the European Commission.

1.11 Criteria for the classification of a substance on the basis of its physicochemical properties are included in Appendix 6, and on the basis of ecotoxicological effects in Appendix 7. These criteria are taken from Annex VI of EC Council Directive 67/548/EEC[3] (as amended by Commission Directive 2001/59/EC of 6 August 2001).

Definition of a hazardous substance

1.12 Under the *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)][1], a hazardous substance means a substance that:

(1) is included on the *List of Designated Hazardous Substances*; or

(2) has been classified as a hazardous substance by the manufacturer or importer in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

1.13 The National Model Regulations do not apply to radioactive and infectious substances, substances that are solely dangerous goods (because of their physicochemical properties), or substances hazardous to the environment. The Approved Criteria therefore do not address these hazards in a legislative way.

1.14 However, criteria enabling the classification of physicochemical and environmental hazards are presented in Appendices 6 and 7, respectively. These criteria may be used to determine the Risk and Safety phrases applicable to a substance hazardous because of its physical properties, or because it is hazardous to the environment. This hazard information may then be included on the label and MSDS of the substance.

1.15 The List contains the more common workplace hazardous substances, but is not a complete list of all hazardous substances.

1.16 The List is the starting point for identifying whether a substance is hazardous. If a substance is included on the List it is a hazardous substance under hazardous substances regulations. If a substance is not on the List it may still be hazardous to health but has not yet been classified.

1.17 Where a substance or, in the case of mixtures, an ingredient, is not included on the List, it will be necessary to assess information about its health effects against the Approved Criteria in order to determine whether it is hazardous or not.

1.18 From such an assessment the nature of the hazard (if any) presented by the substance can be identified and classified with appropriate risk phrases. Classification of substances is important in producing labels and MSDS as required by Australian, State and Territory government regulations introduced in accordance with the National Model Regulations.

The criteria

1.19 Guidance on applying the criteria is provided in **Chapter 3.**

1.20 For determining whether a substance is hazardous to health refer to the following chapters:

Chapters 4 & 5 contain the **health effects criteria** for classifying a substance on the basis of its health effects;

Chapter 6 provides **concentration cut-off levels** for ingredients that have satisfied the health effects criteria of Chapters 4 and 5. There is a concentration cut-off level corresponding to each type of health effect and hazard category;

Chapter 7 lists **formulae** to be used in classifying mixtures that may be hazardous due to the additive effects of ingredients which have satisfied the health effects criteria in Chapters 4 and 5, but whose concentrations do not exceed the concentration cut-off levels in Chapter 6; and

1.21 Substances with similar health effects can produce an additive effect greater than would be suggested by their individual concentrations. Therefore, the concentration cut-off levels of Chapter 6 are designed to provide a practical level of protection and should not be used to imply that an effect cannot occur below that level.

1.22 The health effects criteria (Chapters 4 and 5) are the same as those used by the European Communities in EC Council Directive 67/548/EC3 (as amended by EC Commission Directive 2001/59/EC) for classifying substances hazardous to health.

1.23 The criteria will be revised periodically to maintain consistency with European Commission Council Directives.

1.24 Concentration cut-off levels (Chapter 6) are taken from EC Commission Directive 1999/45/EC[4] relating to the classification, packaging and labeling of dangerous preparations.

1.25 The risk and safety phrases relevant to the different types of health effects (Appendix 3) are taken from EC Council Directive 67/548/EC[3] and its subsequent amendments.

Chapter 2

DEFINITION OF TERMS

Absorption	The process by which a substance enters the body.
Acute toxicity	The adverse effects occurring within a given time (usually 14 days), after administration of a single dose of a substance.
Aerosol	Particles (solid and/or liquid) homogeneously dispersed in air.
Alopecia	Partial or complete lack or loss of hair.
Alveolitis	Inflammation of the pulmonary alveoli.
Aneuploidy	A condition in which a cell or organism has an abnormal total number of chromosomes and/or where numbers of individual chromosomes are not in proportion with the numbers of the other chromosomes. Hyperploidy is the presence of too many chromosomes. Hypoploidy is the presence of too few. A single set of chromosomes (which is half the full complement of genetic material), is present in the reproductive cells (egg and sperm cells) of animals and in the reproductive cells (egg and pollen cells). Human beings have 23 chromosomes in their reproductive cells (haploid) and 46 in their non-reproductive cells (diploid).
Aplasia	A condition that manifests in defective or incomplete tissue development.
Article	An item that is formed to a specific shape, surface, or design during production and has an end function dependent in whole or in part on its shape or design, and which undergoes no change in chemical composition and physical state during its life cycle, including its end use, except as an intrinsic aspect of that end use. Fluids and particles are not considered articles, regardless of the shape or design.
Aspiration hazards	A phrase used with respect to risk phrase R65, whereby low viscosity liquid chemicals can be hazardous to human health if they enter the lung through swallowing or vomiting.
Bradypnea	Abnormal slowness of breathing.
Can	Implies a capability or possibility, or a possibility that is available or that might occur.

Cancer	A malignant tumour that can spread to other organs of the body, as distinct from a benign tumour that cannot. (Although leukaemia and some other malignant diseases are not solid tumours, they meet other criteria for cancer and can be, and often are, included under this definition).
Carcinogen	An agent which is responsible for the formation of a cancer.
Carcinogenesis	The process leading to the development of cancer cells.
Chemical	Any element, compound or complex present as an entity or contained in a mixture.
Chemical Abstracts Service Registry Number (CAS Number or CAS No.)	The unique number assigned to a chemical by the Chemical Abstracts Service, Columbus, Ohio, USA.
Chemosis	Oedema of the conjunctiva.
Chromosome	One of the threadlike, rodlike structures in the nucleus of a cell, which carry the genetic information in the cell. Each species has a characteristic number of chromosomes, which in humans is 46.
Chronic toxicity	A toxic effect that occurs after repeated or prolonged exposure. Chronic effects may occur some time after exposure has ceased.
Classification	The process whereby the toxicological, physicochemical and ecotoxicological properties of a substance are identified and categorised.
Conjunctiva	The mucous membrane covering the anterior portion of the eyeball reflected upon the lids and extending to their free edges.
Corrosivity	The property of a chemical indicating its capacity to cause corrosion.
Cytogenetic	The branch of genetics devoted to study of the cellular constituents concerned with heredity, primarily the structure, function and origin of the chromosomes.
Dangerous Goods	Materials which are either specifically listed in the Australian Dangerous Goods (ADG) Code or meet the classification criteria of the ADG Code, or are deemed to be dangerous goods by the Competent Authorities Panel.

Dangerous Preparations	Mixtures or solutions composed of two or more substances determined to be hazardous according to their physico-chemical properties and human health and environmental effects as defined in sub-points 2.a-o of Article 2 of EC Directive 1999/45/EC.
Deoxyribonucleic acid (DNA)	A large nucleic acid molecule, which contains the genetic sequence or code, found principally in the chromosomes of the nucleus of a cell. The crucial property of DNA is that it consists of two strands that are complementary and joined by weak chemical bonds called hydrogen bonds. A single DNA strand is made up of four molecules called nucleotides, which bind to another DNA strand via base pairs. The bases are called guanine, cytosine, adenine and thymine. Guanine pairs with cytosine and adenine with thymine. It is the specific sequence of these nucleotides that create the genetic code. Damage to the DNA may result in damage to the information carried on the DNA. This may give rise to genetic errors in the cell that may manifest in abnormal growth and metabolism of the cell.
Dermal	Relating to the skin.
Dermal Corrosion	The production of irreversible tissue damage in the skin following the application of a test substance for the duration of from 3 minutes up to 4 hours.
Distribution	The process(es) by which the absorbed substance and/or its metabolites partition within the body.
Dosage	A general term comprising of dose, its frequency and the duration of the dosing.
Dose	The amount of test substance administered. Dose is expressed as weight (grams or milligrams) or as weight of test substance per unit weight of test animal (eg. milligrams per kilogram body weight), or as constant dietary concentrations (milligrams per kilogram of food).
Discriminating dose	Used with reference to the fixed dose procedure, a discriminating dose is the highest out of four fixed dose levels (5, 50, 500 or 2000 mg/kg) that can be administered without causing compound-related mortality (including humane kills).
Dysfunction	A state of abnormal, incomplete or impaired function.
Ecotoxicological properties	Properties that contribute to the toxicity of a substance to the natural environment.
Embryotoxic	Pertaining to anything that is toxic to an embryo.
Entity	A single substance that includes discrete chemical elements, compounds and complexes which may exist in pure or technical grade, or as components in a mixture of substances.

Environmental hazard	Means the hazards to be assessed for the classification "dangerous for the environment".
Epidemiological	Relating to the study of the relationships determining the frequency and distribution of disease in a human community.
Erythema	Redness or inflammation of the skin or mucous membranes.
Eschar	The slough or dry scab that forms, for example, on an area of skin that has been burned.
EuroNorm (EN)	A European Union standard that requires implementation at the national level by EU member countries.
Evident toxicity	The concept 'evident toxicity' is used to designate toxic effects, after exposure to the substance tested, which are so severe that exposure to the next highest fixed dose would probably lead to mortality.
Excretion	The process(es) by which an administered substance, and/or its metabolites, is removed from the body.
Eye irritation	The production of changes in the eye following the application of a test substance to the anterior surface of the eye.
Fertility	The capacity to conceive or induce conception.
Fibrosis	The development of fibrous tissue in a part of an organ.
Fixed dose procedure	See Appendix 2.
Foetotoxic	Pertaining to anything that is toxic to a foetus.
Gastritis	Inflammation of the gastric mucosa.
Gavage	The administration of food or other substances through a stomach tube. Usually the tube is passed through the nose or mouth into the stomach.
Gene	A unit of inheritable genetic material made up of a specific sequence of deoxyribonucleic acid (DNA) on a chromosome.
Genotoxin	A substance capable of causing damage to genetic material, such as DNA.
Germ cell	A sexual reproductive cell in any stage of development, from the primordial embryonic form to the mature gamete.
Granuloma	Chronic inflammatory lesion characterised by large numbers of cells of various types (macrophages, lymphocytes, fibroblasts, giant cells), some of which are involved in tissue degradation and/or tissue repair.

Hazard	An intrinsic capacity associated with an agent or process capable of causing harm.
Hazardous substance	A substance which: • is listed on the National Occupational Health and Safety Commission's *List of Designated Hazardous Substances*; or • has been classified as a hazardous substance by the manufacturer or importer in accordance with the National Occupational Health and Safety Commission's *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].
Health effects criteria	The basis on which a substance is evaluated with respect to its toxicological data.
Hyperplasia	The abnormal multiplication or increase in number of normal cells in normal arrangement in a tissue.
Hypersensitivity	A state of excessive and potentially damaging responsiveness to a chemical or other substance. If immunologically mediated, hypersensitivity often occurs as a result of previous exposure to the substance or closely related substance. If the hypersensitivity is of the immediate type (antibody-mediated), then the response occurs in minutes; in delayed hypersensitivity the response takes longer (about 24hr) and is mediated by primed T cells.
Hypertrophy	Enlargement or overgrowth of an organ or part due to an increase in size of constituent cells.
Hypoplasia	Incomplete development of an organ so that it fails to reach adult size.
Inanition	A condition characterised by marked weakness, extreme weight loss and a decrease in metabolism resulting from a prolonged and severe insufficiency of food.
Ingredient	Any component of a substance (including impurities), in a mixture or combination.
Inhalation	Breathing in.
In vitro	Used to describe the experimental reproduction of biological processes in isolation from the living organism.
In vivo	Observation made in a living organism either in animals or humans.
Label	A set of information on a container that identifies the substance in the container identifies whether the substance is hazardous and provides basic information about the safe use and handling of the substance.

LC_{50}	Median lethal concentration. A statistically derived concentration of a substance that can be expected to cause death during exposure or within a fixed time after exposure in 50% of animals exposed for a specified time. The LC_{50} value is expressed as weight of test substance per standard volume of air (milligrams per litre).
LD_{50}	Median lethal dose. A statistically derived single dose of a substance that can be expected to cause death in 50% of dosed animals. The LD_{50} value is expressed in terms of weight of test substance per unit weight of test animal (milligrams per kilogram).
Lesion	A discontinuity of tissue or loss of function of a part of the body as a result of disease or trauma.
Material Safety Data Sheet (MSDS)	A document that describes the properties and uses of a substance, that is, identity, chemical and physical properties, health hazard information, precautions for use and safe handling information.
Maximum Tolerated Dose (MTD)	The highest dose level eliciting signs of toxicity in animals without having major effects on survival relative to the test in which it is used.
May	Indicates that a requirement is optional.
Metabolism	The process(es) by which the administered substances are structurally changed in the body either by enzymatic or non-enzymatic reactions.
Mixture	A physical combination of chemicals resulting from the deliberate mixing of those chemicals or from a chemical reaction.
Mutagen	An agent capable of producing a mutation.
Mutagenesis	The process of producing a mutation.
Mutagenic	Able to produce a mutation.
Mutation	A change in the genetic material of cells.
Myocardium	The muscular structure of the heart.
Necrosis	Changes that are indicative of cell death.
Neoplasm	Any abnormal growth of new tissue, benign or malignant.
Nephrosis	A syndrome caused by a primary non-inflammatory degeneration of the renal tubules.

NOAEL	The abbreviation for no observed adverse effect level. The highest dose or exposure level where no adverse treatment-related findings are observed.
Ocular	Of the eye or affecting the eye.
Oedema (edema)	Excessive accumulation of fluid in the tissue spaces of the body due to increase transudation of the fluid from the capillaries.
Oogenesis	The process of the formation of the female reproductive cells.
Oral	Ingested or administered via the mouth.
Paresthesia (Paraesthesia)	An abnormal sensation, such as tingling, tickling and formication (sensation of insects crawling on or under the skin).
Particulate	Pertaining to a minute discrete particle or fragment of a substance or material.
Perinatal	Pertaining to or occurring in the period shortly before and after birth.
Phenotype	The visible form of an organism, as contrasted with its genetic character (genotype). In different environments the same genotype may produce different phenotypes.
Point mutation	A heritable change taking place at a single gene position.
Postnatal	Occurring after birth, with reference to the newborn.
Progeny	Offspring or descendants.
Repeated dose/ Sub chronic toxicity	The adverse effects occurring in experimental animals as a result of repeated daily dosing with, or exposure to, a chemical for a short part of their expected life span.
Reproductive hazard	An agent capable of causing abnormalities in a developing foetus, that is, causing birth defects.
Resorption	The process of breaking down and absorbing already formed tissues and structures in an organism. Early resorption of the developing foetus is thought to be caused by errors in development, which may result from chemical damage to the foetus.
Rhinitis	An inflammation of the mucous membranes of the nose.
Risk	The likelihood that a substance will cause harm in the circumstances of its use.
Sensitisation	To become sensitive/allergic to the effects of minute quantities of a substance.

Should	Indicates a recommendation.
Sister chromatid exchange	A technique used for monitoring DNA damage in a pair of chromosomes during one of the phases of cell division. Undamaged segments are exchanged for damaged segments between homologous duplex DNA molecules.
Skin irritation	The production of inflammatory changes in the skin following the application of a test substance.
Somatic cells	Cells of the body other than germ cells.
Spermatogenesis	The process of formation of spermatozoa.
Substance	Any natural or artificial entity, composite material, mixture or formulation, other than an article.
Teratogen	An agent capable of causing abnormalities in a developing foetus, that is, causing birth defects.
Toxicity	The capacity of an agent to produce damage to an organism. This usually refers to functional (systemic) damage but may be developmental in respect of tissue and skeleton in the case of the embryo. The damage may be permanent or transient.
Toxicokinetics	The study of the absorption, distribution, metabolism and excretion of test substances.
Tumour	A swelling or enlargement or an abnormal mass of tissue in which the growth of cells is uncontrolled. A tumour can be either benign (not malignant) or malignant (cancerous). A tumour is also called a 'neoplasm'.
Unscheduled DNA synthesis (UDS)	Unscheduled DNA synthesis (UDS) refers to DNA synthesis occurring outside of the usual replication phase of the cell cycle when chromosomes are duplicated. UDS in animal cells in vitro measures the repair of DNA damage induced by variety of agents including chemicals, radiation and viruses.
Urticaria	A vascular reaction of the skin characterised by the formation of evanescent whitish, pink or red elevations or weals, with itching, stinging or burning.

Chapter 3

HOW TO APPLY THE CRITERIA

3.1 This chapter gives guidance on how to use the health effects criteria given in Chapters 4 and 5 to determine whether a substance is hazardous. If the substance is a mixture, then the criteria in Chapter 6 and Chapter 7 should also be used. Appendix 8 lists non-mandatory classification and labelling requirements for specific mixtures of hazardous substances. See also the flow chart at the end of this chapter.

3.2 Classification must cover the toxicological properties of substances and preparations. Physicochemical and ecotoxicological properties may be considered to give a more complete classification. The addition of physicochemical and ecotoxicological risk phrases to product MSDS and labels will harmonize Australian classification practices with those of the European Commission.

3.3 The guidance given in this chapter is to be used when the substance is not found in the List, or when new toxicology data becomes available on a substance in the List.

3.4 The criteria in this publication are applicable to all substances, including gaseous substances.

3.5 Classifying the substance will involve finding and putting together all the available information on the substance and assessing this information against the criteria. This process will identify the health, physical, and environmental hazards of the substances and the appropriate risk and safety phrases to be used.

3.6 The method of applying the criteria to determine whether a substance is hazardous will depend on:

- whether the substance is an ingredient in a mixture; and
- whether the mixture has been tested as a whole for its effects.

3.7 Information on health effects for a substance can be obtained from a number of different sources. For example:

- scientific reference works and literature;
- practical experience, for example, the health effects of the substance on exposed persons;
- the results of experimental animal testing;
- information required by international rules on the transport of dangerous goods and notification of hazardous substances; and
- existing classifications for substances that have similar structural relationships.

See Appendix 1 for further suggestions on information resources.

3.8 It is not intended that additional animal testing will need to be carried out.

3.9 The classification of substances should include consideration of all the toxicological properties covered in Chapters 4 and 5. These include:

- acute toxicity
- subacute, subchronic and chronic toxicity
- corrosivity
- irritancy
- sensitisation
- other toxicological properties
- carcinogenic effects
- mutagenic effects
- toxicity to reproduction, fertility and development.

3.10 Some substances do not pose a hazard to human health by ingestion, inhalation or contact with the skin in the form in which they are supplied, for example, certain polymers. In these cases, the available information may show that they may be determined not to be hazardous.

3.11 If evidence is available to show that, in practice, the toxic effect of a substance on humans is, or is likely to be, different from that suggested by the results of animal testing, then the substance should be classified according to its toxicity in humans.

3.12 If only some information is available for the substance, then the health effects criteria and other suitable information should be applied as far as possible to classify the substance. For assistance in classification matters that may be difficult or contentious, the relevant Australian, State or Territory government authority should be consulted for assistance.

3.13 The classification of a substance may need to be revised periodically as new information about that substance becomes available.

For substances not in mixtures

3.14 To determine whether a substance is hazardous and to determine its classification, a comparison should be made of the health effects data for the substance with the health effects criteria in Chapters 4 and 5. All the health effects of the substance should be considered.

3.15 For example, a substance with acute lethal effects and an oral LD_{50} of 20mg/kg would be determined to be hazardous and categorised as Very Toxic. If it also causes significant inflammation of the skin, then the substance would be categorised as Very Toxic and Irritant. The most appropriate risk phrases can then be identified for the substance, for example, R28 and R38.

For ingredients in mixtures

Mixtures tested as a whole

3.16 If a mixture has been tested for its health effects as a whole, then it can be classified by applying the health effects criteria in Chapters 4 and 5. The most appropriate risk phrases can then be assigned.

Mixtures not tested as a whole

3.17 If the mixture has not been tested as a whole, then the health effects data of *each ingredient* in the mixture will need to be considered separately against the health effects criteria in Chapters 4 and 5.

3.18 The classification of the mixture is dependent upon:

- the health effects data or other information available for each of the ingredients; and,
- the concentration of each ingredient in the mixture.

3.19 In the case of ingredients that are on the List, the information provided there - including concentration cut-off levels and risk phrases - can be used in the classification of the mixture.

3.20 In the case of ingredients that are not on the List each ingredient should be considered separately as a pure substance to determine its health effects.

3.21 Once all the ingredients in a mixture have been classified, the mixture as a whole can be classified.

3.22 The mixture is a hazardous substance if:

- any of the ingredients of the mixture meet any of the health effects criteria in Chapters 4 and 5, and;
- that ingredient is present in the mixture at a concentration that exceeds the concentration cut-off level given in Chapter 6, for the relevant health effect.

3.23 By use of the concentration cut-off levels, the mixture can be classified overall and the appropriate risk phrases selected.

3.24 For example, if an ingredient, classified as Toxic by virtue of its acute lethal effects, is present in a mixture at a concentration of 15% by weight, then the mixture would only be classified as Harmful (Table 2, Chapter 6).

3.25 **Note:** Identified impurities, additives or individual constituents should be taken into account if their concentration is *greater than or equal* to the cut-off levels specified in Chapter 6. These cut off levels are:

i. 0.1% for liquid or solid substances, and 0.02% for gaseous mixtures that are classified as:

- Very Toxic,
- Toxic,
- Carcinogenic (category 1 or 2),
- Mutagenic (category 1 or 2) or
- Toxic to Reproduction (category 1 or 2);

ii. 1% for liquid or solid substances, and 0.2% for gaseous mixtures that are classified as:

- Harmful,
- Corrosive,
- Irritant,
- Sensitising,
- Carcinogenic (category 3),
- Mutagenic (category 3),
- Toxic to Reproduction (category 3);

unless lower values have been specified in the List[2].

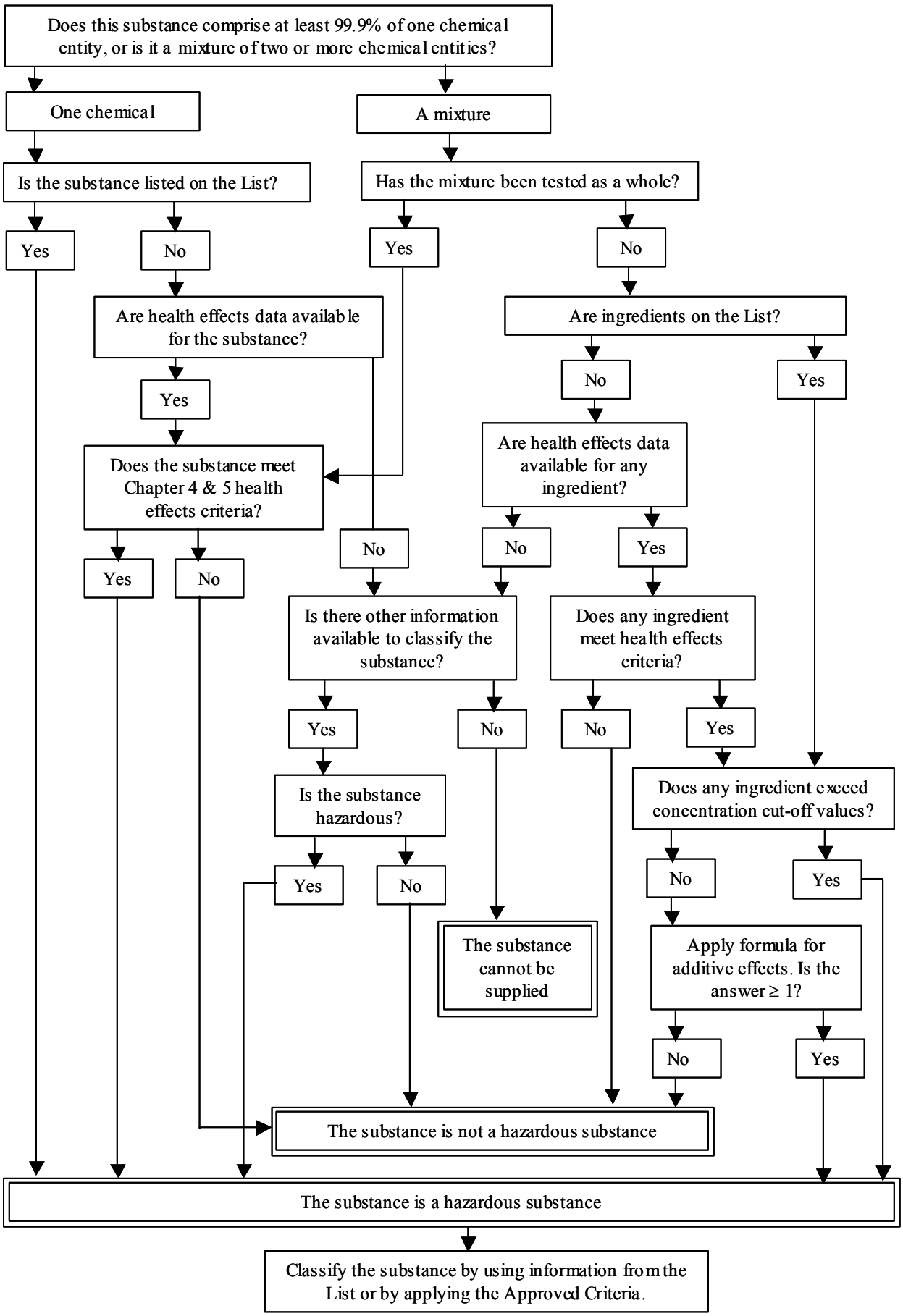
Interaction of substances

3.26 A mixture containing ingredients classified as hazardous on the basis of acute lethal effects, corrosivity or irritancy, carcinogenic effects, mutagenic effects, or toxic effects on reproduction, and present at concentrations below the relevant concentration cut-off levels, may still need to be classified as a hazardous substance. This can be determined by applying the formulae in Chapter 7. These formulae are used for the classification of mixtures containing ingredients with similar and additive health effects that are present individually at concentrations below the cut-off levels.

3.27 An **additive effect** is when the combined toxic effect of a number of individual chemicals in a mixture is equal to the sum of each individual agent, that is, 3+2=5. For example, two organophosphate insecticides that act as cholinesterase enzyme inhibitors will give rise to an additive toxic effect.

3.28 Occasionally the combined effect of multiple exposures is greater than the sum of the effects from the individual components. **Synergism** occurs when both chemicals have an individual effect but the combined effect is more than additive. **Potentiation** occurs when only one chemical is individually effective but the second inactive chemical enhances the first. Subtractive effects are also possible.

Process of determining whether a substance is hazardous



Chapter 4

HEALTH EFFECTS CRITERIA

RISK PHRASES: For a list of relevant risk phrases see the end of chapter 5.

Introduction

4.1 The criteria in this chapter are those used by the European Communities in EC Council Directive 67/548/EC[3] for classifying substances based on their hazards to health. These criteria take into account both short and long-term health effects, and are applicable to both pure substances and mixtures.

4.2 Health effects criteria are to be applied to:

- substances which are not listed on the *List of Designated Hazardous Substances*[2];
- mixtures tested as a whole; and
- ingredients of mixtures that have not been tested as a whole.

4.3 The process of classification results in assigning the substance to a hazard category. Broadly these categories are:

- **very toxic;**
- **toxic;**
- **harmful;**
- **corrosive;**
- **irritant;**
- **sensitiser;** and
- **other toxicological properties.**

4.4 Criteria dealing with **specific effects on human health** (carcinogenicity, mutagenicity, and reproductive toxicology) are described in Chapter 5. As each hazard is identified a corresponding risk phrase is applied to the substance being classified. A substance may have more than one health effect.

Criteria for classification, choice of symbols, indication of danger, choice of risk phrases

4.5 The classification of substances must be made on the basis of experimental data in accordance with the following criteria.
The criteria take into account the magnitude of the observed health effects:

a) For acute, subacute, subchronic or chronic toxicity the criteria in paragraphs 4.9 to 4.22 are to be used.

b) For corrosive and irritant effects the criteria in paragraphs 4.23 to 4.33 are to be used.

c) For sensitising effects the criteria in paragraphs 4.34 to 4.48 are to be used.

d) Risk phrases for other toxicological properties are described in paragraphs 4.49 to 4.52.

e) For specific effects on health (carcinogenicity, mutagenicity and reproductive toxicity) the criteria in Chapter 5 are to be used.

4.6 The guidance criteria set out below are directly applicable when the data in question have been obtained from test methods comparable with those described in Annex V of Council Directive 67/548/EEC. In other cases, the available data must be evaluated by comparing the test methods employed with those indicated in Annex V and the rules specified in this Approved Criteria for determining the appropriate classification and labelling.

4.7 The acute oral toxicity of substances or preparations placed on the market may be established either by a method permitting assessment of the LD_{50} value, or by determining the discriminating dose (the fixed dose method), or by determining the range of exposure where lethality is expected (the acute toxic class method).

4.8 The discriminating dose is the dose that causes evident toxicity but not mortality. Evident toxicity is used to designate toxic effects, after exposure to the substance tested, that are so severe that exposure to the next highest fixed dose would probably lead to mortality (see Appendix 2).

VERY TOXIC (T^+)

4.9 Substances and preparations shall be classified as **very toxic** and assigned the symbol 'T+' and indication of danger 'very toxic' in accordance with the criteria specified below.

4.10 Risk phrases shall be assigned in accordance with the following criteria:

Acute lethal effects

R28 Very toxic if swallowed

Acute toxicity results:

- LD_{50} oral, rat $\leq$ 25 mg/kg,
- less than 100% survival at 5 mg/kg oral, rat by the fixed dose procedure, or
- high mortality at doses $\leq$ 25 mg/kg oral, rat, by the acute toxic class method.

R27 Very toxic in contact with skin

Acute toxicity results:

- LD_{50} dermal, rat or rabbit: $\leq$ 50 mg/kg.

R26 Very toxic by inhalation

Acute toxicity results:

- LC_{50} inhalation, rat, for aerosols or particulates: $\leq$ 0.25 mg/litre/4hr,
- LC_{50} inhalation, rat, for gases and vapours: $\leq$ 0.5 mg/litre/4hr.

Non-lethal irreversible effects after a single exposure

R39 Danger of very serious irreversible effects

Strong evidence that irreversible damage other than the effects referred to in Chapter 5 is likely to be caused by a single exposure by an appropriate route, generally in the above-mentioned dose ranges.

In order to indicate the route of administration or exposure one of the following combinations shall be used: R39/26, R39/27, R39/28, R39/26/27, R39/26/28, R39/27/28, R39/26/27/28.

TOXIC (T)

4.11 Substances and preparations shall be classified as **toxic** and assigned the symbol 'T' and the indication of danger, 'toxic', in accordance with the criteria specified below.

4.12 Risk phrases shall be assigned in accordance with the following criteria:

Acute lethal effects

R25 Toxic if swallowed

Acute toxicity results:

- LD_{50} oral, rat: $25 < LD_{50} \leq 200$ mg/kg,
- Discriminating dose, oral, rat, 5 mg/kg: 100% survival but evident toxicity, or
- high mortality in the dose range > 25 to ≤ 200 mg/kg oral, rat, by the acute toxic class method

R24 Toxic in contact with skin

Acute toxicity results:

- LD_{50} dermal, rat or rabbit: $50 < LD_{50} \leq 400$ mg/kg.

R23 Toxic by inhalation

Acute toxicity results:

- LC_{50} inhalation, rat, for aerosols or particulates: $0.25 < LC_{50} \leq 1$ mg/litre/4hr,
- LC_{50} inhalation, rat, for gases and vapours: $0.5 < LC_{50} \leq 2$ mg/litre/4hr.

Non-lethal irreversible effects after a single exposure

R39 Danger of very serious irreversible effects

Strong evidence that irreversible damage other than the effects referred to in Chapter 5 is likely to be caused by a single exposure by an appropriate route, generally in the above-mentioned dose ranges.

In order to indicate the route of administration/exposure one of the following combinations shall be used: R39/23, R39/24, R39/25, R39/23/24, R39/23/25, R39/24/25, R39/23/24/25.

Severe effects after repeated or prolonged exposure

R48 Danger of serious damage to health by prolonged exposure

Serious damage (clear functional disturbance or morphological change which have toxicological significance) is likely to be caused by repeated or prolonged exposure by an appropriate route.

Substances and preparations are classified **at least as toxic (T)** when these effects are observed at the following levels: -

- inhalation, rat ≤ 0.025 mg/l, 6h/day,
- oral, rat ≤ 5 mg/kg (bodyweight)/day,
- dermal, rat or rabbit ≤ 10 mg/kg (bodyweight)/day.

In order to indicate the route of administration/exposure one of the following combinations shall be used: R48/23, R48/24, R48/25, R48/23/24, R48/23/25, R48/24/25, R48/23/24/25.

HARMFUL (Xn)

4.13 Substances and preparations shall be classified as **harmful** and assigned the symbol 'Xn' and the indication of danger 'harmful' in accordance with the criteria specified below.

4.14 Risk phrases shall be assigned in accordance with the following criteria:

Acute lethal effects

R22 Harmful if swallowed

Acute toxicity results:

- LD_{50} per oral, rat: $200 < LD_{50} \leq 2000$ mg/kg,
- discriminating dose, oral, rat, 50 mg/kg: 100% survival but evident toxicity,
- less than 100% survival at 500 mg/kg, rat oral by the fixed dose procedure, (refer to the evaluation table in Appendix 2), or
- high mortality in the dose range > 200 to $\leq$ 2 000 mg/kg oral, rat, by the acute toxic class method.

R21 Harmful in contact with skin

Acute toxicity results:

- LD_{50} dermal, rat or rabbit: $400 < LD_{50} \leq 2\,000$ mg/kg.

R20 Harmful by inhalation

Acute toxicity results:

- LC_{50} inhalation, rat, for aerosols or particulates: $1 < LC_{50} \leq 5$ mg/litre/4hr,
- LC_{50} inhalation, rat, for gases or vapours: $2 < LC_{50} \leq 20$ mg/litre/4hr.

Aspiration hazard

R65 Harmful: may cause lung damage if swallowed

Liquid substances and preparations presenting an aspiration hazard in humans because of their low viscosity, use:

(a) for substances and preparations containing aliphatic, alicyclic and aromatic hydrocarbons in a total concentration equal to or greater than 10% and having either:

- a flow time of less than 30 sec. in a 3mm International Standards Organisation (ISO) cup according to ISO 2431 (April 1996 / July 1999 edition) relating to 'Paints and varnishes - Determination of flow time by use of flow cups',

- a kinematic viscosity measured by a calibrated glass capillary viscometer in accordance with ISO 3104/3105 of less than 7×10^{-6} m^2/sec at 40°C (ISO 3104, 1994 edition, relating to 'Petroleum products - Transparent and opaque liquids - Determination of kinematic viscosity and calculation of dynamic viscosity'; ISO 3105, 1994 edition, relating to 'Glass capillary kinematic viscometers - Specifications and operating instructions'), or

- a kinematic viscosity derived from measurements of rotational viscometry in accordance with ISO 3219 of less than 7×10^{-6} m^2/sec at 40°C (ISO 3219, 1993 edition, relating to 'Plastics – Polymers/resins in the liquid state or as emulsions or dispersions - Determination of viscosity using a rotational viscometer with defined shear rate').

Note that substances and preparations meeting these criteria need not be classified if they have a mean surface tension greater than 33mN/m at 25°C as measured by the du Nouy tensiometer.

or,

(b) for substances and preparations, based on practical experience in humans.

Non-lethal irreversible effects after a single exposure

R68 Possible risk of irreversible effects

Strong evidence that irreversible damage other than the effects referred to in Chapter 5 is likely to be caused by a single exposure by an appropriate route, generally in the above-mentioned dose ranges.

In order to indicate route of administration/exposure one of the following combinations shall be used: R68/20, R68/21, R68/22, R68/20/21, R68/20/22, R68/21/22, R68/20/21/22.

Severe effects after repeated or prolonged exposure

R48 Danger of serious damage to health by prolonged exposure

Serious damage (clear functional disturbance or morphological change which has toxicological significance) is likely to be caused by repeated or prolonged exposure by an appropriate route.

Substances and preparations are classified **at least as harmful** (Xn) when these effects are observed at levels of the order of:

- inhalation, rat $\leq$ 0.25 mg/l, 6h/day.
- oral, rat $\leq$ 50 mg/kg (bodyweight)/day,
- dermal, rat or rabbit $\leq$ 100 mg/kg (bodyweight)/day,

These guide values can apply directly when severe lesions have been observed in a sub-chronic (90 days) toxicity test. When interpreting the results of a sub-acute (28 days) toxicity test these figures should be increased approximately three fold. If a chronic (two years) toxicity test is available it should be evaluated on a case-by-case basis. If results of studies of more than one duration are available, then those from the study of the longest duration should normally be used.

In order to indicate route of administration/exposure one of the following combinations shall be used: R48/20, R48/21, R48/22, R48/20/21, R48/20/22, R48/21/22, R48/20/21/22.

Comments regarding the use of R48

4.15 Use of this risk phrase refers to the specific range of biological effects within the terms described below. For application of this risk phrase serious damage to health is to be considered to include death, clear functional disturbance or morphological changes that are toxicologically significant. It is particularly important when these changes are irreversible. It is also important to consider not only specific severe changes in a single organ or biological system but also generalised changes of a less severe nature involving several organs, or severe changes in general health status.

4.16 When assessing whether there is evidence for these types of effects reference should be made to the following guidelines:

4.17 Evidence indicating that R48 should be applied:

a) substance-related deaths;

b) (i) major functional changes in the central or peripheral nervous systems, including sight, hearing and the sense of smell, assessed by clinical observations or other appropriate methods (eg. electrophysiology);

(ii) major functional changes in other organ systems (for example the lung);

c) any consistent changes in clinical biochemistry, haematology, or urinalysis parameters, which indicate severe organ dysfunction. Haematological disturbances are considered to be particularly important if the evidence suggests that they are due to decreased bone marrow production of blood cells;

d) severe organ damage noted on microscopic examination following autopsy:

(i) widespread or severe necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity (eg. liver);

(ii) severe morphological changes that are potentially reversible but are clear evidence of marked organ dysfunction (eg. severe fatty change in the liver, severe acute tubular nephrosis in the kidney, ulcerative gastritis); or

(iii) evidence of appreciable cell death in vital organs incapable of regeneration (eg. fibrosis of the myocardium or dying back of a nerve) or in stem cell populations (eg. aplasia or hypoplasia of the bone marrow).

4.18 The above evidence will most usually be obtained from animal experiments. When considering data derived from practical experience special attention should be given to exposure levels.

4.19 Evidence indicating that R48 should not be applied:

The use of this risk phrase is restricted to 'serious damage to health by prolonged exposure'. A number of substance-related effects may be observed in both humans and animals that would not justify the use of R48. These effects are relevant when attempting to determine a no-effect level for a chemical substance.

Examples of well-documented changes that would not normally justify classification with R48, irrespective of their statistical significance, include:

a) clinical observations or changes in bodyweight gain, food consumption or water intake, which may have some toxicological importance but which do not, by themselves, indicate ‘serious damage’;

b) small changes in clinical biochemistry, haematology or urinalysis parameters which are of doubtful or minimal toxicological importance;

c) changes in organ weights with no evidence of organ dysfunction;

d) adaptive responses (eg. macrophage migration in the lung, liver hypertrophy and enzyme induction, hyperplastic responses to irritants). Local effects on the skin produced by repeated dermal application of a substance which are more appropriately classified with R38 'irritating to skin'; or

e) where a species-specific mechanism of toxicity (eg. specific metabolic pathways) has been demonstrated and the observed effect is not applicable to humans.

Comments regarding volatile substances

4.20 For certain substances with a high saturated vapour concentration evidence may be available to indicate effects that give cause for concern. These substances might not be classified as 'harmful' (Xn) under the criteria for health effects described in paragraph 4.13, or not covered under paragraph 4.49 'other toxicological properties'.

4.21 However, due to their high volatility and where there is appropriate evidence that such substances may present a risk in normal handling and use, then classification as Harmful (Xn) with the assignment of risk phrases R20, R21, or R22, may be necessary. This should be determined on a case-by-case basis.

4.22 Such substances may already appear on the List with specific concentration cut-off levels. For example, a very volatile substance such as nitromethane [CAS No. 75-52-5] is classified in the List as harmful, R22, at and above 12.5%, rather than at 25% which is the level normally specified for R22. Very volatile substances will need to be considered and classified appropriately.

CORROSIVE (C)

4.23 A substance or a preparation is considered to be corrosive if, when applied to healthy intact animal skin, it produces full thickness destruction of skin tissue on at least one animal during the test for skin irritation.

4.24 A substance should also be considered corrosive if the result can be predicted, for example from strongly acid or alkaline reactions indicated by a pH of 2 or less, or 11.5 or greater. However, where extreme pH is the basis for classification, acid/alkali reserve[1] may also be taken into consideration. If consideration of alkali/acid reserve suggests the substance may not be corrosive then further testing should be carried out to confirm this, preferably by use of an appropriate validated *in vitro* test. Consideration of acid/alkali reserve should not be used alone to exonerate substances or preparations from classification as corrosive.

4.25 Risk phrases shall be assigned in accordance with the following criteria:

R35 Causes severe burns

- if, when applied to healthy intact animal skin, full thickness destruction of skin tissue occurs as a result of up to three minutes exposure, or if this result can be predicted.

R34 Causes burns

- if, when applied to healthy intact animal skin, full thickness destruction of skin tissue occurs as a result of up to four hours exposure, or if this result can be predicted,
- organic hydroperoxides, except where evidence to the contrary is available.

Note: Where classification is based on results of a validated *in vitro* test R35 or R34 should be applied according to the capacity of the test method to discriminate between these.

Where classification is based upon consideration of extreme pH alone, R35 should be applied.

1 J.R. Young, M.J. How, A.P. Walker and W.M.H. Worth (1988) "Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without testing on animals" *Toxic. In Vitro* **2(1)**: 19-26.

IRRITANT (XI)

4.26 A substance is determined to be hazardous and classified as **Irritant** (Xi) and the indication of danger, 'irritant', if it causes:

- inflammation of the skin;
- eye irritation;
- serious eye effects; or
- irritation to the respiratory system.

4.27 One or more of the following risk phrases are assigned in accordance with the criteria given.

Inflammation of the skin

The following risk phrase shall be assigned in accordance with the criteria given:

R38 Irritating to skin

- Substances and preparations which cause **significant inflammation** of the skin, that persists for at least 24 hours after an exposure period of up to four hours, determined on the rabbit according to the cutaneous irritation test method cited in Annex V of Council Directive 67/548/EEC.

Inflammation of the skin is significant if:

(a) the mean value of the scores for either erythema and eschar formation or oedema formation, calculated over all the animals tested, is 2 or more; or

(b) in the case where the irritant test has been completed using three animals, either erythema and eschar formation or oedema formation equivalent to a mean value of 2 or more calculated for each animal separately has been observed in two or more animals.

In both cases all scores at each of the reading times (24, 48 and 72 hr) for an effect should be used in calculating respective mean values.

Inflammation of the skin is also significant if it persists in at least two animals at the end of the observation time. Particular effects eg. hyperplasia, scaling, discoloration, fissures, scabs and alopecia should be taken into account.

- Substances and preparations which cause significant inflammation of the skin, based on practical observations in humans on immediate, prolonged or repeated contact.
- Organic peroxides, except where evidence to the contrary is available.

Paresthesia

4.28 Paresthesia caused in humans by skin contact with pyrethroid pesticides is not regarded as an irritant effect justifying classification as Xi; R38. The safety phrase S24 should however be applied for substances seen to cause this effect.

Ocular lesions

4.29 The following risk phrases shall be assigned in accordance with the criteria given:

R36 Irritating to eyes

- Substances and preparations which, when applied to the eye of the animal, cause **significant ocular lesions** which occur within 72 hours after exposure and which persist for at least 24 hours.

  Ocular lesions are significant if the mean scores of the eye irritation test cited in Annex V of Council Directive 67/548/EEC have any of the following values:

  - cornea opacity equal to or greater than 2 but less than 3,
  - iris lesion equal to or greater than 1 but not greater than 1.5,
  - redness of the conjunctivae equal to or greater than 2.5,
  - oedema of the conjunctivae (chemosis) equal to or greater than 2,

  or, in the case where the test has been completed using three animals, if the lesions on two or more animals are equivalent to any of the following:

  - cornea opacity equal to or greater than 2 but less than 3,
  - iris lesion equal to or greater than 1 but less than 2,
  - redness of the conjunctivae equal to or greater than 2.5,
  - oedema of the conjunctivae (chemosis) equal to or greater than 2,

  In both cases all scores at each of the reading times (24, 48 and 72 hours) for an effect should be used in calculating the respective mean values.

- Substances or preparations that cause significant ocular lesions, based on practical experience in humans.

- Organic peroxides except where evidence to the contrary is available.

R41 Risk of serious damage to eyes

- Substances and preparations which, when applied to the eye of the animal, cause **severe ocular lesions**, which occur within 72 hours after exposure and which persist for at least 24 hours.

  Ocular lesions are severe if the means of the scores of the eye irritation test have any of the values:

  - cornea opacity equal to or greater than 3,
  - iris lesion greater than 1.5.

  The same shall be the case where the test has been completed using three animals if these lesions, on two or more animals, have any of the values:

  - cornea opacity equal to or greater than 3,
  - iris lesion equal to 2.

  In both cases all scores at each of the reading times (24, 48 and 72 hours) for an effect should be used in calculating the respective mean values.

  Ocular lesions are also severe when they are still present at the end of the observation time.

  Ocular lesions are also severe if the substance or preparation causes irreversible colouration of the eyes.

- Substances and preparations that cause severe ocular lesions, based on practical experience in humans.

Note: When a substance or preparation is classified as corrosive and assigned R34 or R35, the risk of severe damage to eyes is considered implicit and R41 is not included in the label. However, when calculating the sum of quotients by the formulae in Chapter 7 (paragraphs 7.31 and 7.35) substances classified as corrosive should be considered as if R41 had been assigned.

Respiratory system irritation

4.30 The following risk phrase shall be assigned in accordance with the criteria given:

R37 Irritating to respiratory system

- Substances and preparations that cause serious irritation to the respiratory system based on:
  - practical observation in humans
  - positive results from appropriate animal tests.

Comments regarding the use of R37

4.31 In interpreting practical observations in humans, care should be taken to distinguish between effects that lead to classification with R48 (see sections 4.12 and 4.15 to 4.19) from those leading to classification with R37.

4.32 Conditions normally leading to classification with R37 are reversible and usually limited to the upper airways.

4.33 Positive results from appropriate animal tests may include data obtained in a general toxicity test, including histopathological data from the respiratory system. Data from the measurement of experimental bradypnea may also be used to assess airway irritation.

SENSITISATION

Sensitisation by inhalation

4.34 Substances and preparations shall be classified as **sensitising** and assigned the symbol **'Xn'**, the indication of danger **'Harmful'** and the risk phrase **R42** in accordance with the criteria given below.

R42 May cause sensitisation by inhalation

- if there is evidence that the substance or preparation can induce specific respiratory hypersensitivity;
- where there are positive results from appropriate animal tests; or
- if the substance is an isocyanate, unless there is evidence that the specific isocyanate does not cause respiratory hypersensitivity

Comments regarding the use of R42

Human evidence

4.35 Evidence that the substance or preparation can induce specific respiratory hypersensitivity will normally be based on human experience. In this context hypersensitivity is normally seen as asthma, but other hypersensitivity reactions such as rhinitis and alveolitis are also considered. The condition will have the clinical character of an allergic reaction. However, immunological mechanisms do not have to be demonstrated.

4.36 When considering the evidence from human exposure, it is necessary for a decision on classification to take into account, in addition to the evidence from the cases, the:

- size of the population exposed
- extent of exposure.

4.37 The evidence from cases referred to above could be clinical history and data from appropriate lung function tests related to exposure to the substance, and confirmed by other supportive evidence, that may include:

- a chemical structure related to substances known to cause respiratory hypersensitivity;
- an *in vivo* immunological test (eg. skin prick test);
- an *in vitro* immunological test (eg. serological analysis);
- studies indicating other specific but non-immunological mechanisms of action, eg. repeated low-level irritation, pharmacologically mediated effects; or
- data from a positive bronchial challenge test with the substance conducted according to accepted guidelines for the determination of a specific hypersensitivity reaction.

4.38 Clinical history should include both medical and occupational history to determine a relationship between exposure to a specific substance or preparation and development of respiratory hypersensitivity. Relevant information includes aggravating factors both in the home and workplace, the onset and progress of the disease, family history and medical history of the patient in question. The medical history should also include a note of other allergic or airway disorders from childhood, and smoking history.

4.39 The results of positive bronchial challenge tests are considered to provide sufficient evidence for classification on their own. It is however recognised that in practice many of the examinations listed above will already have been carried out.

4.40 Substances that elicit symptoms of asthma by irritation only in people with bronchial hyper-reactivity should not be assigned R42.

Animal studies

4.41 Data from tests, which may be indicative of the potential of a substance or preparation to cause sensitisation by inhalation in humans, may include:

- IgE measurements (eg. in mice), or
- specific pulmonary responses in guinea pigs.

Sensitisation by skin contact

4.42 Substances and preparations shall be classified as **sensitising** and assigned the symbol '**Xi**', the indication of danger **'Irritant'** and the risk phrase **R43** in accordance with the criteria given below:

R43 May cause sensitisation by skin contact

– If practical experience shows the substance or preparation to be capable of inducing a sensitisation by skin contact in a substantial number of persons, or
– where there are positive results from an appropriate animal test.

Comments regarding the use of R43

Human evidence

4.43

a) The following evidence (practical experience) is sufficient to classify a substance or preparation with R43:

- Positive data from appropriate patch testing, normally in more than one dermatological clinic, or
- Epidemiological studies showing allergic contact dermatitis caused by the substance or preparation. Situations in which a high proportion of those exposed exhibit characteristic symptoms are to be looked at with special concern, even if the number of cases is small, or
- Positive data from experimental studies in man.

b) The following is sufficient to classify a substance with R43 when there is supportive evidence:

- Isolated episodes of allergic contact dermatitis, or
- Epidemiological studies where chance, bias or confounders have not been ruled out fully with reasonable confidence.

4.44 Supportive evidence may include:

- data from animal tests performed according to existing guidelines, with a result that does not meet the criteria given in the section on animal studies but is sufficiently close to the limit to be considered significant, or
- data from non-standard methods, or
- appropriate structure-activity relationships.

Animal studies

4.45 Positive results from appropriate animal tests are:

- in the case of an adjuvant type test method a response in at least 30% of the animals tested is considered positive;
- for any other test method a response in at least 15% of the animals is considered positive.

Immunological contact urticaria

4.46 Some substances or preparations, which meet the criteria for R42 (paragraph 4.34), may in addition cause immunological contact urticaria. In these cases, information concerning contact urticaria should be included by the use of appropriate Safety Phrases (S-phrases), usually S24 and S36/37, both on the label and in the Material Safety Data Sheet. See Appendix 3 for definitions of these Safety Phrases.

4.47 For substances or preparations that produce signs of immunological contact urticaria and *do not* fulfil the criteria for R42, consideration should be given to classification with R43 (paragraph 4.42).

4.48 There is no recognised animal model available to identify substances that cause immunological contact urticaria. Therefore, classification will normally be based on human evidence, which will be similar to that for skin sensitisation (R43).

Note: that if the symbol ‘Xn” and the indication of danger ‘harmful’ are assigned, the symbol ‘Xi’ and the indication of danger ‘irritant’ are optional.

OTHER TOXICOLOGICAL PROPERTIES

4.49 Additional risk phrases shall be assigned, in accordance with the following criteria, to substances and preparations classified by virtue of 4.9 to 4.48 above, and/or Chapter 5, and Appendices 6 and 7.

R29 Contact with water liberates toxic gas

For substances and preparations which in contact with water or damp air, evolve very toxic or toxic gases in potentially dangerous amounts, eg. aluminium phosphide, phosphorus pentasulphide.

R31 Contact with acids liberates toxic gas

For substances and preparations which react with acids to evolve toxic gases in dangerous amounts, eg. sodium hypochlorite, barium polysulphide. For substances used by members of the general public, the use of S50 (do not mix with ... (to be specified by the manufacturer)) would be more suitable.

R32 Contact with acids liberates very toxic gas

For substances and preparations that react with acids to evolve very toxic gases in dangerous amounts; eg. salts of hydrogen cyanide, sodium azide. For substances used by members of the general public, the use of S50 (do not mix with ... (to be specified by the manufacturer)) would be more suitable.

R33 Danger of cumulative effects

For substances and preparations when accumulation in the human body is likely and may cause some concern which, however, is not sufficient to justify the use of R48.

For comments on the use of this R-phrase see paragraph 5.62.

R64 May cause harm to breastfed babies

For substances and preparations that are absorbed by women and may interfere with lactation or which may be present (including metabolites) in breast milk in amounts sufficient to cause concern for the health of a breastfed child.

For comments on the use of this R-phrase see paragraphs 5.58 to 5.62.

R66 Repeated exposure may cause skin dryness or cracking

For substances and preparations that may cause concern as a result of skin dryness, flaking or cracking but which do not meet the criteria for R38 based on either:

- practical observation after normal handling and use, or
- relevant evidence concerning their predicted effects on the skin.

Note on the use of R66:

4.50 The criteria in this Approved Criteria are directly applicable when the data has been obtained from test methods equivalent to those described in Annex V to EU Directive 67/548/EEC. In other cases, the available data should be assessed by comparing the test methods used with those in Annex V to Directive 67/548/EEC and by applying the criteria herewith to determine the classification.

4.51 In some cases there may be doubt over the application of the relevant criteria, especially where these require the use of expert judgement. In such cases the manufacturer, distributor, or importer should provisionally classify and label the substance or preparation on the basis of an assessment of the evidence by a competent person.

R67 Vapours may cause drowsiness and dizziness

For volatile substances and preparations containing such substances that cause clear symptoms of central nervous system depression by inhalation, and which are not already classified with respect to acute inhalation toxicity (R20, R23, R26, R68/20, R39/23 or R39/26).

The following evidence may be used:

(a) Data from animal studies showing clear signs of CNS depression such as narcotic effects, lethargy, lack of co-ordination (including loss of righting reflex) and ataxia either:

- at concentrations/exposure times not exceeding 20 mg/l/4h or,
- for which the ratio of the effect concentration at $\leq$ 4 h to the saturated vapour concentration (SVC) at 20ºC is $\leq$ 1/10.

(b) Practical experience in humans (eg. narcosis, drowsiness, reduced alertness, loss of reflexes, lack of co-ordination, vertigo) from well documented reports under comparable exposure conditions to the effects specified above for animals.

4.52 For other supplementary risk phrases see Appendices 6 and 7.

Chapter 5

CLASSIFICATION ON THE BASIS OF SPECIFIC EFFECTS ON HUMAN HEALTH

Introduction

5.1 This chapter sets out the procedure for the classification of substances that are determined to be hazardous because of the following specific effects on human health:

- carcinogenic effects,
- mutagenic effects,
- toxic to reproduction, fertility, and development.

5.2 If a manufacturer, distributor, or importer has information available, which indicates that a substance should be classified and labelled in accordance with the criteria given in this chapter, he shall provisionally label the substance in accordance with these criteria on the basis of the assessment of the evidence by a competent person.

5.3 Where the substance is not already included in NOHSC's *List of Designated Hazardous Substances*, and is not a composite material, mixture or formulation, then the manufacturer or importer has a duty to notify NOHSC of that determination (see Appendix 5).

Criteria for classification, indication of danger, choice of risk phrases

CARCINOGENIC SUBSTANCES

5.4 For the purpose of classification and labelling, and having regard to the current state of knowledge, such substances are divided into three categories:

Category 1

5.5 Substances known to be carcinogenic to man. There is sufficient evidence to establish a causal association between human exposure to a substance and the development of cancer.

Category 2

5.6 Substances that should be regarded as if they are carcinogenic to man. There is sufficient evidence to provide a strong presumption that human exposure to a substance may result in the development of cancer, generally on the basis of:

- appropriate long-term animal studies,
- other relevant information.

Category 3

5.7 Substances that cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies, but this is insufficient to place the substance in Category 2.

5.8 The following symbols and specific risk phrases apply:

Categories 1 and 2:

5.9 Substances classified as carcinogenic category 1 or 2 shall be assigned the symbol **'T'** and the risk phrase:

R45 May cause cancer

5.10 However, substances and preparations which present a carcinogenic risk only when inhaled, for example, as dust, vapour or fumes, (other routes of exposure eg. by swallowing or in contact with skin do not present any carcinogenic risk), shall be assigned the symbol **'T'** and the risk phrase

R49 May cause cancer by inhalation

Category 3:

5.11 Substances classified as carcinogenic category 3 shall be assigned the symbol **'Xn'** and the risk phrase

R40 Limited evidence of a carcinogenic effect

Comments regarding the categorisation of carcinogenic substances.

5.12 The placing of a substance into Category 1 is done on the basis of epidemiological data; placing into Categories 2 and 3 is based primarily on animal experiments.

5.13 For classification as a Category 2 carcinogen either positive results in two animal species should be available or clear positive evidence in one species, together with supporting evidence such as genotoxicity data, metabolic or biochemical studies, induction of benign tumours, structural relationship with other known carcinogens, or data from epidemiological studies suggesting an association.

5.14 Category 3 actually comprises 2 sub-categories:

- substances which are well investigated but for which the evidence of a tumour-inducing effect is insufficient for classification in Category 2. Additional experiments would not be expected to yield further relevant information with respect to classification; and

- substances that are insufficiently investigated. The available date are inadequate, but they raise concern for man. This classification is provisional; further experiments are necessary before a final decision can be made.

5.15 For a distinction between Categories 2 and 3 the arguments listed below are relevant. These reduce the significance of experimental tumour induction in view of possible human exposure. These arguments, especially in combination, would lead in most cases to classification in Category 3, even though tumours have been induced in animals:

- carcinogenic effects only at very high dose levels exceeding the 'maximum tolerated dose'. The maximum tolerated dose is characterised by toxic effects which, although not yet reducing lifespan, go along with physical changes such as 10% retardation in weight gain;

- appearance of tumours, especially at high dose levels, only in particular organs of certain species known to be susceptible to a high spontaneous tumour formation;

- appearance of tumours only at the site of application, in very sensitive test systems (eg. intraperitoneal or subcutaneous application of certain locally active compounds), if the particular target is not relevant to man;

- lack of genotoxicity in short-term tests *in vivo* and *in vitro*;

- existence of a secondary mechanism of action with the implication of a practical threshold above a certain dose level (eg. hormonal effects on target organs or on mechanisms of physiological regulation, chronic stimulation of cell proliferation);

- existence of a species - specific mechanism of tumour formation (eg. by specific metabolic pathways) irrelevant for man.

5.16 For a distinction between *Category 3* and *no classification*, the following should be taken into consideration:

- a substance should not be classified in any of the categories if the mechanism of experimental tumour formation is clearly identified, with good evidence that this process cannot be extrapolated to man;

- if the only available tumour data are liver tumours in certain sensitive strains of mice, without any other supplementary evidence, the substance may not be classified in any of the categories;

- particular attention should be paid to cases where the only available tumour data are the occurrence of neoplasms at sites and in strains where they are well known to occur spontaneously with a high incidence.

MUTAGENIC SUBSTANCES

5.17 For the purposes of classification and labelling, and having regard to the current state of knowledge, such substances are divided into three categories:

Category 1

5.18 Substances known to be mutagenic to man.

There is sufficient evidence to establish a causal association between human exposure to a substance and heritable genetic damage.

Category 2

5.19 Substances that should be regarded as if they are mutagenic to man.

There is sufficient evidence to provide a strong presumption that human exposure to the substance may result in the development of heritable genetic damage, generally on the basis of:

- appropriate animal studies,
- other relevant information.

Category 3

5.20 Substances that cause concern for man owing to possible mutagenic effects.

There is evidence from appropriate mutagenicity studies, but this is insufficient to place the substance in Category 2.

5.21 The following symbols and specific risk phrases apply:

Categories 1 and 2:

5.22 Substances classified as mutagenic category 1 or 2 shall be assigned the symbol **'T'** and the risk phrase

R46 May cause heritable genetic damage

Category 3:

5.23 Substances classified as mutagenic category 3 shall be assigned the symbol **'Xn'** and the risk phrase

R68 Possible risk of irreversible effects

Comments regarding the categorisation of mutagenic substances

Definition of terms:

5.24 A mutation is a permanent change in the amount or structure of the genetic material in an organism, resulting in a change of the phenotypic characteristics of the organism. The alterations may involve a single gene, a block of genes, or a whole chromosome. Effects involving single genes may be a consequence of effects on single DNA bases (point mutations) or of large changes, including deletions, within the gene. Effects on whole chromosomes may involve structural or numerical changes. A mutation in the germ cells in sexually reproducing organisms may be transmitted to the offspring. A mutagen is an agent that gives rise to an enhanced occurrence of mutations.

5.25 It should be noted that substances are classified as mutagens with specific reference to inherited genetic damage. However, the type of results leading to classification of chemicals in Category 3: 'induction of genetically relevant events in somatic cells', is generally also regarded as an alert for possible carcinogenic activity.

5.26 Method development for mutagenicity testing is an ongoing process. For many new tests no standardised protocols and evaluation criteria are presently available. For the evaluation of mutagenicity data the quality of the test performance and the degree of validation of the test method have to be considered.

Category 1

5.27 To place a substance in Category 1, positive evidence from human mutation epidemiology studies will be needed. Examples of such substances are not known to date. It is recognised that it is extremely difficult to obtain reliable information from studies on the incidence of mutations in human populations, or on possible increases in their frequencies.

Category 2

5.28 To place a substance in Category 2, positive results are needed from assays showing:

(a) mutagenic effects;

(b) other cellular interactions relevant to mutagenicity in germ cells of mammals *in vivo*; or

(c) mutagenic effects in somatic cells of mammals *in vivo* in combination with clear evidence that the substance or a relevant metabolite reaches the germ cells.

5.29 With respect to placement in Category 2, at present the following methods are appropriate:

2 (a) *in vivo* germ cell mutagenicity assays:

- specific locus mutation test;
- heritable translocation test;
- dominant lethal mutation test.

These assays actually demonstrate the appearance of affected progeny or a defect in the developing embryo.

2 (b) *in vivo* assays showing relevant interaction with germ cells (usually DNA):

- assays for chromosomal abnormalities, as detected by cytogenetic analysis, including aneuploidy, caused by malsegregation of chromosomes,
- test for sister chromatid exchanges (SCEs),
- test for unscheduled DNA synthesis (UDS),
- assay of (covalent) binding of mutagen to germ cell DNA,
- assaying other kinds of DNA damage.

These assays provide evidence of a more or less indirect nature. Positive results in these assays would normally be supported by positive results from *in vivo* somatic cell mutagenicity assays in mammals or in man (see under Category 3, preferably methods as under 3 (a)).

2 (c) in *vivo* assays showing mutagenic effects in somatic cells of mammals (see under 3 (a)), in combination with toxicokinetic methods, or other methodologies capable of demonstrating that the compound or a relevant metabolite reaches the germ cells.

5.30 For 2 (b) and 2 (c), positive results from host-mediated assays or the demonstration of unequivocal effects in *in vitro* assays can be considered as supporting evidence.

Category 3

5.31 To place a substance in Category 3, positive results are needed in assays showing:

(a) mutagenic effects, or

(b) other cellular interactions relevant to mutagenicity in somatic cells in mammals *in vivo*.

5.32 The latter especially would normally be supported by positive results from *in vitro* mutagenicity assays.

5.33 For effects in somatic cells *in vivo* the following methods are presently appropriate:

3 (a)

- *in vivo* somatic cell mutagenicity assays:
  - bone marrow micronucleus test or metaphase analysis;
  - metaphase analysis of peripheral lymphocytes;
  - mouse coat colour spot test.

3 (b)

- *in vivo* somatic cell DNA interaction assays:
  - test for SCEs in somatic cells,
  - test for UDS in somatic cells,
  - assay for the (covalent) binding of mutagen to somatic cell DNA,
  - assay for DNA damage, eg. by alkaline elution, in somatic cells.

5.34 Substances showing positive results only in one or more *in vitro* mutagenicity assays should normally not be classified. Their further investigation using *in vivo* assays, however, is strongly indicated. In exceptional cases, eg. for a substance showing pronounced responses in several *in vitro* assays, for which no relevant *in vivo* data are available, and which shows resemblance to known mutagens/carcinogens, classification in Category 3 could be considered.

SUBSTANCES TOXIC TO REPRODUCTION

5.35 For the purposes of classification and labeling and having regard to the present state of knowledge, such substances are divided into 3 categories:

Category 1

Substances known to impair fertility in humans

5.36 There is sufficient evidence to establish a causal relationship between human exposure to the substance and impaired fertility.

Substances known to cause developmental toxicity in humans

5.37 There is sufficient evidence to establish a causal relationship between human exposure to the substance and subsequent developmental toxic effects in the progeny.

Category 2

Substances that should be regarded as if they impair fertility in humans

5.38 There is sufficient evidence to provide a strong presumption that human exposure to the substance may result in impaired fertility on the basis of:

- clear evidence in animal studies of impaired fertility in the absence of toxic effects, or, evidence of impaired fertility occurring at around the same dose levels as other toxic effects but which is not a secondary non-specific consequence of the other toxic effects;
- other relevant information.

Substances that should be regarded as if they cause developmental toxicity to humans

5.39 There is sufficient evidence to provide a strong presumption that human exposure to the substance may result in developmental toxicity, generally on the basis of:

- clear results in appropriate animal studies where effects have been observed in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not a secondary non-specific consequence of the other toxic effects;
- other relevant information.

Category 3

(i) *Substances that cause concern for human fertility*

5.40 Generally on the basis of:

- results in appropriate animal studies that provide sufficient evidence to cause a strong suspicion of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects, but which is not a secondary non-specific consequence of the other toxic effects, but where the evidence is insufficient to place the substance in Category 2;
- other relevant information.

(ii) *Substances that cause concern for humans owing to possible developmental toxic effects*

5.41 Generally on the basis of:

- results in appropriate animal studies that provide sufficient evidence to cause a strong suspicion of developmental toxicity in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not a secondary non-specific consequence of the other toxic effects, but where the evidence is insufficient to place the substance in Category 2,
- other relevant information.

5.42 The following symbols and specific risk phrases apply:

Category 1:

5.43

(i) for substances that impair fertility in humans:

Substances classified as *toxic to reproduction category 1* shall be assigned the symbol **'T'** and the risk phrase

R60 May impair fertility

(ii) for substances that cause developmental toxicity:

Substances classified as *toxic to reproduction category 1* shall be assigned the symbol **'T'** and the risk phrase

R61 May cause harm to the unborn child

Category 2:

5.44

(i) for substances that should be regarded as if they impair fertility in humans:

Substances classified as *toxic to reproduction category 2* shall be assigned the symbol '**T**' and the risk phrase

R60 May impair fertility

(ii) for substances that should be regarded as if they cause developmental toxicity in humans:

Substances classified as *toxic to reproduction category 2* shall be assigned the symbol '**T**' and the risk phrase

R61 May cause harm to the unborn child.

Category 3:

5.45

(i) for substances which cause concern for human fertility:

Substances classified as *toxic to reproduction category 3* shall be assigned the symbol '**Xn**' and the risk phrase

R62 Possible risk of impaired fertility

(ii) for substances which cause concern for humans owing to possible developmental toxic effects:

Substances classified as *toxic to reproduction category 3* shall be assigned the symbol '**Xn**' and the risk phrase

R63 Possible risk of harm to the unborn child.

Comments regarding the categorisation of substances toxic to reproduction

5.46 Reproductive toxicity includes impairment of male and female reproductive functions or capacity and the induction of non-inheritable harmful effects on the progeny. This may be classified under two main headings of:

1. Effects on male or female fertility;
2. Developmental toxicity.

5.47 Effects on male or female fertility include adverse effects on libido, sexual behaviour, any aspect of spermatogenesis or oogenesis, or on hormonal activity or physiological response which would interfere with the capacity to fertilise, fertilisation itself or the development of the fertilised ovum up to and including implantation.

5.48 Developmental toxicity is taken in its widest sense to include any effect interfering with normal development, both before and after birth. It includes effects induced or manifested prenatally as well as those manifested postnatally. This includes embryotoxic/foetotoxic effects such as reduced body weight, growth and developmental retardation, organ toxicity, death, abortion, structural defects (teratogenic effects), functional defects, peri-postnatal defects, and impaired postnatal mental or physical development up to and including normal pubertal development.

5.49 Classification of chemicals as toxic to reproduction is intended to be used for chemicals that have an intrinsic or specific property to produce such toxic effects. Chemicals should not be classified as toxic to reproduction where such effects are solely produced as a non-specific secondary consequence of other toxic effects. Chemicals of most concern are those that are toxic to reproduction at exposure levels that do not produce other signs of toxicity.

5.50 The placing of a compound in Category 1 for effects on fertility and/or developmental toxicity is done on the basis of epidemiological data. Placing into Categories 2 or 3 is done primarily on the basis of animal data. Data from *in vitro* studies, or studies on avian eggs, are regarded as 'supportive evidence' and would only exceptionally lead to classification in the absence of *in vivo* data.

5.51 In common with most other types of toxic effect, substances demonstrating reproductive toxicity will be expected to have a threshold below which adverse effects would not be demonstrated. Even when clear effects have been demonstrated in animal studies the relevance for humans may be doubtful because of the doses administered, for example, where effects have been demonstrated only at high doses, or where marked toxicokinetic differences exist, or the route of administration is inappropriate. For these or similar reasons it may be that classification in Category 3, or even no classification, will be warranted.

5.52 If a dose level of at least 1000 mg/kg orally produces no evidence of effects toxic to reproduction, studies at other dose levels may not be considered necessary. If data are available from studies carried out with doses higher than the above limit dose, this data must be evaluated together with other relevant data. Under normal circumstances it is considered that effects seen only at doses in excess of the limit dose would not necessarily lead to classification as 'Toxic to reproduction'.

Effects on fertility

5.53 For the classification of a substance into Category 2 for impaired fertility, there should normally be clear evidence in one animal species, with supporting evidence on mechanism of action or site of action, or chemical relationship to other known anti-fertility agents or other information from humans which would lead to the conclusion that effects would be likely to be seen in humans. Where there are studies in only one species without other relevant supporting evidence then classification in Category 3 may be appropriate.

5.54 Since impaired fertility may occur as a non-specific accompaniment to severe generalised toxicity or where there is severe inanition, classification into Category 2 should only be made where there is evidence that there is some degree of specificity of toxicity for the reproductive system. If it was demonstrated that impaired fertility in animal studies was due to failure to mate, then for classification into Category 2 it would normally be necessary to have evidence on the mechanism of action in order to interpret whether any adverse effect such as alteration in pattern of hormonal release would be likely to occur in humans.

Developmental toxicity

5.55 For classification into Category 2 there should be clear evidence of adverse effects in well conducted studies in one or more species. Since adverse effects in pregnancy or postnatally may result as a secondary consequence of maternal toxicity, reduced food or water intake, maternal stress, lack of maternal care, specific dietary deficiencies, poor animal husbandry, intercurrent infections, and so on, it is important that the effects observed should occur in well conducted studies and at dose levels which are not associated with marked maternal toxicity. The route of exposure is also important. In particular, the injection of irritant material intraperitoneally may result in local damage to the uterus and its contents, and the results of such studies must be interpreted with caution and on their own would not normally lead to classification.

5.56 Classification into Category 3 is based on similar criteria as for Category 2 but may be used where the experimental design has deficiencies that make the conclusions less convincing, or where the possibility that the effects may have been due to non-specific influences such as generalised toxicity cannot be excluded.

5.57 In general, classification in Category 3 or no category would be assigned on an ad hoc basis where the only effects recorded are small changes in the incidences of spontaneous defects, small changes in the proportions of common variants such as are observed in skeletal examinations, or small differences in postnatal developmental assessments.

Effects during lactation

5.58 Substances classified as toxic to reproduction and which also cause concern due to their effects on lactation should in addition be labelled with **R64** (see paragraph 4.49).

5.59 For the purpose of classification, toxic effects on offspring resulting only from exposure via the breast milk, or toxic effects resulting from direct exposure of children, will not be regarded as 'Toxic to reproduction', unless such effects result in impaired development of the offspring.

5.60 Substances which are not classified as toxic to reproduction but which cause concern due to toxicity when transferred to the baby during the period of lactation should be labelled with R64. This risk phrase may also be appropriate for substances that affect the quantity or quality of the milk.

5.61 R64 would normally be assigned on the basis of:

- toxicokinetic studies that would indicate the likelihood that the substance would be present in potentially toxic levels in breast milk, and/or
- on the basis of results of one or two generation studies in animals which indicate the presence of adverse effects on the offspring due to transfer in the milk, and/or
- on the basis of evidence in humans indicating a risk to babies during the lactational period.

5.62 Substances which are known to accumulate in the body and which subsequently may be released into milk during lactation may be labelled with R33 and R64.

LIST OF RISK PHRASES

R1	Explosive when dry
R2	Risk of explosion by shock, friction, fire or other sources of ignition
R3	Extreme risk of explosion by shock, friction, fire or other sources of ignition
R4	Forms very sensitive explosive metallic compounds
R5	Heating may cause an explosion
R6	Explosive with or without contact with air
R7	May cause fire
R8	Contact with combustible material may cause fire
R9	Explosive when mixed with combustible material
R10	Flammable
R11	Highly flammable
R12	Extremely flammable
R14	Reacts violently with water
R15	Contact with water liberates extremely flammable gases
R16	Explosive when mixed with oxidising substances
R17	Spontaneously flammable in air
R18	In use, may form flammable/explosive vapour-air mixture
R19	May form explosive peroxides
R20	Harmful by inhalation
R21	Harmful in contact with skin
R22	Harmful if swallowed
R23	Toxic by inhalation
R24	Toxic in contact with skin
R25	Toxic if swallowed
R26	Very toxic by inhalation
R27	Very toxic in contact with skin
R28	Very toxic if swallowed
R29	Contact with water liberates toxic gas
R30	Can become highly flammable in use
R31	Contact with acid liberates toxic gas
R32	Contact with acid liberates very toxic gas
R33	Danger of cumulative effects
R34	Causes burns

R35 Causes severe burns

R36 Irritating to eyes

R37 Irritating to respiratory system

R38 Irritating to skin

R39 Danger of very serious irreversible effects

R40 Limited evidence of a carcinogenic effect (See R68 for previous description applied to R40)

R41 Risk of serious eye damage

R42 May cause sensitisation by inhalation

R43 May cause sensitisation by skin contact

R44 Risk of explosion if heated under confinement

R45 May cause cancer

R46 May cause heritable genetic damage

R48 Danger of serious damage to health by prolonged exposure

R49 May cause cancer by inhalation

R50 Very toxic to aquatic organisms

R51 Toxic to aquatic organisms

R52 Harmful to aquatic organisms

R53 May cause long-term adverse effects in the aquatic environment

R54 Toxic to flora

R55 Toxic to fauna

R56 Toxic to soil organisms

R57 Toxic to bees

R58 May cause long-term adverse effects in the environment

R59 Dangerous for the ozone layer

R60 May impair fertility

R61 May cause harm to the unborn child

R62 Possible risk of impaired fertility

R63 Possible risk of harm to the unborn child

R64 May cause harm to breastfed babies

R65 Harmful: may cause lung damage if swallowed

R66 Repeated exposure may cause skin dryness or cracking

R67 Vapours may cause drowsiness and dizziness

R68 Possible risk of irreversible effects (previously this description was R40)

CHAPTER 6

CONCENTRATION LIMITS TO BE USED IN THE EVALUATION OF HEALTH HAZARDS

6.1 Concentration cut-off levels are used to determine whether or not a mixture or preparation is hazardous on the basis of its ingredients, and to classify the mixture on the basis of its health effects. The concentration cut-off levels are designed to provide a practical level of protection and information provision, but should not be used to imply that an effect cannot occur below that level.

6.2 Mixtures are hazardous if any ingredient meets any of the health effects criteria of Chapters 4 and 5, and is present at a concentration above the minimum concentration cut-off level for that ingredient, as shown in Tables 1 to 14 (see also Paragraphs 3.17-3.28).

6.3 For the purposes of classification, health effects are subdivided into:

- acute lethal effects (R20-28);
- non-lethal irreversible effects after a single exposure (R39, R68);
- severe effects after repeated or prolonged exposure (R48);
- cumulative effects (R33);
- corrosive effects (R34, R35);
- irritant effects (R36, R37, R38, R41);
- sensitising effects (R42, R43);
- carcinogenic effects (R40, R45, R49);
- mutagenic effects (R46);
- reproductive effects (R60-64); and,
- other toxicological effects (R65-R67).

6.4 A substance may have more than one health effect.

6.5 Unless a mixture has been tested and hence classified as a whole, the mixture is assessed by consideration of the health effects of each ingredient in the mixture, and classified according to the concentrations of each hazardous ingredient in the mixture.

6.6 Tables 1 to 14 are provided for determining whether an ingredient in a mixture exceeds its concentration cut-off level and, if so, the hazard classification of the mixture. The concentration cut-off levels from the Tables are used in the absence of specific concentration limits for the substance under consideration in the List.

6.7 For example, a mixture that contains an ingredient hazardous to health on the basis of its acute lethal effects may be classified as Very Toxic, Toxic or Harmful depending on the concentration of the hazardous substance contained therein (see Table 2).

6.8 Tables are provided for both solid and liquid mixtures, and for gaseous mixtures. For solid and liquid mixtures, concentrations are expressed on a weight/weight (w/w) basis. For gaseous mixtures, concentrations are on a volume/volume (v/v) basis.

6.9 To read the tables:

- identify the ingredient classification in the left-hand vertical column of the table, titled 'Classification of the Ingredient';
- compare the concentration of the ingredient in the mixture with the concentration cut-off levels listed in the table for the ingredient classification; and
- determine the mixture classification by reading the column heading for the concentration range matching the ingredient concentration in the mixture.

6.10 The hazardous ingredients of mixtures have risk phrases that are based on their health effects. Use of the tables in this chapter enables appropriate risk phrases to be selected for mixtures.

6.11 For example, a mixture with 15% of an ingredient classified as Toxic on the basis of its health effects, is classified as Harmful with risk phrases of R20, R21 or R22 (see Table 2).

6.12 Appropriate risk phrases for substances that are hazardous on the basis of their health effects are listed in Appendix 3.

6.13 In some instances, the hazard classification of a mixture may be different to the hazard classifications of the individual ingredients.

6.14 For example, a mixture containing a Corrosive ingredient (risk phrase R35) at 3% w/w will be classified as Irritant (risk phrases R36 or R38) (see Table 8).

6.15 Tables 1 to 14 have been adapted from Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999, (as amended by Commission Directive 2001/60/EC of 7 August 2001) concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of preparations.

Lower limits of concentration

6.16 Mixtures containing substances classified as hazardous on the basis of their health and/or environmental effects, whether they are present as impurities or additives, shall be taken into consideration when their concentrations are equal to or greater than those defined in Table 1, unless lower concentration cut-off values are given in either the List or in subsequent Tables in this chapter.

Table 1

Category of danger of the substance	**Concentration to take into consideration for**	
	gaseous mixtures % vol/vol	other preparations % w/w
Very toxic	≥ 0.02	≥ 0.1
Toxic	≥ 0.02	≥ 0.1
Carcinogenic, Category 1 or 2	≥ 0.02	≥ 0.1
Mutagenic, Category 1 or 2	≥ 0.02	≥ 0.1
Toxic for reproduction, Category 1 or 2	≥ 0.02	≥ 0.1
Harmful	≥ 0.2	≥ 1
Corrosive	≥ 0.02	≥ 1
Irritant	≥ 0.2	≥ 1
Sensitising	≥ 0.2	≥ 1
Carcinogenic, Category 3	≥ 0.2	≥ 1
Mutagenic, Category 3	≥ 0.2	≥ 1
Toxic for reproduction, Category 3	≥ 0.2	≥ 1
Dangerous for the environment, N		≥ 0.1
Dangerous for the environment, ozone	≥ 0.1	≥ 0.1
Dangerous for the environment		≥ 1

ACUTE LETHAL EFFECTS

6.17 The concentration limits in Tables 2 and 3 determine the classification of the mixture in relation to the individual concentration of the substance(s) present whose classification is shown.

6.18 In general, the Risk phrases to be assigned to the mixture will be those applicable to the substance(s) present in the concentration that gives rise to the most severe classification.

Table 2 Solid and liquid mixtures (includes aerosols and particulates)

INGREDIENT - CLASSIFICATION (*start*)- ⬇	**MIXTURE – CLASSIFICATION (*result*)**		
	Very Toxic (T^+) (R26, R27, R28)	**Toxic (T) (R23, R24, R25)**	**Harmful (Xn) (R20, R21, R22)**
Very Toxic (T^+) (R26, R27, R28) ➔	**conc ≥ 7%**	**1% ≤ conc < 7%**	**0.1% ≤ conc < 1%**
Toxic (T) (R23, R24, R25) ➔		**conc ≥ 25%**	**3% ≤ conc < 25%**
Harmful (Xn) (R20, R21, R22) ➔			**conc ≥ 25%**

Concentrations are in % w/w.

Table 3 Gas and Vapour Mixtures

INGREDIENT - CLASSIFICATION (*start*)- ⬇	**MIXTURE – CLASSIFICATION (*result*)**		
	Very Toxic (T^+) (R26, R27, R28)	**Toxic (T) (R23, R24, R25)**	**Harmful (Xn) (R20, R21, R22)**
Very Toxic (T^+) (R26, R27, R28) ➔	**conc ≥ 1%**	**0.2% ≤ conc < 1%**	**0.02% ≤ conc < 0.2%**
Toxic (T) (R23, R24, R25) ➔		**conc ≥ 5%**	**0.5% ≤ conc < 5%**
Harmful (Xn) (R20, R21, R22) ➔			**conc ≥ 5%**

Concentrations are in % v/v.

NON-LETHAL IRREVERSIBLE EFFECTS AFTER A SINGLE EXPOSURE

6.19 For substances that produce non-lethal irreversible effects after a single exposure (R39/route of exposure, R68/route of exposure), the individual concentration limits specified in Tables 4 and 5 determine, when appropriate, the classification of the mixture.

Table 4 Solid and liquid mixtures

INGREDIENT - CLASSIFICATION (*start*)- ↓	**MIXTURE – CLASSIFICATION (*result*)**		
	Very Toxic (T^+) R39 (*)[1]	**Toxic (T) R39 (*)[2]**	**Harmful (Xn) R68 (*)[3]**
Very Toxic (T^+) (with R39/route of exposure) →	**conc ≥ 10%**	**1% ≤ conc < 10%**	**0.1% ≤ conc < 1%**
Toxic (T) (with R39/route of exposure) →		**conc ≥ 10%**	**1% ≤ conc < 10%**
Harmful (Xn) (with R68/route of exposure) →			**conc ≥ 10%**

Concentrations are in % w/w.

(*) To indicate the route of administration/exposure one of the combination risk phrases listed below should be used.

Very Toxic (T^+)[1]	**Toxic (T)[2]**	**Harmful (Xn)[3]**
R39/26, R39/27, R39/28,	R39/23, R39/24, R39/25	R68/20, R68/21, R68/22
R39/26/27, R39/26/28,	R39/23/24, R39/23/25,	R68/20/21, R68/20/22,
R39/27/28	R39/24/25	R68/21/22
R39/26/27/28	R39/23/24/25	R68/20/21/22

Table 5 Gaseous mixtures

INGREDIENT - CLASSIFICATION (*start*)- ↓	**MIXTURE – CLASSIFICATION (*result*)**		
	Very Toxic (T^+) R39 (*)[1]	**Toxic (T) R39 (*)[2]**	**Harmful (Xn) R68 (*)[3]**
Very Toxic (T^+) (with R39/route of exposure) →	**conc ≥ 1%**	**0.2% ≤ conc < 1%**	**0.02% ≤ conc < 0.2%**
Toxic (T) (with R39/route of exposure) →		**conc ≥ 5%**	**0.5% ≤ conc < 5%**
Harmful (Xn) (with R68/route of exposure) →			**conc ≥ 5%**

Concentrations are in % v/v.

(*) To indicate the route of administration/exposure one of the combination risk phrases listed below should be used.

Very Toxic (T^+)[1]	**Toxic (T)[2]**	**Harmful (Xn)[3]**
R39/26, R39/27, R39/28,	R39/23, R39/24, R39/25	R68/20, R68/21, R68/22
R39/26/27, R39/26/28,	R39/23/24, R39/23/25,	R68/20/21, R68/20/22,
R39/27/28	R39/24/25	R68/21/22
R39/26/27/28	R39/23/24/25	R68/20/21/22

SEVERE EFFECTS AFTER REPEATED OR PROLONGED EXPOSURE

6.20 For substances that produce severe effects after repeated or prolonged exposure (R48/ route of exposure), the individual concentration limits specified in Tables 6 and 7 determine, when appropriate, the classification of the mixture.

Table 6 Solid and liquid mixtures

INGREDIENT - CLASSIFICATION (*start*)- ↓	**MIXTURE – CLASSIFICATION (*result*)**	
	Toxic (T) R48 (*)[1]	**Harmful (Xn) R48 (*)[2]**
Toxic (T) (with **R48/route of exposure)** →	**concentration ≥ 10%**	**1% ≤ conc < 10%**
Harmful (Xn) (with R48/route of exposure) →		**concentration ≥ 10%**

Concentrations are in % w/w.

(*) To indicate the route of administration/exposure one of the combination risk phrases listed below should be used.

Toxic (T)[1]	**Harmful (Xn)[2]**
R48/23, R48/24, R48/25	R48/20, R48/21, R48/22
R48/23/24, R48/23/25,	R48/20/21, R48/20/22,
R48/24/25	R48/21/22
R48/23/24/25	R48/20/21/22

Table 7 Gaseous mixtures

INGREDIENT - CLASSIFICATION (*start*)- ↓	**MIXTURE – CLASSIFICATION (*result*)**	
	Toxic (T) R48 (*)[1]	**Harmful (Xn) R48 (*)[2]**
Toxic (T) (with **R48/route of exposure)** →	**concentration ≥ 5%**	**0.5% ≤ conc < 5%**
Harmful (Xn) (with R48/route of exposure) →		**concentration ≥ 5%**

Concentrations are in % v/v.

(*) To indicate the route of administration/exposure one of the combination risk phrases listed below should be used.

Toxic (T)[1]	**Harmful (Xn)[2]**
R48/23, R48/24, R48/25	R48/20, R48/21, R48/22
R48/23/24, R48/23/25, R48/24/25	R48/20/21, R48/20/22, R48/21/22
R48/23/24/25	R48/20/21/22

CORROSIVE AND IRRITANT EFFECTS INCLUDING SERIOUS DAMAGE TO THE EYE

6.21 For substances that produce corrosive effects (R34, R35) or irritant effects (R36, R37, R38, R41), the individual concentration limits specified in Tables 8 and 9 determine, when appropriate, the classification of the mixture.

Table 8 Solid and liquid mixtures

INGREDIENT-CLASSIFICATION (*start*)- ↓	**MIXTURE – CLASSIFICATION (*result*)**			
	C with R35	C with R34	Irritant Xi with R41	Irritant Xi with R36, R37, R38
Corrosive (C) (with R35) →	**≥ 10%**	**5% ≤ conc < 10%**	**5%(*)**	**1% ≤ conc < 5% R36/38 obligatory**
Corrosive (C) (with R34) →		**conc ≥ 10%**	**10%(*)**	**5% ≤ conc < 10% R36/38 obligatory**
Irritant (Xi) (with R41) →			**conc ≥ 10%**	**5% ≤ conc < 10% R36 obligatory**
Irritant (Xi) (with R36, R37, R38) →				**conc ≥ 20% R36, R37, R38 obligatory**

Concentrations are in w/w%

(*) Corrosive ingredients assigned risk phrases R35 or R34 should be considered as assigned risk phrase R41, that is, capable of causing serious eye damage. Consequently, if the mixture contains corrosive substances with R35 or R34 below the concentration cut off levels for a classification of the mixture as corrosive, such ingredients can contribute to a classification of the mixture as irritant (R41) or irritant (R36).

Therefore, when the formulae for classifying mixtures at paragraphs 7.28 and 7.32 of Chapter 7 are applied the following concentration cut-off levels should be used:

Formula at 7.28 The concentration cut off levels to be used for $L_{Xi.R41}$ in the formula are:	*Formula at 7.32 The concentration cut off levels to be used for $L_{Xi.R36}$ in the formula are:*
10% for ingredients Xi.R41 *10% for ingredients C.R34* *5% for ingredients C.R35*	*20% for ingredients Xi.R36* *5% for ingredients Xi.R41* *5% for ingredients C.R34* *1% for ingredients C.R35*

Note: Simple application of the conventional method to preparations containing substances classified as corrosive or irritant may result in under-classification or over-classification of the hazard, if other relevant factors (eg. pH of the preparation) are not taken into account. Therefore, in classifying for corrosivity, consider the advice given in paragraphs 4.23 to 4.25, and effects such as potentiation that would under-estimate the toxicological hazard, and antagonism that would over-estimate the toxicological hazard. Potentiation and antagonistic effects shall be taken into account in classifying the preparation.

Table 9 Gaseous mixtures

INGREDIENT-CLASSIFICATION (*start*)- ⬇	**MIXTURE – CLASSIFICATION (*result*)**			
	C with R35	**C with R34**	**Xi with R41**	**Xi with R36, R37, R38**
Corrosive (C) (with R35) ➔	**conc ≥ 1% R35 obligatory**	**0.2% ≤ conc < 1% R34 obligatory**	**0.2%(*)**	**0.02% ≤ conc < 0.2% R36/37/38 obligatory**
Corrosive (C) (with R34) ➔		**conc ≥ 5% R34 obligatory**	**5%(*)**	**0.5% ≤ conc < 5% R36/37/38 obligatory**
Irritant (Xi) (with R41) ➔			**conc ≥ 5% R41 obligatory**	**0.5% ≤ conc < 5% R36 obligatory**
Irritant (Xi) (with R36, R37, R38) ➔				**conc ≥ 5% R36, R37, R38 obligatory as appropriate**

Concentrations are in v/v%

(*) Corrosive ingredients assigned risk phrases R35 or R34 must also be considered as being assigned risk phrase R41 (i.e. capable of causing serious eye damage). Consequently, if the mixture contains corrosive ingredients with R35 or R34 below the concentration cut-off level for a classification of the mixture as corrosive, such ingredients can contribute to a classification of the mixture as irritant with R41 or irritant with R36.

Therefore when the formulae for classifying mixtures at paragraphs 7.28 and 7.32 of Chapter 7 are applied the following concentration cut off levels should be used:

Formula at 7.28: The concentration cut-off levels to be used for $L_{Xi\ R41}$ in the formula are:	*Formula at 7.32: The concentration cut-off levels to be used for $L_{Xi\ R36}$ in the formula are:*
5% for the ingredients Xi R41 *5% for the ingredients C R34* *0.2% for the ingredients C R35*	*5% for the ingredients Xi R36* *0.5% for the ingredients Xi R41* *0.5% for the ingredients C R34* *0.02% for the ingredients C R35*

Note: Simple application of the conventional method to preparations containing substances classified as corrosive or irritant may result in under-classification or over-classification of the hazard, if other relevant factors (eg. pH of the preparation) are not taken into account. Therefore, in classifying for corrosivity, consider the advice given in paragraphs 4.23 to 4.25, and effects such as potentiation that would under-estimate the toxicological hazard, and antagonism that would over-estimate the toxicological hazard. Potentiation and antagonistic effects shall be taken into account in classifying the preparation.

SENSITISING EFFECTS

6.22 Preparations that produce such effects are classified as sensitising and assigned:

- the symbol Xn and phrase R42 if this effect can be produced by inhalation,
- the symbol Xi and phrase R43 if this effect can be produced through contact with the skin.

6.23 The individual concentration limits specified in Tables 10 and 11 determine, when appropriate, the classification of the mixture.

Table 10 Solid and liquid mixtures

INGREDIENT-CLASSIFICATION (*start*)- ⬇	**MIXTURE – CLASSIFICATION *(result)***	
	Sensitising with R42 (Xn)	**Sensitising with R43 (Xi)**
Sensitising with R42 ➔	**concentration ≥ 1% R42 obligatory**	
Sensitising with R43 ➔		**concentration ≥ 1% R43 obligatory**

Concentrations are in % w/w.

Table 11 Gaseous mixtures

INGREDIENT-CLASSIFICATION (*start*)- ⬇	**MIXTURE – CLASSIFICATION *(result)***	
	Sensitising with R42 (Xn)	**Sensitising with R43 (Xi)**
Sensitising with R42 ➔	**concentration ≥ 0.2% R42 obligatory**	
Sensitising with R43 ➔		**concentration ≥ 0.2% R43 obligatory**

Concentrations are in % v/v.

CARCINOGENIC / MUTAGENIC / TOXIC EFFECTS FOR REPRODUCTION

(i) Solid and liquid mixtures.

6.24 For substances that produce such effects, the concentration limits laid down in Table 12, expressed as a weight/weight percentage, shall determine, where appropriate, the classification of the mixture. The following symbol and risk phrases are assigned:

Carcinogenic categories 1 and 2:	T; R45 or R49
Carcinogenic category 3:	Xn; R40
Mutagenic categories 1 and 2:	T; R46
Mutagenic category 3:	Xn; R68
Toxic for reproduction fertility categories 1 and 2:	T; R60
Toxic for reproduction development categories 1 and 2:	T; R61
Toxic for reproduction fertility category 3:	Xn; R62
Toxic for reproduction development category 3:	Xn; R63

Table 12

Classification of the substance (start ↓)	**CLASSIFICATION OF THE MIXTURE (RESULT)**	
	Categories 1 and 2	**Category 3**
carcinogenic substances of category 1 or 2 with R45 or R49	**concentration ≥ 0.1% carcinogenic R45, R49 obligatory as appropriate**	
carcinogenic substances of category 3 with R40		**concentration ≥ 1% carcinogenic R40 obligatory**
mutagenic substances of category 1 or 2 with R46	**concentration ≥ 0.1% mutagenic R46 obligatory**	
mutagenic substances of category 3 with R68		**concentration ≥ 1% mutagenic R68 obligatory**
substances 'toxic for reproduction' of category 1 or 2 with R60 (fertility)	**concentration ≥ 0.5% toxic for reproduction (fertility) R60 obligatory**	
substances 'toxic for reproduction' of category 3 with R62 (fertility)		**concentration ≥ 5% toxic for reproduction (fertility) R62 obligatory**
substances 'toxic for reproduction' of category 1 or 2 with R61 (development)	**concentration ≥ 0.5% toxic for reproduction (development) R61 obligatory**	
substances 'toxic for reproduction' of category 3 with R63 (development)		**concentration ≥ 5% toxic for reproduction (development) R63 obligatory**

(ii) Gaseous mixtures.

6.25 For gases that produce such effects, the concentration limits laid down in Table 13, expressed as a volume/volume percentage, shall determine, where appropriate, the classification of the mixture. The following symbol and risk phrases are assigned:

Carcinogenic categories 1 and 2:	T; R45 or R49
Carcinogenic category 3:	Xn; R40
Mutagenic categories 1 and 2:	T; R46
Mutagenic category 3:	Xn; R68
Toxic for reproduction fertility categories 1 and 2:	T; R60
Toxic for reproduction development categories 1 and 2:	T; R61
Toxic for reproduction fertility category 3:	Xn; R62
Toxic for reproduction development category 3:	Xn; R63

Table 13

Classification of the substance (start ↓)	CLASSIFICATION OF THE MIXTURE (RESULT)	
	Categories 1 and 2	**Category 3**
carcinogenic substances of category 1 or 2 with R45 or R49	**concentration ≥ 0.1% carcinogenic R45, R49 obligatory as appropriate**	
carcinogenic substances of category 3 with R40		**concentration ≥ 1% carcinogenic R40 obligatory**
mutagenic substances of category 1 or 2 with R46	**concentration ≥ 0.1% mutagenic R46 obligatory**	
mutagenic substances of category 3 with R68		**concentration ≥ 1% mutagenic R68 obligatory**
substances 'toxic for reproduction' of category 1 or 2 with R60 (fertility)	**concentration ≥ 0.2% toxic for reproduction (fertility) R60 obligatory**	
substances 'toxic for reproduction' of category 3 with R62 (fertility)		**concentration ≥ 1% toxic for reproduction (fertility) R62 obligatory**
substances 'toxic for reproduction' of category 1 or 2 with R61 (development)	**concentration ≥ 0.2% toxic for reproduction (development) R61 obligatory**	
substances 'toxic for reproduction' of category 3 with R63 (development)		**concentration ≥ 1% toxic for reproduction (development) R63 obligatory**

OTHER TOXICOLOGICAL EFFECTS

Table 14 Solid, liquid and gaseous mixtures

INGREDIENT-CLASSIFICATION (*start*)- ↓	MIXTURE – CLASSIFICATION (*result*)
	Harmful (Xn)
R33 →	concentration ≥ 1% R33
R64 →	concentration ≥ 1% R64
R65 →	concentration ≥ 10.0% R65

Concentrations are in % w/w for solids and liquids and %v/v for gases.

CHAPTER 7

METHODS FOR THE EVALUATION OF HEALTH HAZARDS OF MIXTURES

Introduction

7.1 An assessment must be made for all the health effects corresponding to the health effects of substances contained in a mixture. This chapter details a method which is applicable to all preparations and mixtures, and which takes into consideration all the health hazards of substances contained in the mixture. For that purpose the adverse health effects have been subdivided into:

1. acute lethal effects;
2. non-lethal irreversible effects after a single exposure;
3. severe effects after repeated or prolonged exposure;
4. corrosive effects,
5. irritant effects;
6. sensitising effects;
7. carcinogenic effects, mutagenic effects, toxic effects for reproduction.

7.2 The health effects of a preparation are to be assessed using individual concentration limits:

(a) where the ingredients of a mixture are listed in the *List of Designated Hazardous Substances* (the List), and are assigned concentration limits necessary for the application of the method of assessment described in this chapter, these concentration limits must be used;

(b) where the ingredients of the mixture do not appear in the List or appear there without concentration limits, the concentration limits must be assigned in accordance with the specifications in Chapter 6 of the Approved Criteria.

7.3 The classification of the substance(s) and the resulting classification of the preparation are expressed:

- either by a symbol and one or more risk phrases, or
- by categories (category 1, category 2 or category 3) also assigned risk phrases when substances and preparations are shown to be carcinogenic, mutagenic or toxic for reproduction. Therefore it is important to consider, in addition to the symbol, all the phrases denoting specific risks, which are assigned to each substance under consideration.

7.4 The systematic assessment of all the adverse health effects is expressed by means of concentration limits expressed as a weight/weight percentage, except for gaseous preparations where they are expressed as a volume/volume percentage, and in conjunction with the classification of the substance.

7.5 Where they are not given in the List the concentration limits to be taken into account are those set out in Chapter 6 of the Approved Criteria.

Procedure for evaluation of health hazards.

7.6 The following formulae provide a safeguard, as substances with similar health effects can produce an additive effect greater than would be suggested by their individual concentrations.

7.7 For calculating the additive effects of hazardous ingredients in mixtures in order to determine the hazard classification of the mixture, the following procedure is used:

(i) identify the ingredient classification in the first column of the appropriate table in Chapter 6.

(ii) check to see if two or more ingredients are classified with very toxic, toxic, harmful, corrosive or irritant, sensitizing, carcinogenic, mutagenic, or toxic to reproduction effects.

(iii) for each type of health effect use the formulae listed below to classify the mixture, beginning with the most severe classification for each health effect.

For example, determine whether the mixture is Very Toxic (T^+) before determining whether it is Toxic (T).

(iv) for each denominator in the equation select the concentration cut-off level for the ingredient that is appropriate for the mixture classification.

For example, in the case of a Very Toxic (T^+) ingredient, the concentration cut-off level (Table 2) is 7% for a Very Toxic (T^+) mixture, 1% for a Toxic mixture, and 0.1% for a Harmful mixture.

(v) Where a concentration range is indicated in Chapter 6, use the lowest concentration cut-off level as the denominator in the equation.

For example, use 3% if the range shown in Table 2 is $3\% \leq \text{conc} < 25\%$.

ACUTE LETHAL EFFECTS

7.8 Lethality resulting from different routes of exposure is considered to be additive for the purpose of applying the following formulae. The appropriate combination risk phrase is then applied to the mixture.

Very toxic (T^+) mixtures with R26, R27, R28.

7.9 *The following preparations are to be classified as* ***very toxic***:

7.10 Owing to their **acute lethal effects** and assigned the symbol $\mathbf{T^+}$, the indication of danger '**very toxic**', and the risk phrases **R26**, **R27** or **R28**;

(i) preparations containing one or more substances classified as very toxic that produce such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 2 or 3 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

(ii) preparations containing more than one substance classified as very toxic in lower individual concentrations than the limits specified under (i)(a) or (b) if:

$$\sum\left(\frac{P_T^+}{L_T^+}\right)\geq 1$$

where:

P_{T+} = is the percentage by weight or by volume of each very toxic substance in the preparation,

L_{T+} = is the very toxic limit specified for each very toxic substance, expressed as a percentage by weight or by volume;

7.11 owing to their **non-lethal irreversible effects after a single exposure** and assigned the symbol **T**$^{+}$, the indication of danger '**very toxic**', and the risk phrase **R39/route of exposure**.

(i) preparations containing at least one substance that produces such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 4 or 5 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

Toxic (T) mixtures with R23, R24, R25

7.12 *The following preparations shall be classified as* ***toxic***:

7.13 owing to their **acute lethal effects** and assigned the symbol **T**, the indication of danger '**toxic**', and the risk phrases **R23**, **R24** or **R25**;

(i) preparations containing one or more substances classified as very toxic or toxic that produce such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 2 or 3 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

(ii) preparations containing more than one substance classified as very toxic or toxic in lower individual concentrations than the limits specified under (i)(a) or (b) if:

$$\sum\left(\frac{P_T^{+}}{L_T}+\frac{P_T}{L_T}\right)\geq 1$$

where:

P_T^{+} = is the percentage by weight or by volume of each very toxic substance in the preparation,

P_T = is the percentage by weight or by volume of each toxic substance in the preparation,

L_T = is the respective toxic limit specified for each very toxic or toxic substance, expressed as a percentage by weight or by volume;

7.14 owing to their **non-lethal irreversible effects after a single exposure** and assigned the symbol **T**, the indication of danger '**toxic**', and the risk phrase **R39/route of exposure**.

(i) preparations containing at least one substance classified as very toxic or toxic that produce such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 4 or 5 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

7.15 owing to their **long-term effects** and assigned the symbol **T**, the indication of danger '**toxic**' and the risk phrase **R48/route of exposure**.

(i) preparations containing at least one substance that produces such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 6 or 7 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

Harmful (Xn) mixtures with R20, R21, R22.

7.16 *The following preparations shall be classified as **harmful***:

7.17 owing to their **acute lethal effects** and assigned the symbol **Xn**, and the indication of danger '**harmful**', and the risk phrases **R20**, **R21** or **R22**;

(i) preparations containing one or more substances classified as very toxic, toxic or harmful and that produce such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 2 or 3 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

(ii) preparations containing more than one substance classified as very toxic, toxic or harmful in lower individual concentrations than the limits specified under (i)(a) or (b) if:

$$\sum\left(\frac{P_{T^+}}{L_{Xn}}+\frac{P_T}{L_{Xn}}+\frac{P_{Xn}}{L_{Xn}}\right)\geq 1$$

where:

P_{T+} = is the percentage by weight or by volume of each very toxic substance in the preparation,

P_T = is the percentage by weight or by volume of each toxic substance in the preparation,

P_{Xn} = is the percentage by weight or by volume of each harmful substance in the preparation,

L_{Xn} = is the respective harmful limit specified for each very toxic, toxic or harmful substance, expressed as percentage by weight or by volume.

7.18 owing to their **acute effects to the lungs if swallowed** and assigned the symbol **Xn**, and the indication of danger '**harmful**', and the risk phrase **R65**.

(i) preparations classified as harmful according to the criteria specified in paragraph 4.14 (aspiration hazard) of Chapter 4.

(ii) in applying the method according to 7.17(ii), no account shall be taken of the classification of a substance as R65;

7.19 owing to their **non-lethal irreversible effects after a single exposure** and assigned the symbol **Xn**, the indication of danger '**harmful**', and the risk phrase **R68/route of exposure**.

(i) preparations containing at least one substance classified as very toxic, toxic or harmful that produces such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 4 or 5 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.20 owing to their **long-term effects** after repeated or prolonged exposure and assigned the symbol **Xn**, the indication of danger '**harmful**', and the risk phrase **R48/route of exposure**.

(i) preparations containing at least one substance classified as toxic or harmful that produces such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 6 or 7 where the substance or substances do not appear in the List or appear in it without concentration limits.

CORROSIVE (C) MIXTURES WITH R34, R35.

7.21 The following preparations are to be classified as **corrosive (R35),** and assigned the symbol **C**, the indication of danger '**corrosive**' and the risk phrase **R35**:

7.22 preparations containing one or more substances classified as corrosive to which is assigned the phrase R35 in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 8 or 9 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

7.23 preparations containing more than one substance classified as corrosive to which is assigned phrase R35 in lower individual concentrations than the limits specified under 7.22(a) or (b) if:

$$\sum\left(\frac{P_{C.R35}}{L_{C.R35}}\right)\geq 1$$

where:

$P_{C\,R35}$ = is the percentage by weight or by volume of each corrosive substance which is assigned phrase R35 in the preparation,

$L_{C\,R35}$ = is the corrosive R35 limit specified for each corrosive substance to which is assigned phrase R35, expressed as a percentage by weight or by volume;

7.24 The following preparations are to be classified as **corrosive (R34),** and assigned the symbol **C**, the indication of danger '**corrosive**' and the risk phrase **R34**:

7.25 preparations containing one or more substances classified as corrosive to which is assigned the phrase R35 or R34 in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 8 or 9 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.26 preparations containing more than one of the substances classified as corrosive to which is assigned the phrase R35 or R34 in lower individual concentrations than the limits specified under 7.25(a) or (b) if:

$$\sum\left(\frac{P_{C.R35}}{L_{C.R34}} + \frac{P_{C.R34}}{L_{C.R34}}\right) \geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$L_{C\ R34}$ = is the respective corrosive R34 limit specified for each corrosive substance to which is assigned phrase R35 or R34, expressed as a percentage by weight or by volume.

IRRITANT (XI) MIXTURES WITH R36, R37, R38, R41.

7.27 *The following preparations are to be classified as irritants*:

7.28 *Irritant mixtures with risk of serious eye damage (R41)*

7.29 liable to cause **serious eye damage** and assigned the symbol **Xi**, the indication of danger '**irritant**', and the risk phrase **R41**:

7.30 preparations containing one or more substances classified as irritant to which is assigned phrase R41 in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 8 or 9 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.31 preparations containing more than one of the substances classified as irritant and to which is assigned phrase R41, or classified as corrosive and to which is assigned phrase R35 or R34, in lower individual concentrations than the limits specified under 7.30(a) or (b) if:

$$\sum\left(\frac{P_{C.R35}}{L_{Xi.R41}}+\frac{P_{C.R34}}{L_{Xi.R41}}+\frac{P_{Xi.R41}}{L_{Xi.R41}}\right)\geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$P_{Xi\ R41}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R41 in the preparation,

$L_{Xi\ R41}$ = is the respective irritant R41 limit specified for each corrosive substance to which is assigned phrase R35 or R34 or irritant substance to which is assigned phrase R41, expressed as percentage by weight or by volume;

7.32 *Eye irritant mixtures (R36)*

7.33 **irritant to eyes** and assigned the symbol **Xi**, the indication of danger '**irritant**', and the risk phrase **R36**:

7.34 preparations containing one or more substances classified as corrosive to which is assigned phrase R35 or R34, or as irritant and to which is assigned phrase R41 or R36, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 8 or 9 of chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.35 preparations containing more than one substance classified as irritant to which is assigned phrase R41 or R36, or as corrosive and to which is assigned phrase R35 or R34, in lower individual concentrations than the limits specified under 7.34(a) or (b) if:

$$\sum\left(\frac{P_{C,\ R35}}{L_{Xi,\ R36}} + \frac{P_{C,\ R34}}{L_{Xi,\ R36}} + \frac{P_{Xi,\ R41}}{L_{Xi,\ R36}} + \frac{P_{Xi,\ R36}}{L_{Xi,\ R36}}\right) \geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$P_{Xi\ R41}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R41 in the preparation,

$P_{Xi\ R36}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R36 in the preparation,

$L_{Xi\ R36}$ = is the respective irritant R36 limit specified for each corrosive substance to which is assigned phrase R35 or R34 or irritant substance to which is assigned phrase R41, or R36 expressed as percentage by weight or by volume;

7.36 *Skin irritant mixtures (R38)*

7.37 **irritant to skin** and assigned the symbol **Xi**, the indication of danger '**irritant**', and the risk phrase **R38**;

7.38 preparations containing one or more substances classified as irritant and to which is assigned phrase R38, or as corrosive and to which is assigned phrase R35 or R34, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 8 or 9 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.39 preparations containing more than one of the substances classified as irritant and to which is assigned phrase R38, or as corrosive and to which is assigned phrase R35 or R34, in lower individual concentrations than the limits specified under 7.38(a) or (b) if:

$$\sum\left(\frac{P_{C.R35}}{L_{Xi.R38}}+\frac{P_{C.R34}}{L_{Xi.R38}}+\frac{P_{Xi.R38}}{L_{Xi.R38}}\right)\geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$P_{Xi\ R38}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R38 in the preparation,

$L_{Xi\ R38}$ = is the respective irritant R38 limit specified for each corrosive substance to which is assigned phrase R35 or R34 or irritant substance to which is assigned phrase R38, expressed as percentage by weight or by volume;

7.40 *Respiratory irritant mixtures (R37)*

7.41 **irritant to respiratory system** and assigned the symbol **Xi**, the indication of danger '**irritant**', and the risk phrase **R37**;

7.42 preparations containing one or more substances classified as irritant, and to which is assigned phrase R37 in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 8 or 9 of Chapter 6 where the substance or the substances do not appear in the List or appear in it without concentration limits;

7.43 preparations containing more than one substance classified as irritant and to which is assigned phrase R37 in lower individual concentrations than the limits specified under 7.42(a) or (b) if:

$$\sum\left(\frac{P_{Xi.R37}}{L_{Xi.R37}}\right)\geq 1$$

where:

$P_{Xi\ R37}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R37 in the preparation,

$L_{Xi\ R37}$ = is the irritant R37 limit specified for each irritant substance to which is assigned phrase R37, expressed as percentage by weight or by volume;

7.44 gaseous preparations containing more than one of the substances classified as irritant to which is assigned phrase R37, or as corrosive and to which is assigned phrase R35 or R34, in lower individual concentrations than the limits specified under 7.42(a) or (b) if:

$$\sum\left(\frac{P_{C.R35}}{L_{Xi.R37}}+\frac{P_{C.R34}}{L_{Xi.R37}}+\frac{P_{Xi.R37}}{L_{Xi.R37}}\right)\geq 1$$

where:

$P_{C\ R35}$ = is the percentage by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$P_{Xi\ R37}$ = is the percentage by volume of each irritant substance to which is assigned phrase R37 in the preparation,

$L_{Xi\ R37}$ = is the respective irritant R37 limit specified for each gaseous corrosive substance to which is assigned phrase R35 or R34 or gaseous irritant substance to which is assigned phrase R37, expressed as percentage by weight or by volume.

MIXTURES CLASSIFIED AS SENSITIZING

7.45 *The following preparations are to be classified as **sensitising***:

7.46 by **skin contact** and assigned the symbol **Xi**, the indication of danger '**irritant**' and the risk phrase **R43**.

7.47 preparations containing at least one substance classified as sensitising and to which is assigned phrase R43 that produces such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 10 or 11 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.48 by **inhalation** and assigned the symbol **Xn**, the indication of danger '**harmful**' and the risk phrase **R42**.

7.49 preparations containing at least one substance classified as sensitising to which is assigned phrase R42 that produces such effects in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 10 or 11 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

CARCINOGENIC MIXTURES

7.50 *The following preparations are to be classified as **carcinogenic***:

7.51 those of **category 1 or 2** which are assigned the symbol **T** and the phrase **R45** or **R49**;

7.52 preparations containing at least one substance producing such effects, classified as carcinogenic and to which is assigned phrase R45 or R49 which denotes carcinogenic substances in category 1 and category 2, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.53 those of **category 3** which are assigned the symbol **Xn** and the phrase **R40**;

7.54 preparations containing at least one substance producing such effects classified as carcinogenic and to which is assigned phrase R40 which denotes carcinogenic substances in category 3, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

MUTAGENIC MIXTURES

7.55 *The following preparations are to be classified as* ***mutagenic***:

7.56 those of **category 1 or 2** which are assigned the symbol **T** and the phrase **R46;**

7.57 preparations containing at least one substance producing such effects, classified as mutagenic and to which is assigned phrase R46 which denotes mutagenic substances in category 1 and category 2, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.58 those of **category 3** which are assigned the symbol **Xn** and the phrase **R68**;

7.59 preparations containing at least one substance producing such effects, classified as mutagenic and to which is assigned phrase R68, which denotes mutagenic substances in category 3, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 and 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

MIXTURES TOXIC FOR REPRODUCTION

7.60 *The following preparations are to be classified as toxic for **reproduction***:

7.61 those of **category 1 or 2** which are assigned the symbol **T** and the phrase **R60** (fertility);

7.62 preparations containing at least one substance producing such effects, classified as toxic for reproduction, and to which is assigned phrase R60 which denotes substances toxic for reproduction of category 1 and category 2, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.63 those of **category 3** which are assigned the symbol **Xn** and the phrase **R62** (fertility);

7.64 preparations containing at least one substance producing such effects, classified as toxic for reproduction, and to which is assigned phrase R62, which denotes substances toxic for reproduction of category 3 in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.65 those of **category 1 or 2** which are assigned the symbol **T** and the phrase **R61** (development);

7.66 preparations containing at least one substance producing such effects, classified as toxic for reproduction and to which is assigned phrase R61, which denotes substances toxic for reproduction of category 1 and category 2, in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits;

7.67 those of **category 3** which are assigned the symbol **Xn** and the phrase **R63** (development);

7.68 preparations containing at least one substance producing such effects, classified as toxic for reproduction, and to which is assigned phrase R63, which denotes substances toxic for reproduction of category 3 in individual concentrations equal to or greater than:

(a) either the concentration specified in the List for the substance or substances under consideration, or

(b) the concentration specified in Table 12 or 13 of Chapter 6 where the substance or substances do not appear in the List or appear in it without concentration limits.

APPENDICES

Appendix 1

INFORMATION SOURCES

Although not an exhaustive listing, the following information sources described in this appendix may be useful in the process of collating and interpreting data on the health effects of a substance.

Books, monographs and other publications

A1.1 Clayton, G. D. and Clayton, F. E, Patty's Industrial Hygiene and Toxicology, 5th edition. John Wiley & Sons, Inc., Brisbane, 2000. (Web site: http://www3.interscience.wiley.com/reference.html)

A1.2 International Agency for Research on Cancer, IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, International Agency for Research on Cancer, Lyon, France. (Web site: http://www.iarc.fr)

These monographs are critical reviews of the literature on chemicals, industrial processes and industries associated with human cancer by the various IARC Working Groups. Summary evaluations, list of agents and exposures evaluated and their classification and information on ordering can be found at http://monographs.iarc.fr.

A1.3 International Agency for Research on Cancer, IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Supplement 7 (IARC Monographs, Volumes 1 to 78 - continuing), International Agency for Research on Cancer, Lyon, France, 1987.

The supplement summarises the data reviewed in the IARC Monographs, Volumes 1 to 42, and provides a cumulative index. Note that the website http://www.iarc.fr provides summaries of the carcinogenic properties of chemicals studied in these monographs.

A1.4 International Agency for Research on Cancer, IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Supplement 6 (Genetic and Related Effects: An Updating of Selected IARC Monographs, Volumes 1 to 42), International Agency for Research on Cancer, Lyon, France, l987.

This is a tabulation of the published literature on the genotoxic effects of 200 IARC evaluated chemicals and agents.

A1.5 International Programme on Chemical Safety, Environmental Health Criteria, World Health Organisation, Geneva, Switzerland.

These criteria are reviews of environmental and toxicological literature on chemicals and physical agents published as a joint venture of the United Nations Environment Programme, the International Labour Organisation and the World Health Organisation. These publications are freely available at: http://www.inchem.org/ehc.html.

A1.6 Klaasen, C.D., Amdur, M.O. and Doull, J., Casarett and Doull's Toxicology: The Basic Science of Poisons, 6th Edition. McGraw Hill Companies, Inc., New York, USA, 2001.

This is a textbook covering theoretical aspects of toxicology including concepts and mechanisms.

A1.7 Schardein, J.L., Chemically Induced Birth Defects, 3rd Edition. Marcel Dekker, New York, USA, 2000.

This is a valuable reference text on chemicals and their interaction with the processes of development and growth.

A1.8 Shepard, T.H., Catalogue of Teratogenic Agents, 7th Edition, Johns Hopkins University Press, Baltimore, USA, 1992.

This is a comprehensive listing of teratogens, as abstracted from the published literature. This is also available as a database on TOMES Plus.

A1.9 The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC).

ECETOC publishes a range of reports varying in scope from those on specific chemicals (eg the Joint Assessment of Commodity Chemicals reports (JACC)) to those dealing with the fundamental principles underlying the various branches of science in toxicology and ecotoxicology (eg. Monographs and Technical Reports). ECETOC publications are produced by Task Forces composed of appropriate experts drawn from member companies and other organisations. Abstracts of recent reports and monograph ordering information can be found on the ECETOC site: http://www.ecetoc.org/entry.htm.

The European Centre for Ecotoxicology and Toxicology of Chemicals
Avenue E, Van Nieuwenhuyse, 4-B6
B-1160 Brussels, Belgium.
Email: info@ecetoc.org

Computer databases

A1.10 There are two principal types of computer databases available:

(a) Factual - a listing of information on the properties of a chemical. For example, RTECS and HSDB; and

(b) Bibliographic - a list of references in the scientific literature, usually with abstracts or summaries. For example, TOXLINE, CISDOC, HSELINE, MEDLINE and NIOSHTIC.

A1.11 Factual databases have the advantage of allowing immediate access to information, for example, specific physical properties of a chemical or toxicity values. Retrieving information by searching a bibliographic database is more time consuming as it involves obtaining copies of the articles from books and journals. However, it should be noted that reference to articles in the scientific literature will generally provide more current information in a greater amount of detail.

A1.12 Searching databases containing chemical information demands a knowledge and experience of the different search techniques. Searching by inexperienced users may yield results which are not a true representation of the information available. It is generally recommended that advice from an experienced user should be sought before commencing a search.

A1.13 Databases are available either by online (web) access or on a CD-ROM. Some databases, such as RTECS, are available from a number of different database suppliers both via the web and through CD-ROM products. Online database suppliers provide access to hundreds of databases and very powerful search engines. Account holders are charged for what they use, usually on a monthly basis. This method of searching can prove expensive for the inexperienced or untrained user.

A1.14 There are an increasing number of information products containing one or a package of several databases which are purchased via annual subscription to either web-based or CD-ROM access and updated during the year. For the frequent user this may prove more cost effective as once the subscription fees are paid no charge is made for access.

A1.15 There are currently several hundred databases worldwide providing occupational health and safety information. Some of the more widely used databases providing information on chemicals are described below. Where a database is freely available on the web, there is a link directly to that resource (hyperlinked from the resource title). A selection of database suppliers appends the following list, linked from each particular database's details.

Factual Databases

A1.16 CCRIS - Chemical Carcinogenesis Research Information System. CCRIS contains scientifically evaluated data derived from carcinogenicity, mutagenicity, tumour promotion, and tumour inhibition studies on over 2500 chemicals.
CIS | TOXNET

A1.17 CHEMINFO - produced by the Canadian Centre for Occupational Health and Safety (CCOHS), Cheminfo contains property information, exposure limit values, NFPA hazard assessments and toxicity data.
CCINFO

A1.18 CHEMLIST - The Regulated Chemicals Listing contains identifying and US regulatory information for chemical substances listed on the US EPA Toxic Substances Control Act Inventory or subject to regulation under TSCA; the Australian Inventory of Chemical Substances (AICS); the Canadian Domestic Substances List (DSL) and Non-Domestic Substances List (NDSL); the Korean Existing Chemicals List (ECL), the European Inventory of Existing Commercial Chemicals Substances (EINECS) and the European List of Notified Chemical Substances (ELINCS), and the Japanese Chemical Inventory (ECN).
STN | SciFinder

A1.19 CHEMSAFE - contains evaluated safety characteristics of flammable substances. More than 40 properties, such as flash points, explosion limits, minimum ignition energy and autoignition temperature are provided. Sources include technical laws, collections of safety parameters and accident prevention regulations.
STN

A1.20 CHEMTOX - provides a collection of environmental, health and safety data for chemical substances regulated or which are candidates for regulation in the US. The database contains identifying information, physical and chemical properties, US regulatory information, toxicity data, and emergency and disposal guidelines for 6,000 chemicals.
Dialog Corp

A1.21 CHRIS 2000- Chemical Hazard Response Information System from the US Coast Dept of Transportation (CoastGuard) contains information to assist with emergency response, accident response, accident prevention and safety procedure design, and transportation of chemicals. This database is available through the following database collections:
CIS | SilverPlatter | TOMES Plus | STN

A1.22 GENE-TOX - contains mutagenicity data on over 3,000 chemicals assembled from expert review of the open scientific literature from the US EPA.
TOXNET

A1.23 HAZARDTEXT - provides information to assist with the management of hazardous chemical incidents such as spills or leaks - toxicity, fire and explosion data, chemical reactivity, personal protective equipment and disposal guidelines. A good source of information on personal protective equipment.
TOMES Plus

A1.24 HSDB - Hazardous Substances Databank from the US National Library of Medicine's TOXNET system: broad scope in human and animal toxicity, safety and handling, environmental fate, and more. Scientifically peer-reviewed.
STN | TOXNET | SilverPlatter | CIS | TOMES Plus

A1.25 IRIS - Integrated Risk Information System, sponsored by the US EPA, provides EPA health risk and regulatory information on over 600 chemicals. Carcinogenic (eg unit risks) and non-carcinogenic (eg reference doses) risk assessment data is provided for the oral and inhalation routes of exposure.
TOXNET | CIS | TOMES Plus

A1.26 NATIONAL CHEMICAL INVENTORIES CD-ROM - includes identifying data (chemical names, synonyms and trade names, and if available molecular formulae and structure diagrams) for over 175,000 substances taken from the following national inventories: Australian Inventory of Chemical Substances (AICS), United States (TSCA); Canada (DSL, NDSL); The European Communities (EINECS/ELINCS); Japan (ECN), Philippines (PICCS), Taiwan, Israel and Korea (ECL).
CAS

A1.27 REGISTRY FILE - contains over 15 million unique chemical substance records identified by the Chemical Abstracts Service (CAS). Records contain identifying information such as CAS Registry numbers, CA index names, commonly used synonyms and some trade names, polymer class terms, molecular formula and structure diagrams. The Registry file is unique to STN and the locator field indicates which other files (indexed by CAS numbers) on the STN system contain information on the chemical - thus it will indicate whether there is a record for the chemical in RTECS, HSDB, Chemlist, Medline, Toxline, Toxlit etc.
STN | SciFinder

A1.28 REPROTEXT - is produced by Micromedex and provides information on the acute and chronic clinical effects of chemicals and physical agents. Each chemical has a dual hazard rating, one for general toxicity and one for reproductive hazard.
TOMES Plus

A1.29 RTECS - Registry of Toxic Effects of Chemical Substances is produced by the US National Institute for Occupational Safety and Health (NIOSH). RTECS provides data for over 133,000 chemicals including identifying information such as CAS number, chemical names and synonyms. Toxicity data include acute and chronic animal tests data, human data, skin and eye irritation data, Threshold Limit Values, IARC determinations, *in vitro* toxicity test data, US National Toxicology Programme (NTP) and TSCA Inventory data. RTECS provides the original reference for each value given.
STN | CIS | CCINFO | SilverPlatter | TOMES Plus

A1.30 TERIS - Teratogen Information System provides current information on the teratogenic effects of drugs and environmental agents. Agent summaries derived from thorough literature reviews rate reproductive risk and explain data used to determine the rating. Produced by the University of Washington.
TOMES Plus

Bibliographic Databases

A1.31 CANCERLIT - Produced by the US National Cancer Institute, Cancerlit covers all areas of the international literature on cancer. It covers material on carcinogens and mutagens.
Dialog Corp | Ovid | STN | SilverPlatter

A1.32 CHEMICAL ABSTRACTS - This huge database (over 13 million records) is produced by the Chemical Abstracts Service and covers worldwide literature in all areas of chemistry, biochemistry and chemical engineering from 1967 to the present. It indexes over 9,000 journals as well as patents, conference papers, technical reports, books and theses. Chemical Abstracts is available from several online suppliers but only STN contains the abstracts.
STN | Dialog Corp | Questel-Orbit | SciFinder

A1.33 CISDOC - is produced by the International Labour Organisation and indexes worldwide literature in OHS. CIS abstracts information on the toxicology of industrial chemicals, chemical hazards and industrial hygiene. It is a source of European regulatory information as it indexes OH&S information from the Official Journal of the European Communities and EC Directives.
CCINFO | SilverPlatter

A1.34 CSNB - Chemical Safety Newsbase, indexes sources such as journals, books, conference papers, legislation and press releases in areas relating to fire and explosions, storage and transport, toxicity and waste removal of chemicals, particularly in chemical or allied industries and in chemical and biochemical laboratories. It is produced by the Royal Society of Chemistry.
Dialog Corp | STN

A1.35 EMBASE - is equivalent to the printed Excerpta Medica and covers worldwide literature in the biomedical and pharmaceutical fields, including biological science, biochemistry, environmental science, toxicology and pharmacology. It indexes more than 3,500 journals as well as monographs, conference proceedings, dissertations and reports.
Dialog Corp | Ovid | STN

A1.36 ENVIRONMENTAL CHEMISTRY HEALTH AND SAFETY - is produced by the Royal Society of Chemistry. It does not index the toxicological literature as comprehensively as does Toxline but has good coverage of regulatory information and chemical industry literature on industrial chemicals.
Dialog Corp

A1.37 HSELINE - is produced by the UK Health and Safety Executive and covers all areas of health and safety at work. It is a good source for UK and European regulatory information.
Dialog Corp | SilverPlatter

A1.38 KOSMET - Indexes world literature related to cosmetics and perfumes, with an emphasis on scientific and technical aspects.
Dialog Corp | STN

A1.39 MEDLINE - Produced by the US National Library of Medicine. Medline covers all areas of medicine and contains over 8.4 million references from 1966 to the present. Medline indexes over 4,700 international health and medical journals and is the online equivalent of the printed *Index Medicus, Index to Dental Literature* and *International Nursing Index.* The Medline database is available at the US National Library of Medicine.
NLM | STN | Dialog Corp | Ovid | SilverPlatter | SciFinder

A1.40 NAPRALERT - The Natural Products Alert database contains bibliographic and factual data on natural products and covers pharmacological, biological activity and chemistry of plant, microbial and animal extracts. The database indexes journals, books, patents, conference papers, government reports and newsletters.
STN

A1.41 NIOSHTIC - is produced by the US National Institute for Occupational Safety and Health and indexes both US and international literature in all areas of OH&S including toxicology, hazardous wastes and industrial hygiene. It covers a broad range of literature in toxicology and includes references to both animal and human studies. This is a legacy database that closed in 1998: the indexing of material in this field has been taken over by 'OSHLINE with NIOSHTIC' through CCINFO. The second version, NIOSHTIC-2, only indexes literature produced and sponsored by NIOSH and is available through SilverPlatter.
Dialog Corp | CCINFO | SilverPlatter

A1.42 TOXLINE - Produced by the US National Library of Medicine. Toxline indexes the literature on pharmacological, biochemical, physiological and toxicological effects of chemicals. Toxline consists of 16 different files, including TSCATS and indexes journals, patents, government reports and criteria documents. This file closed in 2001, it still contains over 20 years of citations prior to this however and all future medical citations dealing with toxicology will be indexed through the National Library of Medicine's TOXLINE Core & TOXLINE Special collections, and through the broader database MEDLINE.
NLM | TOXNET

A1.43 TOXCENTER – (Toxicology Center) is a new bibliographic database available from Chemical Abstracts Service (CAS) through STN. It replaces TOXLINE and TOXLIT on STN. The database covers the pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals.
STN

A1.44 TSCATS - (Toxic Substances Control Act Test Submissions) enables users to identify unpublished health and safety studies submitted to the US EPA under various sections of the US Toxic Substances Control Act. TSCATS is updated quarterly and provides access to over 50,000 test submissions on over 6,500 chemicals substances. It can be searched separately on CIS or as a subfile of the TOXLINE special database via TOXNET.
TOXNET | CIS

Database suppliers

A1.45 **CAS** - The Chemical Abstracts Service, a division of the American Chemical Society, produces Chemical Abstracts, the Chemical Registry File and CASReact as well as a number of CD-ROM databases (including the National Chemical Inventories CD-ROM). It also produces SciFinder and is one of the partners in producing STN (see below).

CAS - Chemical Abstract Service
2540 Olentangy River Road
PO Box 3012
Columbus, Ohio, 43210
USA
Email: help@cas.org
Web site: http://www.cas.org/
NCI Web site: http://www.cas.org/Support/substance.html

A1.46 **CCINFO** is a series of products published by CCOHS (Canadian Centre of Occupational Health and Safety). Products available in the series include: MSDS (contains over 100,000 material safety datasheets prepared by over 550 US or Canadian chemical suppliers or manufacturers); The CHEMpendium Collection (including Cheminfo, CESARS, CHRIS 2000) ; NIOSHTIC; RTECS and INCHEM. CCINFO is available by subscription both as a set of CD-ROMs, or via the web.

CCOHS
250 Main Street East
Hamilton, Ontario,
L8N 1H6.
Ph: 905 570 8094
Fax: 905 572 2206
Email: custserv@ccohs.ca
Web site: http://www.ccohs.ca

A1.47 **CIS** - (Chemical Information Systems) provides access to a series of databases containing information on specific chemical substances, including toxicological and carcinogenic research data, hazardous materials handling information, chemical/physical property information, regulatory information, spectroscopic data, and pharmaceutical data. CIS does not have an Australian representative, however, they can be contacted directly at:

National Information Services Corporation
Wyman Towers, 3100 St. Paul Street
Baltimore, Maryland
21218 USA
Ph: +1 410 2430797
Fax: +1 410 2430982
EMAIL: sales@nisc.com
Web site: http://www.nisc.com/cis/

(CIS provides access to CCRIS, CHRIS, HSDB, RTECS, TSCATS, and other more specific databases).

A1.48 **Dialog Corporation** - provides access to over 600 databases in all areas of science and technology, business and company information and social sciences and humanities through its three systems DIALOG, Datastar and Profound. Contact details:

The Dialog Corporation
100 Harris Street
PYRMONT, NSW 2009
Tel: 02 8587 7700
Fax: 02 8587 7720
email: contact_australia@dialog.com
Web site: http://www.dialog.com/info/home/australia/

(Chemical Abstracts, Medline, NIOSHTIC, HSELINE, Cancerlit, KOSMET, and Toxline)

A1.49 **National Library of Medicine (USA)** – Provides free online access to a number of databases primarily dealing with medical issues, but with substantial access to toxicology, cancer and occupational and environmental medicine information.

National Library of Medicine
8600 Rockville Pike
Bethesda, MD 20894
Ph: 1 301 496 6531
Fax: 1 301 480 3537
Web site: http://www.nlm.nih.gov

(Medline, Toxline)

A1.50 **Ovid Technologies** - provides access to over 90 Databases either online or in stand-alone or network configurations at your site. Databases are concentrated mainly in medical and health sciences but include some databases in the areas of business, science and social science and humanities. Contact:

Ovid Technologies
Suite 1702, Level 17
25 Bligh Street
SYDNEY NSW 2000
Ph: 02 9231 5599
Fax: 02 9231 5086
Freecall: 1800 22 6474.
Email: ausupport@ovid.com
Web site: http://www.ovid.com/index.cfm

(Cancerlit, Embase, Chemical Abstracts, Medline)

A1.51 **Questel-Orbit Inc**. - provides online access to some 200 databases concentrated in the areas of business, science and engineering and patents through its two database systems Questel and Orbit. Questel-Orbit is represented in Australia and can be contacted at:

Questel-Orbit
TransData Corporation Pty Ltd.
Level 23, The Royal Exchange Building
Sydney NSW 2000
AUSTRALIA
Phone: 02 9252 2644
Fax: 02 9252 5108
Email: tracy@transdatacorp.com
Australian Web site: http://www.transdatacorp.com
International We site: http://www.questel.orbit.com/

(Chemical Abstracts)

A1.52 **SciFinder** – is a desktop research tool that provides access to chemical identification data (Registry File); regulation of chemicals (Regulated Chemicals List) ; indexes to the literature (Chemical Abstracts and Medline) and chemical reaction data (CASReact). It is produced by the Chemical Abstracts Service.

SciFinder
Dr Damon Ridley
School of Chemistry, F11
University of Sydney
SYDNEY NSW 2006
Ph: 02 9351 2180, Fax: 02 9351 6650
Email: dridley@chem.usyd.edu.au
Web site: http://www.cas.org/SCIFINDER/scicover2.html

(CHEMLIST, REGISTRY FILE, CHEMICAL ABSTRACTS, Medline)

A1.53 **SilverPlatter** – provides access to over 200 bibliographic and full text databases. The subject coverage is broad, with the following databases of particular interest to this forum.

CHEM-BANK contains the five fulltext databases; RTECS, HSDB, OHMTADS, CHRIS 2000 and IRIS.

OSHROM contains the seven bibliographic databases HSELine, CISDOC, MHIDAS, Medline (OEM), RILOSH, NIOSHTIC and NIOSHTIC-2.

MEDLINE contains the National Library of Medicine database covering a huge range of the medical literature; including the occupational and environmental medicine subset.

POLTOX I (Pollution and Toxicology) provides access to pollution and toxicology databases containing citations to the world's pollution and toxicology literature. Topics covered include air, water, land, radiation, and noise pollution; environmental risks; food additives, pharmaceutical side effects and biochemistry; agrochemicals; industrial chemicals; legislation and standards; ecology; and health and safety.

SilverPlatter
Suite 1702, Level 17
25 Bligh Street
SYDNEY NSW 2000
Ph: 02 9231 5599 Fax: 02 9231 5086
Freecall: 1800 22 6474.
Ph: 02 9267 9055, Fax: 02 9267 9430.
Email: australia@silverplatter.com
Web site: http://www.silverplatter.com/au/contact-sydney.htm

A1.54 **STN** - (Scientific and Technical Network) is a joint operation by CAS (Chemical Abstracts Service), a division of the American Chemical Society in the US; FIZ Karlsruhe in Europe and JICST (The Japan Information Centre of Science and Technology) in Japan. The STN system provides access to some 200 databases in all areas of science and technology. STN is represented in Australia by:

Dr Damon Ridley
School of Chemistry, F11
University of Sydney
SYDNEY NSW 2006
Ph: 02 9351 2180, Fax: 02 9351 6650
Email: dridley@chem.usyd.edu.au
Web site: http://www.cas.org/stn.html

(Registry File, Chemical Abstracts, Chemlist, HSDB, RTECS, Chemsafe, CSNB, Medline, Napralert, Cancerlit, Toxcenter.)

A1.55 **TOMES Plus** is produced by the US company Micromedex Inc. It contains the following fulltext databases: Meditext, Hazardtext, Saratext, Reprorisk, Reprotext, RTECS, HSDB, IRIS, OHM/TADS, CHRIS 2000, DOT Emergency Response Guides. TOMES Plus is available in Australia from:

MICROMEDEX
A Division of Thomson Financial Services Pty. Ltd.
Level 7/34 Hunter Street
Sydney NSW 2000
Ph: 02 9235 3252
Fax: 02 9223 5308
Web site: http://www.micromedex.com

A1.56 **TOXNET** – is produced by the National Library of Medicine and is a cluster of databases on toxicology, hazardous chemicals, and related areas.

Specialized Information Services
National Library of Medicine
8600 Rockville Pike
Bethesda, MD 20894
Ph: 1 301 496 6531
Fax: 1 301 480 3537
Email: tehip@teh.nlm.nih.gov
Web site: http://toxnet.nlm.nih.gov/

(CCRIS, DART, EMICBACK, ETICBACK, GENE-TOX, HSDB, IRIS, RTECS, TOXLINE and TRI)

Libraries and Information Centres

A1.57 Many of the larger research libraries (such as state and university libraries) subscribe to some of the products listed above and provide access to the public for free or for a nominal sum. In addition, some libraries provide a fee-based search service and will conduct searches on online databases and/or CD-ROM databases specific to the information needs of the client.

A1.58 **The National Occupational Health and Safety Commission Library** has access to most of the databases listed above (either on CD-ROM or online) as well as an excellent collection of reference books, monographs and journals in the area of toxicology, hazardous substances and regulation of chemicals. The Library supplies information to the general public through the Australian inter-library loan system (contact your local library for assistance), and by working to support the State & Territory OHS Authority libraries and information services.

Internet resources

A1.59 Internet resources, in particular address details, are subject to change. This short list is provided as a starting point for a few direct resources with many links to other Internet sites with chemical safety resources. Wherever possible, large organisations, academic institutions or government agencies have been selected. This list was current as of November 2001.

A1.60 Arbete och Hälsa: http://www.niwl.se/ah/default_en.htm

A scientific report series published by the National Institute for Working Life in Sweden. The series publishes scientific original works, dissertations, criteria documents and literature surveys. Note that there is considerable material on occupational health and safety issues in addition to the criteria documents and occupational standards.

A1.61 ATSDR: http://www.atsdr.cdc.gov/toxpro2.html

The Agency for Toxic Substances and Disease Registry (ATSDR) in the USA produces "toxicological profiles" for hazardous substances found at National Priorities List (NPL) sites. The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for 256 hazardous substances. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties.

A1.62 ChemFinder: http://chemfinder.camsoft.com

For those interested in chemical identification Cambridge Soft provide a useful search tool online, ChemFinder. The company also provides ChemDraw, a useful structural drawing program. Demonstration versions of this product may be downloaded from this site by following links.

A1.63 CHEMINFO: http://www.indiana.edu/~cheminfo/

CHEMINFO is a list of links to chemical resources on the Internet, it is a good starting place for any search for chemical information and is organised into subject areas including MSDS sources and guides to chemical safety or toxicology information.

A subset of CHEMINFO with a slightly different format is found at: http://www.indiana.edu/~cheminfo/cisindex.html. This is the Index to Selected Internet Resources for Chemistry (SIRCh). It is arranged alphabetically rather than by subject area.

A1.64 ECDIN: http://ecdin.etomep.net/

An online factual databank created under the Environmental Research Programme of the European Commission, Joint Research Centre at the ISPRA (I) site and provides identification, pharmacological, toxicological and epidemiological data, health hazard evaluation and legislative information for chemicals listed as priorities by the EC.

A1.65 Hardin MD: http://www.arcade.uiowa.edu/hardin-www/md-tox.html

Hosted by the University of Iowa, the *Hardin Meta Directory - Toxicology* is one of the best sites for toxicology resources. It is short, quick to load and refers to excellent toxicology sites.

A1.66 IDLH: http://www.cdc.gov/niosh/idlh/intridl4.html

Produced by the US National Institute of Occupational Safety & Health (NIOSH) IDLHs document the criteria and information sources that have been used to determine immediately dangerous to life or health concentrations of chemicals.

A1.67 International Clearing House for Major Chemical Incidents: http://www.healthchem.uwic.ac.uk/

Hosted by the Welsh Combined Centres for Public Health as part of the WHO collaborating centre, this site provides public health and policy guidance information on chemical incidents worldwide.

A1.68 IPCS: http://www.who.int/pcs/

The International Programme on Chemical Safety or IPCS established in 1980, is a joint program of three cooperating organisations, ILO, UNEP and WHO, implementing activities related to chemical safety. It is provided as another useful starting place with many links and some of their own resources, including: International Chemical Safety Cards and International Chemical Assessment Documents.

A1.69 MSDS Online: http://www.ilpi.com/msds/index.html

Hosted by Interactive Learning Paradigms, this site collates the major collections of material safety data sheets online into a vortal on MSDS resources. The site includes links to MSDS collections, advice on the use of MSDS, and providers of MSDS: both from government (mainly US & European) sites and chemical companies.

A1.70 NICNAS: http://www.nicnas.gov.au/

Australia's National Industrial Chemicals Notification and Assessment Scheme scientifically assesses industrial chemicals for their health and environmental effects and makes recommendations for safe use. Provides access to Public Chemical Assessment Reports.

A1.71 NIOSH: http://www.cdc.gov/niosh/homepage.html

NIOSH, the National Institute for Occupational Safety and Health of the USA maintains a series of links and some databases for chemical safety information searching. This is a good site to catch up on conferences and current topics of worker safety in general in the United States.

A1.72 NOHSC: http://www.nohsc.gov.au/

Australia's National Occupational Health & Safety Commission provides a wide range of guidance material on a range of occupational health and safety issues including the *List of Designated Hazardous Substances* and an exposure standards database. It also provides information on the national hazardous substances regulatory environment.

A1.73 NTP Reports: http://ehis.niehs.nih.gov/ntp/docs/01-99-doc.html

Produced by the US Environmental Health Information Service, the NTP site includes NTP Toxicology and Carcinogenesis Reports (TR Reports) and NTP Toxicity Reports (TOX Reports). Abstracts are available online.

A1.74 RTK Net: http://www.rtk.net

RTK Net, or the Right To Know network, provides free access to numerous databases, text files, and conferences on the environment, housing, and sustainable development. This reference is often not directly related to chemical safety but if your interests are environmental with respect to chemicals or toxicology, it should prove useful.

Chemical Information Discussion List

If you have an email address, keep up with discussions about chemical information or ask questions yourself, using the chemical information discussion list. You can join this discussion list here: http://listserv.indiana.edu/scripts/wa.exe?SUBED1=chminf-l&A=1

Appendix 2

ACUTE TOXICITY - NOTES ON THE FIXED DOSE PROCEDURE

A2.1 The fixed dose procedure is conducted in two stages - a preliminary sighting study, and a main study.

In a preliminary sighting study, the effects of various doses administered orally by gavage to single animals of one sex are investigated in a sequential manner. The sighting study yields information on the dose-toxicity relationship, including an estimate of the minimum lethal dose.

In the main study, the substance is administered orally by gavage to groups of five male and five female animals at one of the pre-set dose levels (5, 50, 500 or 2,000 mg/kg). The dose used is derived from the sighting study and is that which is likely to produce evident toxicity but no deaths.

A2.2 The discriminating dose is the dose that causes evident toxicity but not mortality, and should be one of the four dosage levels specified: 5, 50, 500 or 2000 mg per kg per body weight. The concept “evident toxicity” is used to designate toxic effects after exposure to the substance tested which are so severe that exposure to the next highest fixed dose would probably lead to mortality.

The results of testing at a particular dose may be either:

- less than 100% survival,
- 100% survival, but evident toxicity,
- 100% survival, but no evident toxicity.

A2.3 Further details of the fixed dose method can be found in Annex V to the Dangerous Substances Directive 67/548/EEC.

Evaluation and interpretation

DOSE	RESULTS	INTERPRETATION
5 mg/kg	Less than 100% survival	Compounds that are VERY TOXIC
	100% survival; but evident toxicity	Compounds that are TOXIC
	100% survival; no evident toxicity	See results at 50 mg/kg.
50 mg/kg	Less than 100% survival	Compounds that may be TOXIC or VERY TOXIC. See results at 5 mg/kg.
	100% survival; but evident toxicity	Compounds that are HARMFUL.
	100% survival; no evident toxicity	See results at 500 mg/kg.
500 mg/kg	Less than 100% survival	Compounds that may be TOXIC or HARMFUL. See results at 50 mg/kg.
	100% survival, but evident toxicity	Compounds considered as having no significant acute toxicity.
	100% survival; no evident toxicity	See results at 2,000 mg/kg
2000 mg/kg	Less than 100% survival	See results at 500mg/kg
	100% survival; with or without evident toxicity	Compounds that do not have significant acute toxicity.

Appendix 3

RISK AND SAFETY PHRASES

Risk phrases

The following risk phrases and combination risk phrases are those adopted by the European Communities in EC Council Directive 67/548/EC3 to describe health effects. These are applicable in Australia.

R20	Harmful by inhalation.
R21	Harmful in contact with skin.
R22	Harmful if swallowed.
R23	Toxic by inhalation.
R24	Toxic in contact with skin.
R25	Toxic if swallowed.
R26	Very toxic by inhalation.
R27	Very toxic in contact with skin.
R28	Very toxic if swallowed.
R29	Contact with water liberates toxic gas.
R31	Contact with acids liberates toxic gas.
R32	Contact with acids liberates very toxic gas.
R33	Danger of cumulative effects.
R34	Causes burns.
R35	Causes severe burns.

R36	Irritating to eyes.
R37	Irritating to respiratory system.
R38	Irritating to skin.
R39	Danger of very serious irreversible effects.
R40	Limited evidence of a carcinogenic effect.
R41	Risk of serious eye damage.
R42	May cause sensitisation by inhalation.
R43	May cause sensitisation by skin contact.
R45	May cause cancer.
R46	May cause heritable genetic damage.
R48	Danger of serious damage to health by prolonged exposure.
R49	May cause cancer by inhalation.
R60	May impair fertility.
R61	May cause harm to the unborn child.
R62	Possible risk of impaired fertility.
R63	Possible risk of harm to the unborn child.
R64	May cause harm to breastfed babies.
R65	Harmful: may cause lung damage if swallowed.
R66	Repeated exposure may cause skin dryness or cracking.

R67	Vapours may cause drowsiness and dizziness.
R68	Possible risk of irreversible effects.
R20/21	Harmful by inhalation and in contact with skin.
R20/22	Harmful by inhalation and if swallowed.
R20/21/22	Harmful by inhalation, in contact with skin and if swallowed.
R21/22	Harmful in contact with skin and if swallowed.
R23/24	Toxic by inhalation and in contact with skin.
R23/25	Toxic by inhalation and if swallowed.
R23/24/25	Toxic by inhalation, in contact with skin and if swallowed.
R24/25	Toxic in contact with skin and if swallowed.
R26/27	Very toxic by inhalation and in contact with skin.
R26/28	Very toxic by inhalation and if swallowed.
R26/27/28	Very toxic by inhalation, in contact with skin and if swallowed.
R27/28	Very toxic in contact with skin and if swallowed.
R36/37	Irritating to eyes and respiratory system.
R36/38	Irritating to eyes and skin.
R36/37/38	Irritating to eyes, respiratory system and skin.
R37/38	Irritating to respiratory system and skin.
R39/23	Toxic: danger of very serious irreversible effects through inhalation.

R39/24	Toxic: danger of very serious irreversible effects in contact with skin.
R39/25	Toxic: danger of very serious irreversible effects if swallowed.
R39/23/24	Toxic: danger of very serious irreversible effects through inhalation and in contact with skin.
R39/23/25	Toxic: danger of very serious irreversible effects through inhalation and if swallowed.
R39/24/25	Toxic: danger of very serious irreversible effects in contact with skin and if swallowed.
R39/23/24/25	Toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed.
R39/26	Very toxic: danger of very serious irreversible effects through inhalation.
R39/27	Very toxic: danger of very serious irreversible effects in contact with skin.
R39/28	Very toxic: danger of very serious irreversible effects if swallowed.
R39/26/27	Very toxic: danger of very serious irreversible effects through inhalation and in contact with skin.
R39/26/28	Very toxic: danger of very serious irreversible effects through inhalation and if swallowed.
R39/27/28	Very toxic: danger of very serious irreversible effects in contact with skin and if swallowed.
R39/26/27/28	Very toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed.
R68/20	Harmful: possible risk of irreversible effects through inhalation.
R68/21	Harmful: possible risk of irreversible effects in contact with skin.
R68/22	Harmful: possible risk of irreversible effects if swallowed.
R68/20/21	Harmful: possible risk of irreversible effects through inhalation and in contact with skin.
R68/20/22	Harmful: possible risk of irreversible effects through inhalation and if swallowed.
R68/21/22	Harmful: possible risk of irreversible effects in contact with skin and if swallowed.

R68/20/21/22	Harmful: possible risk of irreversible effects through inhalation, in contact with skin and if swallowed.
R42/43	May cause sensitisation by inhalation and skin contact.
R48/20	Harmful: danger of serious damage to health by prolonged exposure through inhalation.
R48/21	Harmful: danger of serious damage to health by prolonged exposure in contact with skin.
R48/22	Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R48/20/21	Harmful: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin.
R48/20/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed.
R48/21/22	Harmful: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed.
R48/20/21/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.
R48/23	Toxic: danger of serious damage to health by prolonged exposure through inhalation.
R48/24	Toxic: danger of serious damage to health by prolonged exposure in contact with skin.
R48/25	Toxic: danger of serious damage to health by prolonged exposure if swallowed.
R48/23/24	Toxic: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin.
R48/23/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed.
R48/24/25	Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed.
R48/23/24/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.

Safety phrases

Safety advice phrases (S-phrases) may be assigned to hazardous substances and dangerous goods preparations in accordance with the following general criteria.
The 'manufacturer' referred to below is the person responsible for placing the substance or preparation on the market.

- *The following safety phrases and combination safety phrases are those adopted by the European Communities in EC Council Directive 67/548/EC[3] to describe health effects. In Europe, these safety phrases apply to dangerous substances. `Dangerous Substances` are defined as explosive, oxidising, flammable, toxic, harmful, corrosive, irritant, sensitising, carcinogenic, mutagenic, toxic to reproduction and development and environmental toxins. Substances are chemical elements and compounds in the natural state including preservatives and stabilisers. In Australia, these safety phrases should be used where there is a requirement to do so, in accordance with Occupational Health and Safety regulations.*

S1 Keep locked up

Applicability:

- very toxic, toxic and corrosive substances and preparations.

Criteria for use:

- *obligatory* for those substances and preparations mentioned above if sold to the general public.

S2 *Keep out of the reach of children*

Applicability:

- all dangerous substances and preparations.

Criteria for use:

- *obligatory* for all dangerous substances and preparations sold to the general public, except for those only classified as dangerous for the environment.

S3 *Keep in a cool place*

Applicability:

- organic peroxides;
- other dangerous substances and preparations having a boiling point $\leq$ 40° C.

Criteria for use:

- *obligatory* for organic peroxides unless S47 is used;
- recommended for other dangerous substances and preparations having a boiling point $\leq$ 40°C.

S4 *Keep away from living quarters*

Applicability:

- very toxic and toxic substances and preparations.

Criteria for use:

- normally limited to very toxic and toxic substances and preparations when appropriate to supplement S13; for example when there is an inhalation risk and the substance or preparation should be stored away from living quarters. The advice is not intended to preclude proper use of the substance or preparation in living quarters.

S5 *Keep contents under ... (appropriate liquid to be specified by the manufacturer)*

Applicability:

- spontaneously flammable solid substances and preparations.

Criteria for use:

- normally limited to special cases, eg. sodium, potassium or white phosphorous.

S6 *Keep under ... (inert gas to be specified by the manufacturer)*

Applicability:

- dangerous substances and preparations, which must be kept under an inert atmosphere.

Criteria for use:

- normally limited to special cases, eg. certain organo-metallic compounds.

S7 *Keep container tightly closed*

Applicability:

- organic peroxides;
- substances and preparations which can give off very toxic, toxic, harmful or extremely flammable gases;
- substances and preparations, which in contact with moisture, give off extremely flammable gases;
- highly flammable solids.

Criteria for use:

- *obligatory* for organic peroxides;
- recommended for the other fields of application mentioned above.

S8 *Keep container dry*

Applicability:

- substances and preparations that may react violently with water;
- substances and preparations that on contact with water liberate extremely flammable gases;
- substances and preparations, which on contact with water, liberate very toxic or toxic gases.

Criteria for use:

- normally limited to the fields of application mentioned above when necessary to reinforce warnings given by R14, R15 in particular, and R29.

S9 *Keep container in a well-ventilated place*

Applicability:

- volatile substances and preparations that may give off very toxic, toxic or harmful vapours;
- extremely flammable or highly flammable liquids and extremely flammable gases.

Criteria for use:

- recommended for volatile substances and preparations that may give off very toxic, toxic or harmful vapours;
- recommended for extremely flammable or highly flammable liquids or extremely flammable gases.

S12 *Do not keep the container sealed*

Applicability:

- substances and preparations that will, by giving off gases or vapours, be liable to burst the container.

Criteria for use:

- normally limited to the special cases mentioned above.

S13 *Keep away from* food, *drink and animal feeding stuffs*

Applicability:

- very toxic, toxic and harmful substances and preparations.

Criteria for use:

- recommended when such substances and preparations are likely to be used by the general public.

S14 *Keep away from ... (incompatible materials to be indicated by the manufacturer)*

Applicability:

- organic peroxides.

Criteria for use:

- *obligatory* for and normally limited to organic peroxides. However, may be useful in exceptional cases when incompatibility is likely to produce a particular risk.

S15 *Keep away from heat*

Applicability:

- substances and preparations which may decompose or which may react spontaneously under the effect of heat.

Criteria for use:

- normally limited to special cases, eg. monomers, but not assigned if risk phrases R2, R3 and/or R5 have already been applied.

S16 *Keep away from sources of ignition - No smoking*

Applicability:

- extremely flammable or highly flammable liquids and extremely flammable gases.

Criteria for use:

- recommended for the substances and preparations mentioned above but not assigned if risk phrases R2, R3 and/or R5 have already been applied.

S17 *Keep away from combustible material*

Applicability:

- substances and preparations that may form explosive or spontaneously flammable mixtures with combustible material.

Criteria for use:

- available for use in special cases, eg. to emphasise R8 and R9.

S18 *Handle and open container with care*

Applicability:

- substances and preparations liable to produce an overpressure in the container;
- substances and preparations that may form explosive peroxides.

Criteria for use:

- normally limited to the above-mentioned cases when there is risk of damage to the eyes and/or when the substances and preparations are likely to be used by the general public.

S20 *When using do not eat or drink*

Applicability:

- very toxic, toxic and corrosive substances and preparations.

Criteria for use:

- normally limited to special cases (eg. arsenic and arsenic compounds; fluoracetates) in particular when any of these are likely to be used by the general public.

S21 *When using do not smoke*

Applicability:

- substances and preparations that produce toxic products on combustion.

Criteria for use

- normally limited to special cases (eg. halogenated compounds).

S22 *Do not breathe dust*

Applicability:

- all solid substances and preparations dangerous for health.

Criteria for use:

- *obligatory* for those substances and preparations mentioned above to which R42 is assigned;
- recommended for those substances and preparations mentioned above which are supplied in the form of an inhalable dust and for which the health hazards following inhalation are not known.

S23 *Do not breathe gas/fumes/vapour/spray (appropriate wording to be specified by the manufacturer)*

Applicability:

- all liquid or gaseous substances and preparations dangerous to health.

Criteria for use:

- *obligatory* for those substances and preparations mentioned above to which R42 is assigned;
- *obligatory* for substances and preparations intended for use by spraying. Either S38 or S51 must be ascribed in addition;
- recommended when it is necessary to draw the attention of the user to inhalation risks not mentioned in the risk phrases that have to be ascribed.

S24 *Avoid contact with skin*

Applicability:

- all substances and preparations dangerous for health.

Criteria for use:

- *obligatory* for those substances and preparations to which R43 has been ascribed, unless S36 has also been ascribed;
- recommended when it is necessary to draw the attention of the user to skin contact risks not mentioned in the risk phrases (eg. paresthesia), which have to be ascribed. However, may be used to emphasise such risk phrases.

S25 *Avoid contact with eyes*

Applicability:

- all substances and preparations dangerous to health.

Criteria for use:

- recommended when it is necessary to draw the attention of the user to eye contact risks not mentioned in the risk phrases that have to be applied. However, may be used to emphasise such risk phrases;
- recommended for substances ascribed R34, R35, R36 or R41, which are likely to be used by the general public.

S26 *In case of contact with eyes, rinse immediately with plenty of water and seek medical advice*

Applicability:

- corrosive or irritant substances and preparations.

Criteria for use:

- *obligatory* for corrosive substances and preparations and those to which R41 has already been ascribed;
- recommended for irritant substances and preparations to which the risk phrase R36 has already been ascribed.

S27 *Take off immediately all contaminated clothing.*

Applicability:

- very toxic, toxic or corrosive substances and preparations.

Criteria for use:

- *obligatory* for very toxic substances and preparations to which R27 has been ascribed and which are likely to be used by the general public;
- recommended for very toxic substances and preparations to which R27 has been ascribed. However, this safety phrase should not be used if S36 has been ascribed;
- recommended for toxic substances and preparations to which R24 has been ascribed, as well as corrosive substances and preparations that are likely to be used by the general public.

S28 *After contact with skin, wash immediately with plenty of ... (to be specified by the manufacturer).*

Applicability:

- very toxic, toxic or corrosive substances and preparations.

Criteria for use:

- *obligatory* for very toxic substances and preparations;
- recommended for the other substances and preparations mentioned above, in particular when water is not the most appropriate rinsing fluid;
- recommended for corrosive substances and preparations that are likely to be used by the general public.

S29 *Do not empty into drains*

Applicability:

- extremely or highly flammable liquids immiscible with water;
- very toxic and toxic substances and preparations;
- substances and preparations dangerous for the environment.

Criteria for use:

- *obligatory* for substances and preparations dangerous for the environment and assigned the symbol 'N', which are likely to be used by the general public, unless this is the intended use;
- recommended for other substances and preparations mentioned above which are likely to be used by the general public, unless this is the intended use.

S30 *Never add water to this product*

Applicability:

- substances and preparations that react violently with water.

Criteria for use:

- normally limited to special cases (eg. sulphuric acid) and may be used, as appropriate, to give the clearest possible information, either to emphasise R14 or as an alternative to R14.

S33 *Take precautionary measures against static discharges*

Applicability:

- extremely or highly flammable substances and preparations.

Criteria for use:

- recommended for substances and preparations used in industry which do not absorb moisture. Virtually never used for substances and preparations placed on the market for use by the general public.

S35 *This material and its container must be disposed of in a safe way.*

Applicability:

- all dangerous substances and preparations

Criteria for use:

- recommended for substances and preparations where special guidance is needed to ensure proper disposal.

S36 *Wear suitable protective clothing*

Applicability:

- organic peroxides;
- very toxic, toxic or harmful substances and preparations;
- corrosive substances and preparations.

Criteria for use:

- *obligatory* for very toxic and corrosive substances and preparations;
- *obligatory* for those substances and preparations to which either R21 or R24 has been ascribed;
- *obligatory* for category 3 carcinogens, mutagens and substances toxic to reproduction unless the effects are produced solely by inhalation of the substance or preparation;
- *obligatory* for organic peroxides;
- recommended for toxic substances and preparations if the LD_{50} dermal value is unknown but the substance or preparation is likely to be toxic through skin contact;
- recommended for substances and preparations used in industry which are liable to damage health by prolonged exposure.

S37 *Wear suitable gloves*

Applicability:

- very toxic, toxic, harmful or corrosive substances and preparations;
- organic peroxides;
- substances and preparations irritating to the skin or causing sensitisation by skin contact.

Criteria for use

- *obligatory* for very toxic and corrosive substances and preparations;
- *obligatory* for those substances and preparations to which R21, R24 or R43 has been ascribed;
- *obligatory* for Category 3 carcinogens, mutagens and substances toxic to reproduction unless the effects are produced solely by inhalation of the substances and preparations;
- *obligatory* for organic peroxides;
- recommended for toxic substances and preparations if the LD_{50} dermal value is unknown but the substance or preparation is likely to be harmful by skin contact;
- recommended for substances and preparations irritating to the skin.

S38 *In case of insufficient ventilation, wear suitable respiratory equipment*

Applicability:

- very toxic or toxic substances and preparations.

Criteria for use:

- normally limited to special cases involving the use of very toxic or toxic substances and preparations in industry or in agriculture.

S39 *Wear eye/face protection*

Applicability:

- organic peroxides;
- corrosive substances and preparations, including irritants that give rise to risk of serious damage to the eyes;
- very toxic and toxic substances and preparations.

Criteria for use:

- *obligatory* for those substances and preparations to which R34, R35 or R41 have been ascribed;
- *obligatory* for organic peroxides;
- recommended when it is necessary to draw the attention of the user to eye contact risks not mentioned in the risk phrases that have to be ascribed;
- normally limited to exceptional cases for very toxic and toxic substances and preparations, where there is a risk of splashing and they are likely to be easily absorbed by the skin.

S40 *To clean the floor and all objects contaminated by this material use ... (to be specified by the manufacturer)*

Applicability:

- all dangerous substances and preparations.

Criteria for use:

- normally limited to those dangerous substances and preparations for which water is not considered to be a suitable cleansing agent (eg. where absorption by powdered material, dissolution by solvent etc. is necessary) and where it is important for health and/or safety reasons to provide a warning on the label.

S41 *In case of fire and/or explosion do not breathe fumes*

Applicability:

- dangerous substances and preparations, which on combustion give off very toxic or toxic gases.

Criteria for use:

- normally limited to special cases.

S42 *During fumigation/spraying wear suitable respiratory equipment (appropriate wording to be specified by the manufacturer)*

Applicability:

- substances and preparations intended for such use but which may endanger the health and safety of the user unless proper precautions are taken.

Criteria for use:

- normally limited to special cases.

S43 *In case of fire use ... (indicate in the space the precise type of fire-fighting equipment. If water increases the risk add: 'Never use water')*

Applicability:

- extremely flammable, highly flammable and flammable substances and preparations.

Criteria for use:

- *obligatory* for substances and preparations which, in contact with water or damp air, evolve extremely flammable gases;
- recommended for extremely flammable, highly flammable and flammable substances and preparations, particularly when they are immiscible with water.

S45 *In case of accident or if you feel unwell seek medical advice immediately (show the label where possible).*

Applicability:

- very toxic substances and preparations;
- toxic and corrosive substances and preparations;
- substances and preparations causing sensitisation by inhalation.

Criteria for use:

- *obligatory* for the substances and preparations mentioned above.

S46 *If swallowed, seek medical advice immediately and show this container or label*

Applicability

- all dangerous substances and preparations other than those that are very toxic, toxic, corrosive or dangerous to the environment.

Criteria for use:

- *obligatory* for all dangerous substances and preparations mentioned above which are likely to be used by the general public, unless there is no reason to fear any danger from swallowing, particularly by children.

S47 *Keep at temperature not exceeding ... ° C (to be specified by the manufacturer)*

Applicability:

- substances and preparations that become unstable at a certain temperature.

Criteria for use:

- normally limited to special cases (eg. certain organic peroxides).

S48 *Keep wetted with .... (appropriate material to be specified by the manufacturer)*

Applicability:

- substances and preparations that may become very sensitive to sparks, friction or impact if allowed to dry out.

Criteria for use:

- normally limited to special cases, eg. nitrocelluloses.

S49 *Keep only in the original container*

Applicability:

- substances and preparations sensitive to catalytic decomposition.

Criteria for use:

- substances and preparations sensitive to catalytic decomposition eg. certain organic peroxides.

S50 *Do not mix with ... (to be specified by the manufacturer)*

Applicability:

- substances and preparations that may react with the specified product to evolve very toxic or toxic gases;
- organic peroxides.

Criteria for use

- recommended for substances and preparations mentioned above which are likely to be used by the general public, when it is a better alternative to R31 or R32;
- *obligatory* with certain peroxides which may give violent reaction with accelerators or promoters.

S51 *Use only in well-ventilated areas*

Applicability:

- substances and preparations likely to or intended to produce vapours, dusts, sprays, fumes, mists, etc. which give rise to inhalation risks or to a fire or explosion risk

Criteria for use:

- recommended when use of S38 would not be appropriate. Thus important when such substances and preparations are likely to be used by the general public.

S52 *Not recommended for interior use on large surface areas*

Applicability:

- volatile, very toxic, toxic and harmful substances and preparations containing them.

Criteria for use:

- recommended when damage to health is likely to be caused by prolonged exposure to these substances and preparations by reason of their volatilisation from large treated surfaces in the home or other enclosed places where persons congregate.

S53 *Avoid exposure - Obtain special instructions before use*

Applicability:

- substances and preparations that are carcinogenic, mutagenic and/or toxic to reproduction.

Criteria for use:

- *obligatory* for the above-mentioned substances and preparations to which at least one of the following R-phrases has been assigned: R45, R46, R49, R60 or R61.

S56 *Dispose of this material and its container at hazardous or special waste collection point.*

Applicability:

- all dangerous substances and preparations.

Criteria for use:

- recommended for all dangerous substances and preparations likely to be used by the general public for which special disposal is required.

S57 *Use appropriate containment to avoid environmental contamination*

Applicability:

- substances and preparations that have been assigned the symbol 'N'.

Criteria for use:

- normally limited to substances and preparations not likely to be used by the general public.

S59 *Refer to manufacturer for information on recovery/recycling*

Applicability:

- all dangerous substances and preparations.

Criteria for use:

- *obligatory* for substances and preparations dangerous for the ozone layer;
- recommended for other substances and preparations for which recovery/recycling is recommended.

S60 *This material and its container must be disposed of as hazardous waste*

Applicability:

- all dangerous substances and preparations.

Criteria for use:

- recommended for substances and preparations not likely to be used by the general public and where S35 is not assigned.

S61 *Avoid release to the environment. Refer to special instructions/Material Safety Data Sheets.*

Applicability:

- substances and preparations dangerous for the environment.

Criteria for use:

- normally used for substances and preparations that have been assigned the symbol 'N';
- recommended for all substances and preparations classified as 'dangerous for the environment' not covered above.

S62 *If swallowed, do not induce vomiting: seek medical advice immediately and show this container or label.*

Applicability:

- substances and preparations classified as harmful with R65 in accordance with the criteria in section 4.9;
- not applicable to substances and preparations which are placed on the market in aerosol containers.

Criteria for use:

- *obligatory* for substances and preparations mentioned above, if sold to, or likely to be used by the general public, except when S45 or S46 are obligatory;
- recommended for the substances and preparations mentioned above when used in industry, except where S45 or S46 are obligatory.

S63 *In case of accident by inhalation: remove casualty to fresh air and keep at rest.*

Applicability:

- very toxic and toxic substances and preparations (gases, vapours, particulates, volatile liquids);
- substances and preparations causing respiratory sensitisation.

Criteria for use:

- *obligatory* for substances and preparations to which R26, R23 or R42 has been assigned which are likely to be used by the general public in a way that could result in inhalation.

S64 *If swallowed, rinse mouth with water, (only if the person is conscious).*

Applicability:

- corrosive or irritant substances and preparations.

Criteria for use:

- recommended for the above substances and preparations that are likely to be used by the general public and where the above treatment is suitable.

Appendix 4

APPLYING THE CRITERIA TO CLASSIFY A HAZARDOUS SUBSTANCE - EXAMPLES

Example 1: A substance containing 0.5% w/w Parathion

A4.1 The data show that parathion is Very Toxic on the basis of its acute lethal effects (risk phrase R27/R28).

A4.2 Therefore, parathion meets the health effects criteria of Chapter 4. The concentration cut-off levels of Chapter 6 should now be applied.

A4.3 According to Table 2, a mixture with 0.5% w/w of a Very Toxic substance is to be classified as **Harmful**, as the concentration is below the concentration cut-off level for a Very Toxic mixture (7%). It is also below the concentration cut-off level for a Toxic mixture (1%), but within the range (0.1-1%) for a Harmful mixture. The substance is therefore a hazardous substance and is classified as **Harmful** with R21/22 the most appropriate risk phrase.

Example 2: A substance containing 7% w/w Acetyl chloride

A4.4 The data show that acetyl chloride is Corrosive (risk phrase R34).

A4.5 Therefore, acetyl chloride meets the health effects criteria of Chapter 4. The concentration cut-off levels of Chapter 6 should now be applied.

A4.6 According to Table 8, a mixture with 7% w/w of a Corrosive substance is to be classified as **Irritant**, as the concentration is in the range 5 -10%, but below the cut-off level for a Corrosive mixture (10%). The substance is therefore a hazardous substance and is classified as **Irritant** with R36/38 the most appropriate risk phrase.

Example 3: a substance containing 70% w/w 3a,4,7,7a-tetrahydro-4,7-methanoindene and 30% w/w amyl alcohol

A4.7 As the substance is a mixture its classification depends on whether the mixture has been tested as a whole and whether it has health effects that meet the criteria in Chapter 4. If the mixture has not been tested as a whole, the availability of health effects data on the individual ingredients (3a,4,7,7a-Tetrahydro-4,7-methanoindene and Amyl alcohol) need to be considered.

A4.8 The data available for 3a,4,7,7a-tetrahydro-4,7-methanoindene and amyl alcohol show that:

- 3a,4,7,7a-tetrahydro-4,7-methanoindene is Harmful by inhalation or if swallowed on the basis of its acute lethal effects (risk phrases R20, R22), and is an Irritant (risk phrase R36/37/38); and
- amyl alcohol is Harmful by inhalation on the basis of its acute lethal effects (risk phrase R20).

A4.9 Both 3a,4,7,7a-tetrahydro-4,7-methanoindene and amyl alcohol meet the health effects criteria of Chapter 4. The concentration cut-off levels of Chapter 6 should now be applied.

A4.10 According to Table 2 a mixture containing a Harmful substance (risk phrases R20, R22) at a concentration above 25% w/w is a hazardous substance. The mixture is classified as **Harmful** with risk phrases R20, R22 considered appropriate for the mixture.

A4.11 According to Table 8 a mixture containing an Irritant (risk phrase R36/37/38) at a concentration above 20% w/w is a hazardous substance and the mixture is classified as **Irritant**, with risk phrase R36/37/38 considered appropriate.

A4.12 Therefore, according to the health effects criteria of Chapter 4 and the concentration cut-off levels of Chapter 6, a 70% 3a,4,7,7a-tetrahydro-4,7-methanoindene and 30% amyl alcohol mixture is a hazardous substance. The mixture is classified as **Harmful** and **Irritant**, with R20, R22 and R36/37/38 the most appropriate risk phrases.

Example 4: A substance containing 0.5% w/w 3,3-Dichlorobenzidine;

A4.13 The data show that 3,3-dichlorobenzidine is:

- a Category 2 carcinogen (R45);
- harmful by skin contact on the basis of its acute lethal effects (R21); and,
- a skin sensitiser (R43).

A4.14 Therefore, 3,3-Dichlorobenzidine meets the health effects criteria of Chapters 4 and 5. The concentration cut-off levels of Chapter 6 should now be applied.

A4.15 According to Table 2, a mixture with 0.5% w/w of a Harmful substance is not a hazardous substance on the basis of its acute lethal effects.

A4.16 According to Table 10, a mixture with 0.5% w/w of a skin sensitiser is not a hazardous substance on the basis of its sensitising effects.

A4.17 According to Table 12, a mixture with 0.5% w/w of a Category 2 Carcinogen is to be classified as Toxic, with risk phrase R45 to be assigned to the mixture.

A4.18 The substance is therefore a hazardous substance and is classified as **Toxic** with risk phrase R45.

Example 5: A substance containing 10% w/w Methyl mercaptan, 20% w/w 1,2,4-Trimethylbenzene, and 2% w/w 2,4,6-Trinitrophenol;

A4.19 The data show that:

- methyl mercaptan is Harmful (Xn) by inhalation on the basis of its acute lethal effects (risk phrase R20);
- 1,2,4-trimethylbenzene is Harmful (Xn) by inhalation on the basis of its acute lethal effects (risk phrase R20), and is Harmful (Xi) on the basis of its irritant effects (R36/37/38); and,
- 2,4,6-trinitrophenol is Toxic if swallowed, by inhalation, or by contact with the skin on the basis of its acute lethal effects (risk phrase R23/24/25).

A4.20 Therefore, each of the three ingredients in the mixture meet the health effects criteria of Chapter 4. The concentration cut-off levels of Chapter 6 should now be applied.

A4.21 According to Table 2, a mixture with less than 25% w/w of a Harmful ingredient is not classified as a hazardous substance on the basis of its acute lethal effects.

A4.22 Similarly, a mixture with less than 3% w/w of a Toxic ingredient is not classified as a hazardous substance on the basis of its acute lethal effects.

A4.23 1,2,4-Trimethylbenzene is present at 20%, which in Table 8 (Chapter 6) is at the cut-off for classification as an irritant by virtue of R36/37/38. The mixture is therefore classified as Harmful (Xi) with R36/37/38.

A4.24 Since all the other hazardous ingredients in the mixture are in concentrations below their respective cut-off levels and they have similar health effects, the formulae of Chapter 7 should be used to determine whether the mixture overall is a hazardous substance on the basis of acute lethal effects.

A4.25 Assuming that the three ingredients have additive health effects the appropriate formulae in Chapter 7 can be applied.

Step 1 Consider the concentration cut-off levels for a **Toxic** mixture. These are in Table 2 for acute lethal effects. That is:

- for a Toxic ingredient, 25% w/w;
- for a Harmful ingredient, no concentration cut-off level is given in the table, as it is not appropriate.

Applying the formula from Section 7.13 for a Toxic mixture:

$$\sum\left(\frac{P_T^+}{L_T}+\frac{P_T}{L_T}\right)\geq 1$$

where:

P_T^+ = is the percentage by weight or by volume of each very toxic substance in the preparation,

P_T = is the percentage by weight or by volume of each toxic substance in the preparation,

L_T = is the respective toxic limit specified for each very toxic or toxic substance, expressed as a percentage by weight or by volume;

The only toxic ingredient (2,4,6-Trinitrophenol) is present at a concentration below the cut-off level of 25% w/w and the sum is less than 1.

That is:

$$\frac{P_T}{L_T} = \frac{2}{25}$$ (cut-off for T ingredient)

Therefore, the mixture is not classified as Toxic.

Step 2 Consider now the concentration cut-off levels for a Harmful mixture (Table 2). That is:

- for a Very Toxic ingredient, 0.1% w/w;
- for a Toxic ingredient, 3% w/w; and
- for a Harmful ingredient, 25% w/w.

The formula for a Harmful mixture from Section 7.16 can be applied.

$$\sum\left(\frac{P_T^+}{L_{Xn}} + \frac{P_T}{L_{Xn}} + \frac{P_{Xn}}{L_{Xn}}\right) \geq 1$$

where,

P_{T+} = the percentage by weight of each Very Toxic (R26, R27, R28) ingredient in the mixture;

P_T = the percentage by weight of each Toxic (R23, R24, R25) ingredient in the mixture;

P_{Xn} = the percentage by weight of each Harmful (R20, R21, R22) ingredient in the mixture; and

L_{Xn} = the concentration cut-off level specified for each Very Toxic (R26, R27, R28), Toxic (R23, R24, R25), or Harmful (R20, R21, R22) ingredient, expressed as a percentage by weight.

- There are no Very Toxic ingredients, so there is no PT^+ value.

$$\frac{P_{T+}}{L_{Xn}} = \frac{0}{0.1}$$ (Harmful cut-off for T^+ ingredient)

- 2,4,6-Trinitrophenol is the only Toxic ingredient, so:

$$\frac{P_T}{L_{Xn}} = \frac{2}{3}$$ (Harmful cut-off for T ingredient)

- methyl mercaptan and 1,2,4-trimethylbenzene are both Harmful ingredients, so:

$$\frac{P_{Xn}}{L_{Xn}} = \frac{10}{25} + \frac{20}{25} = \frac{30}{25}$$ (Harmful cut-off for Xn ingredient)

- applying the formula:

$$\sum\left(\frac{P_T^+}{L_{Xn}} + \frac{P_T}{L_{Xn}} + \frac{P_{Xn}}{L_{Xn}}\right) \geq 1$$

$$\frac{0}{0.1} + \frac{2}{3} + \frac{30}{25} = 1.9$$

As the sum is greater than 1 the mixture is a hazardous substance and is classified as:

- **Harmful (Xn)** with **R20** the most appropriate risk phrase on the basis of its acute lethal effects; and,
- **Harmful (Xi)** with **R36/37/38** as the appropriate risk phrase on the basis of its irritant effects.

Example 6: A substance containing 15% w/w 3-Chlorophenol and 10% w/w Bromobenzene

A4.26 The available data show that:

- 3-chlorophenol is Harmful on the basis of its acute lethal effects (risk phrase R20/21/22); and
- bromobenzene is Irritant on contact with the skin (risk phrase R38).

A4.27 Each of the two ingredients in the mixture meets the health effects criteria of Chapter 4. The concentration cut-off levels in Chapter 6 should now be applied.

A4.28 According to Table 2, a mixture containing less than 25% w/w of a Harmful ingredient is not classified as a hazardous substance on the basis of its acute lethal effects.

According to Table 8, a mixture containing less than 20% w/w of an Irritant is not classified as a hazardous substance on the basis of its irritant effects.

A4.29 As the health effects for each ingredient are different they are not additive, and so it is not necessary to apply the formulae in Chapter 7. The mixture is therefore not a hazardous substance.

Example 7: A substance containing 5.7% w/w Lead azide

A4.30 The data show that lead azide is:

- a Category 1 - Toxic for Reproduction (development) substance (R 61),
- a Category 3 - Harmful for Reproduction (fertility) substance (R62),
- harmful by inhalation and if swallowed on the basis of its acute lethal effects (R20/22); and
- accumulation in the human body is likely (R33).

A4.31 Lead azide meets the health effects criteria of Chapter 4. The concentration cut-off levels of Chapter 6 should now be applied.

A4.32 According to Section 6.18 and Table 12 a mixture containing 0.5% w/w or more of a category 1 - Toxic for reproduction substance is to be classified as **Toxic**, with risk phrase **R61** to be assigned to the mixture.

A4.33 According to Section 6.18 and Table 12 a mixture containing 5% w/w or more of a Category 3 - Toxic for Reproduction substance is to be classified as **Harmful** with risk phrase **R62**. The hazard category 'Harmful' is redundant and not assigned as the 'Toxic' hazard classification from above, which is valid at concentrations of 0.5% w/w and above, takes precedence.

A4.34 According to Table 2 a mixture containing less than 25% w/w of a Harmful substance is not classified as a hazardous substance on the basis of its acute lethal effects.

A4.35 According to Table 14 a mixture containing a substance likely to accumulate in the body, at a concentration of 1% or more, shall be assigned risk phrase **R33**.

A4.36 Therefore, according to the health effects criteria of Chapter 4, and the concentration cut-off levels of Chapter 6, a 5.7% lead azide mixture is a hazardous substance and is classified as **Toxic** with risk phrases **R61**, **R62**, and **R33**.

Example 8: A substance containing 2.5% w/w Aqueous Ammonia solution, 0.4% w/w Sodium hydroxide, and 2.4% w/w Bis(3-(trimethoxysilyl)propyl) amine;

A4.37 Information, current in 2001 and included in the *List of Designated Hazardous Substances*, shows the following classification and cut-off information.

	CLASSIFICATION	CUT-OFFS
Ammonia solution	C; R34	Conc ≥ 10%: C; R34 5% ≤ Conc < 10%: Xi; R36/37/38
Sodium hydroxide	C; R35	Conc ≥ 5%: C; R35 2% ≤ Conc < 5%: C; R34 **0.5% ≤ Conc < 2%: Xi; R36/38**
Bis(3-(trimethoxysilyl) propyl)amine	Xi; R41	Conc ≥ 10%: Xi; R41 5% ≤ Conc < 10%: Xi; R36

A4.38 The data show that:

- ammonia solution is corrosive causing burns (risk phrase R34);
- sodium hydroxide is corrosive causing severe burns (risk phrase R35); and,
- bis(3-(trimethoxysilyl)propyl)amine causes serious damage to eyes (risk phrase R41).

A4.39 Each of the three ingredients in the mixture meets the health effects criteria of Chapter 4. The concentration cut-off levels of Chapter 6 should now be applied.

A4.40 According to Table 8:

- a mixture with less than 5% w/w of a Corrosive (ammonia, R34) ingredient is not classified as a hazardous substance (Irritant) on the basis of its corrosive effects, and
- a mixture with less than 5% w/w of an ingredient with a risk of serious damage to eyes (Bis(3-(trimethoxysilyl)propyl)amine) is not classified as a hazardous substance on the basis of its irritant effects.

Additionally,

- a mixture with less than 0.5% sodium hydroxide is not classified as a hazardous substance on the basis of its corrosive effects.

Note that sodium hydroxide has been assigned specific cut-offs in the List and these must be applied, not the generic cut-offs in Table 8.

A4.41 Since all hazardous ingredients in the mixture are in concentrations below their respective cut-off levels, and they have similar health effects, the formulae of Chapter 7 should be used to determine whether the mixture overall is a hazardous substance.

A4.42 Assuming that the three ingredients have additive health effects, the appropriate formulae in Chapter 7 can be applied.

Note: Classification begins with the most hazardous classification in the family and proceeds to the next hazardous classification if classification is not satisfied at any level.

Step 1 Normally the concentration cut-off levels for the most hazardous substance in a mixture are taken from the appropriate Table(s) in Chapter 6.

For a Corrosive/Irritant mixture this is Table 8.

Sodium hydroxide however, has cut-off levels specified in the List. These values are applied.
For R35 corrosive effects, the cut-off for sodium hydroxide is 5% w/w. No others apply.

Step 2 The most severe classification for corrosive / irritant effects is R35. Sodium hydroxide is the only ingredient of the mixture with an R35 classification and it is present in the mixture at a concentration less than the corresponding concentration cut-off for the mixture to be classified as R35 (that is a cut-off level of 5% w/w). A classification of R35 for the mixture does not apply.

Step 3 For R34 corrosive classification the cut-offs are 2% for sodium hydroxide, and 10% for ammonia solution.

Applying the formula from Section 7.26

$$\sum\left(\frac{P_{C.R35}}{L_{C.R34}} + \frac{P_{C.R34}}{L_{C.R34}}\right) \geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$L_{C\ R34}$ = is the respective corrosive limit R34 specified for each corrosive substance to which is assigned phrase R35 or R34, expressed as a percentage by weight or by volume,

the result is $= 0.4 / 2.0 + 2.5 / 10 = 0.45 < 1$
Since the value of 1 is not met or exceeded the substance is not classified as hazardous in terms of R34.

Step 4 Consider the concentration cut-off levels for an R41 mixture (causing serious eye damage) in Table 8:

- for sodium hydroxide 5.0% w/w;
- for a R34 ingredient, 10% w/w; and
- for a R41 ingredient, 10% w/w.

The formula for an irritant mixture causing serious damage to eyes (R41) from Section 7.31 can be applied:

$$\sum\left(\frac{P_{C.R35}}{L_{Xi.R41}}+\frac{P_{C.R34}}{L_{Xi.R41}}+\frac{P_{Xi.R41}}{L_{Xi.R41}}\right)\geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$P_{Xi\ R41}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R41 in the preparation,

$L_{Xi\ R41}$ = is the respective irritant limit R41 specified for each corrosive substance to which is assigned phrase R35 or R34, or irritant substance to which is assigned phrase R41, expressed as percentage by weight or by volume,

$= 0.4 / 5.0 + 2.5 / 10 + 2.4 / 10 = 0.57 < 1$

Since the value of 1 is not met or exceeded, the substance is not classified as hazardous in terms of R41.

Step 5 Consider the concentration cut-off levels for an irritant mixture with risk phrase R36 (eye irritation). From Table 8, and the List for sodium hydroxide, the relevant cut-offs for R36 are:

- for sodium hydroxide 0.5% w/w;
- for a R34 ingredient, 5% w/w; and
- for a R41 ingredient, 5% w/w.

The formula for an irritant mixture with R36 (Section 7.35) can be applied.

$$\sum\left(\frac{P_{C,\ R35}}{L_{Xi,\ R36}} + \frac{P_{C,\ R34}}{L_{Xi,\ R36}} + \frac{P_{Xi,\ R41}}{L_{Xi,\ R36}} + \frac{P_{Xi,\ R36}}{L_{Xi,\ R36}}\right) \geq 1$$

where:

$P_{C\ R35}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R35 in the preparation,

$P_{C\ R34}$ = is the percentage by weight or by volume of each corrosive substance to which is assigned phrase R34 in the preparation,

$P_{Xi\ R41}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R41 in the preparation,

$P_{Xi\ R36}$ = is the percentage by weight or by volume of each irritant substance to which is assigned phrase R36 in the preparation,

$L_{Xi\ R36}$ = is the respective irritant limit R36 specified for each corrosive substance to which is assigned phrase R35 or R34 or irritant substance to which is assigned phrase R41, or R36 expressed as percentage by weight or by volume;

$= 0.4 / 0.5 + 2.5 / 5 + 2.4 / 5 = 1.78 > 1$

Since the value of 1 is exceeded, the substance is classified as hazardous i.e. an **Eye Irritant (Xi)** with the risk phrase **R36**.

Step 6 Consider the concentration cut-off levels for this irritant mixture with risk phrase R38 (skin irritant). From the List and Table 8:

- for sodium hydroxide 0.5% w/w;
- for ammonia solution 5% w/w.

The formula for an irritant mixture with R38 (Section 7.39) can be applied.

$$\sum\left(\frac{P_{C.R35}}{L_{Xi.R38}}+\frac{P_{C.R34}}{L_{Xi.R38}}+\frac{P_{Xi.R38}}{L_{Xi.R38}}\right)\geq 1$$

where:

$P_{C.R35}$ = is the percentage by weight or by volume of each Corrosive ingredient with risk phrase R35 in the mixture,

$P_{C.R34}$ = is the percentage by weight or by volume of each Corrosive ingredient with risk phrase R34 in the mixture,

$P_{Xi.R38}$ = is the percentage by weight or by volume of each Irritant ingredient with risk phrase R38 in the mixture,

$L_{Xi.R38}$ = is the Irritant (Xi) concentration cut-off level specified for each Corrosive ingredient assigned with risk phrase R35 or R34 or Irritant ingredient with risk phrase R38 expressed as a percentage by weight or volume, and

$= 0.4 / 0.5 + 2.5 / 5 = 1.3 > 1$

Since the value of 1 is exceeded, the substance is classified as hazardous ie. a **Skin Irritant** with the risk phrase **R38**.

The overall classification of the mixture is Harmful (Xi) R36, R38.

Appendix 5

NOTIFICATION OF HAZARDOUS SUBSTANCES

Hazardous substances regulations have been implemented by State, Territory and the Australian governments in accordance with the National Occupational Health and Safety Commission's *National Model Regulations for the Control of Workplace Hazardous Substances.* The National Model Regulations require manufacturers or importers to determine if a substance to be used in the workplace is a hazardous substance.

If the substance meets the National Occupational Health and Safety Commission's *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] and that hazardous substance is not already included in NOHSC's *List of Designated Hazardous Substances*, and provided the substance is not a composite material, mixture or formulation, then the manufacturer or importer has a duty to notify NOHSC of that determination.

This Notification Form is provided for manufacturers/importers to advise NOHSC of their determination of a hazardous substance and the associated hazard classification assigned for that substance. In order for NOHSC to keep an accurate and complete register of all notifications the notifier is required to complete this Notification Form.

The information contained in this form is not regarded as confidential

Completed forms should be forwarded to:

Manager
Improving Regulatory Framework
Chemicals Framework Team
National Occupational Health and Safety Commission
GPO Box 1577
Canberra City ACT 2601

<u>NOHSC staff will acknowledge all notifications received</u>

NOTIFIER'S DETAILS

Date:

Company name:

ACN:

Contact name and position:

Address:

Phone number:

Facsimile number:

Email address:

Tick which is applicable: Manufacturer [ ] Supplier [ ]

SUBSTANCE IDENTIFICATION

Chemical name:

Synonyms:

Product or Trade names:

Chemical Abstract Services Registry (CAS) Number:

If a CAS number is not available, please supply:

Molecular Formula:

AND

Structural Formula:

PROPOSED CLASSIFICATION

Risk Phrase(s):_____

Safety Phrase(s):_____

Note(s): _____
Concentration cut-offs:

Xn **Harmful**	**T** **Toxic**	**T+** **Very Toxic**	**Xi** **Irritant**	**C** **Corrosive**

Please state how this classification determination was reached:

_____

_____

_____

Appendix 6

CLASSIFICATION ON THE BASIS OF PHYSICOCHEMICAL PROPERTIES

Introduction

A6.1 The criteria used by the European Commission for the classification of substances on the basis of their physicochemical properties is presented here for information only. It may be used to supplement the classification resulting from the use of the *Australian Dangerous Goods Code* (ADG Code) criteria, and the *National Standard for the Storage and Handling of Workplace Dangerous Goods* [NOHSC:1015(2001)].

A6.2 The test methods relating to explosive, oxidising and flammable properties are referenced from Annex V of EC Council Directive 67/548/EEC. Classification criteria follow directly from the test methods in Annex V as far as they are mentioned.

A6.3 If adequate information is available to demonstrate in practice that the physicochemical properties of substances and preparations (apart from organic peroxides) are different from those revealed by the test methods given in Annex V, then such substances and preparations should be classified according to the hazard they present, if any, to those handling the substances and preparations or to other persons.

Criteria for classification, choice of symbols, indication of danger and choice of risk phrases

Explosive

A6.4 Substances and preparations shall be classified as **explosive** and assigned the symbol '**E**' and the indication of danger '**explosive**' in accordance with the results of the tests given in Annex V and in so far as the substances and preparations are explosive as placed on the market.
One risk phrase is obligatory and is to be specified on the basis of the following:

R2 ***Risk of explosion by shock, friction, fire or other sources of ignition***

Includes substances and preparations except those set out below.

R3 ***Extreme risk of explosion by shock, friction, fire or other source of ignition***

Includes substances and preparations that are particularly sensitive such as picric acid salts or PETN.

Oxidising

A6.5 Substances and preparations shall be classified as **oxidising** and assigned the symbol '**O**' and the indication of danger '**oxidising**' in accordance with the results of the tests given in Annex V.

A6.6 One risk phrase is obligatory and is to be specified on the basis of the test results but subject to the following:

R7 ***May cause fire***

Organic peroxides which have flammable properties even when not in contact with other combustible material.

R8 ***Contact with combustible material may cause fire***

Other oxidising substances and preparations, including inorganic peroxides, which may cause fire or enhance the risk of fire when in contact with combustible material.

R9 ***Explosive when mixed with combustible material***

Other substances and preparations, including inorganic peroxides, which become explosive when mixed with combustible materials, eg. certain chlorates.

Remarks concerning peroxides

A6.7 For the explosive properties, an organic peroxide or preparation thereof in the form in which it is placed on the market is classified according to the criteria in section A6.6 on the basis of tests carried out in accordance with the methods given in Annex V.

A6.8 For the oxidising properties the existing methods in Annex V cannot be applied to organic peroxides.

A6.9 For substances, organic peroxides not already classified as explosive are classified as dangerous on the basis of their structure (eg. R-O-O-H; R_1-O-O-R_2).
Preparations not already classified as explosive shall be classified using the calculation method, based on the percentage of active oxygen, shown in Section 9.5 of Annex VI of Commission Directive 67/548/EEC (as amended by Commission Directive 2001/59/EC).

A6.10 Any organic peroxide or preparation thereof not already classified as explosive is classified as oxidising if the peroxide or its formulation contains:

- more than 5% of organic peroxides; or
- more than 0.5% available oxygen from the organic peroxides, and more than 5% hydrogen peroxide.

Extremely flammable

A6.11 Substances and preparations shall be classified as **extremely flammable** and assigned the symbol '**F^+**' and the indication of danger **'extremely flammable'** in accordance with the results of the tests given in Annex V. The risk phrase shall be assigned in accordance with the following criteria:

R12 ***Extremely flammable***

- Liquid substances and preparations which have a flash point lower than 0°C, and a boiling point (or in case of a boiling range the initial boiling point) lower than or equal to 35°C.
- Gaseous substances and preparations that are flammable in contact with air at ambient temperature and pressure.

Highly flammable

A6.12 Substances and preparations shall be classified as **highly flammable** and assigned the symbol '**F**' and the indication of danger '**highly flammable**' in accordance with the results of the tests given in Annex V. Risk phrases shall be assigned in accordance with the following criteria:

R11 ***Highly flammable***

- Solid substances and preparations that may readily catch fire after brief contact with a source of ignition and which continue to burn or to be consumed after removal of the source of ignition.
- Liquid substances and preparations having a flash point below 21°C but which are not extremely flammable.

R15 ***Contact with water liberates extremely flammable gases***

Substances and preparations, which, in contact with water or damp air, evolve extremely flammable gases in dangerous quantities at a minimum rate of one litre per kilogram per hour.

R17 ***Spontaneously flammable in air***

Substances and preparations that may become hot and finally catch fire in contact with air at ambient temperature without any input of energy.

Flammable

A6.13 Substances and preparations shall be classified as **flammable** in accordance with the results of the tests given in Annex V. The risk phrase shall be assigned in accordance with the criteria mentioned below.

R10 ***Flammable***

Liquid substances and preparations having a flash point equal to or greater than 21°C, and less than or equal to 55°C.

A6.14 In practice, however, it has been shown that a preparation having a flash point equal to or greater than 21°C and less than or equal to 55°C need not be classified as flammable if the preparation could not in any way support combustion and only so long as there is no reason to fear risks to those handling these preparations or to other persons.

Other physicochemical properties

A6.15 Additional risk phrases shall be assigned to substances and preparations which have been classified by virtue of Sections 6.4 to 6.9 above, or by Chapters 4 and 5, or by Appendix 7 of the Approved Criteria, in accordance with the following criteria:

R1 ***Explosive when dry***

For explosive substances and preparations put on the market in solution or in a wetted form, eg. nitrocellulose with more than 12.6% nitrogen.

R4 ***Forms very sensitive explosive metallic compounds***

For substances and preparations which may form sensitive explosive metallic derivatives, eg. picric acid, styphnic acid.

R5 ***Heating may cause an explosion***

For thermally unstable substances and preparations not classified as explosive, eg. perchloric acid >50%.

R6 ***Explosive with or without contact with air***

For substances and preparations which are unstable at ambient temperatures, eg. acetylene.

R7 ***May cause fire***

For reactive substances and preparations, eg. fluorine, sodium hydrosulphite.

R14 ***Reacts violently with water***

For substances and preparations that react violently with water, eg. acetyl chloride, alkali metals, titanium tetrachloride.

R16 ***Explosive when mixed with oxidising substances***

For substances and preparations which react explosively with an oxidising agent, eg. red phosphorus.

R18 ***In use, may form flammable/explosive vapour-air mixture***

For preparations not in themselves classified as flammable, which contain volatile components that are flammable in air.

R19 ***May form explosive peroxides***

For substances and preparations which may form explosive peroxides during storage, eg. diethyl ether, 1,4-dioxan.

R30 ***Can become highly flammable in use***

For preparations not in themselves classified as flammable, which may become flammable due to the loss of non-flammable volatile components.

R44 ***Risk of explosion if heated under confinement***

For substances and preparations not in themselves classified as explosive in accordance with paragraph A6.4 above but which may nevertheless display explosive properties in practice if heated under sufficient confinement. For example, certain substances which would decompose explosively if heated in a steel drum do not show this effect if heated in less-strong containers.

A6.16 For other additional risk phrases see Appendix 3.

Appendix 7

CLASSIFICATION ON THE BASIS OF ENVIRONMENTAL EFFECTS

Introduction

A7.1 The adopted criteria of the European Commission for the classification of substances on the basis of their ecotoxicological properties are presented here for information only. They may be used to supplement the classification of a substance that has been classified on the basis of its health effects and physicochemical properties.

A7.2 The primary objective of classifying substances and preparations dangerous for the environment is to alert the user to the hazards these substances and preparations present to ecosystems. Although the present criteria refer to aquatic ecosystems it is recognised that certain substances and preparations may simultaneously or alternatively affect other ecosystems whose constituents may range from soil microflora and microfauna to primates.

A7.3 The criteria set out below follow directly from the test methods set out in Annex V of EC Council Directive 67/548/EEC. Classified substances may be subject to review in the light of new data.

A7.4 For the purposes of classification and labelling, and having regard to the current state of knowledge, such substances and preparations are divided into two groups according to their acute and/or long term effects in aquatic systems, or their acute and/or long-term effects in non-aquatic systems.

A7.5 The classification of **substances** is usually made on the basis of experimental data for acute aquatic toxicity, degradation, and log Pow (or BCF if available).

A7.6 The classification of **preparations** shall normally be carried out on the basis of a conventional method referred to in Annex III, Parts A and B of Directive 1999/45/EC. In this case, the classification is based on the individual concentration limits specified: -

- in the List, or
- in Annex III, Part B to Directive 1999/45/EC where the substance or substances do not appear in the List, or appear in it without concentration limits.

Criteria for classification, indication of danger, choice of risk phrases

Aquatic environment

A7.7 Substances shall be classified as **dangerous for the environment** and assigned the symbol '**N**' and the appropriate indication of danger, and assigned risk phrases in accordance with the following criteria:

R50 ***Very toxic to aquatic organisms***

and

R53 ***May cause long-term adverse effects in the aquatic environment***

used together when:-

Acute toxicity:		96 hr LC_{50} (for fish)	$\leq$ 1 mg/l
	or	48 hr EC_{50} (for Daphnia)	$\leq$ 1 mg/l
	or	72 hr IC_{50} (for algae)	$\leq$ 1 mg/l
and	-	the substance is not readily degradable,	
	or		
	-	the log Pow (log octanol/water partition coefficient) > 3.0 (unless the experimentally determined BCF $\leq$ 100).	

R50 ***Very toxic to aquatic organisms***

Acute toxicity:		96 hr LC_{50} (for fish)	$\leq$ 1 mg/l
	or	48 hr EC_{50} (for Daphnia)	$\leq$ 1 mg/l
	or	72 hr IC_{50} (for algae)	$\leq$ 1 mg/l

R51 ***Toxic to aquatic organisms***

and

R53 ***May cause long-term adverse effects in the aquatic environment***

used together when:-

Acute toxicity:		96 hr LC_{50} (for fish)	1 mg/l < $LC_{50} \leq$ 10 mg/l
	or	48 hr EC_{50} (Daphnia)	1 mg/l < $EC_{50} \leq$ 10 mg/l
	or	72 hr IC_{50} (for algae)	1 mg/l < $IC_{50} \leq$ 10 mg/l
and	-	the substance is not readily degradable	
	or		
	-	the log Pow > 3.0 (unless the experimentally determined BCF $\leq$ 100).	

A7.8 Substances shall be classified as **dangerous for the environment** in accordance with the criteria set out below. Risk phrases shall also be assigned in accordance with the following criteria:

R52 ***Harmful to aquatic organisms***

and

R53 ***May cause long-term adverse effects in the aquatic environment***

used together when:-

Acute toxicity:		96 hr LC_{50} (for fish)	10 mg/l < $LC_{50} \leq$ 100 mg/l
	or	48 hr EC_{50} (for Daphnia)	10 mg/l < $EC_{50} \leq$ 100 mg/l
	or	72 hr IC_{50} (for algae)	10 mg/l < $IC_{50} \leq$ 100 mg/l
and			
	-	the substance is not readily degradable.	

A7.9 This criterion applies unless there exists additional scientific evidence concerning degradation and/or toxicity sufficient to provide an adequate assurance that neither the substance nor its degradation products will constitute a potential long-term and/or delayed danger to the aquatic environment. Such additional scientific evidence could include:

(i) a proven potential to degrade rapidly in the aquatic environment,

(ii) an absence of chronic toxicity effects at a concentration of 1.0 mg/litre, eg. a no-observed effect concentration of greater than 1.0 mg/litre determined in a prolonged toxicity study with fish or Daphnia.

R52 ***Harmful to aquatic organisms***

Substances not falling under the criteria listed above in this Appendix, but which on the basis of the available evidence concerning their toxicity may nevertheless present a danger to the structure and/or functioning of aquatic ecosystems.

R53 ***May cause long-term adverse effects in the aquatic environment***

Substances not falling under the criteria listed above, but which, on the basis of the available evidence concerning their persistence, potential to accumulate, and predicted or observed environmental fate and behaviour may nevertheless present a long-term and/or delayed danger to the structure and/or functioning of aquatic ecosystems.

For example, poorly water-soluble substances, i.e. substances with a solubility of less than 1mg/l will be covered by this criterion if:

(a) they are not readily degradable; and

(b) the log Pow $\geq$ 3.0 (unless the experimentally determined BCF $\leq$ 100).

A7.10 This criterion applies to substances unless there exists additional scientific evidence concerning degradation and/or toxicity sufficient to provide an adequate assurance that neither the substance nor its degradation products will constitute a potential long-term and/or delayed danger to the aquatic environment.

Such additional scientific evidence could include:

(i) a proven potential to degrade rapidly in the aquatic environment;

(ii) an absence of chronic toxicity effects at the solubility limit eg. a no-observed effect concentration of greater than the solubility limit determined in a prolonged toxicity study with fish or Daphnia.

Comments on the determination of IC_{50} for algae and of degradability

A7.11 Where it can be demonstrated in the case of highly coloured substances that algal growth is inhibited solely as a result of a reduction in light intensity, then the 72h IC_{50} for algae should not be used as a basis for classification.

A7.12 Substances are considered readily degradable if the following criteria hold true.

(a) If in 28-day biodegradation studies the following levels of degradation are achieved

- in tests based upon dissolved organic carbon: 70%,
- in tests based upon oxygen depletion or carbon dioxide generation: 60% of the theoretical maxima.

These levels of biodegradation must be achieved within 10 days of the start of degradation, which point is taken as the time when 10% of the substance has been degraded.

or

(b) if in those cases where only COD and BOD5 data are available when the ratio of BOD5/COD is greater than or equal to 0.5;

or

(c) if other convincing scientific evidence is available to demonstrate that the substance can be degraded (biotically and/or abiotically) in the aquatic environment to a level of >70% within a 28-day period.

Non - aquatic environment

A7.13 Substances and preparations shall be classified as **dangerous for the environment** and assigned the symbol '**N**' and the appropriate indication of danger, and assigned risk phrases in accordance with the following criteria:

R54 ***Toxic to flora***

R55 ***Toxic to fauna***

R56 ***Toxic to soil organisms***

R57 ***Toxic to bees***

R58 ***May cause long-term adverse effects in the environment***

Substances and preparations which, on the basis of the available evidence concerning their toxicity, persistence, potential to accumulate and predicted or observed environmental fate and behaviour, may present a danger, immediate or long-term and/or delayed, to the structure and/or functioning of natural ecosystems other than those covered under paragraphs A7.7 to A7.12 above.

A7.14 Substances and preparations shall be classified as **dangerous for the environment**, and assigned the symbol '**N**' and the appropriate indication of danger, where applicable, and assigned risk phrases in accordance with the following criteria:

R59 ***Dangerous for the ozone layer***

Substances which, on the basis of the available evidence concerning their properties and their predicted or observed environmental fate and behaviour, may present a danger to the structure and/or the functioning of the stratospheric ozone layer.

Appendix 8

CLASSIFICATION GUIDANCE FOR CONSUMER PRODUCTS SUPPLIED TO / USED BY THE GENERAL PUBLIC AND/OR WORKPLACES

A8.1 Manufacturers and Importers of chemical substances supplied for use at workplaces in Australia are required to determine whether such substances are hazardous to health, prior to supply. The criteria that determine the hazardous nature of chemicals are provided in Chapters 1-7 of this document known as the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

A8.2 The Australian Approved Criteria are based on those used in Europe, as NOHSC has a process by which these criteria are updated in line with changes in European classifications. In Australia, the Approved Criteria described in Chapters 1-7 are mandatory and are given effect under the *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)] (National Model regulations) and the Australian, State and Territory regulations introduced in accordance with the National Model Regulations.

A8.3 The provisions described in this Appendix (Appendix 8) are those enforced under EU regulations and largely provide information for the classification of consumer products that contain dangerous preparations[2], in Europe.

A8.4 In Australia, classification and labelling instructions for consumer chemical products are provided in the SUSDP. Therefore, the provisions in Appendix 8 are not mandatory under current Australian workplace chemicals regulations, except where such provisions appear in the Approved Criteria (Chapters 1-7), and as such are provided here for information only.

A8.5 However, labels and MSDS of chemicals imported from, and classified in accordance with the criteria of Europe, may bear some or all of the specific provisions outlined in Appendix 8. As such, manufacturers and importers of chemicals intended for consumer use in Australia should refer to the requirements of the SUSDP for labelling.

-Products supplied to the general public

A8.6 The labels on packages of –products containing dangerous preparations, which are intended to be supplied to the general public must bear relevant safety phrase S1, S2, S45 or S46 in accordance with the Approved Criteria and the *National Code of Practice for the Labelling of Workplace Substances.*

[2] Dangerous preparations are mixtures or solutions composed of two or more substances determined to be hazardous according to their physico-chemical properties and human health and environmental effects as defined in sub-points 2.a-o of Article 2 of EC Directive 1999/45/EC.

A8.7 When products referred to in sub-paragraph (8.6) are classified as very toxic, toxic or corrosive, and where it is physically impossible to give the information on the package itself, packages containing such preparations must be accompanied by precise and easily understandable instructions for use including, where appropriate, instructions for the destruction of the empty package and disposal of un-used product.

Products intended for use by spraying

A8.8 The labels on packages containing dangerous preparations intended to be used for spraying shall bear the safety phrase S23 and safety phrase S38 or S51 assigned in accordance with the Approved Criteria and the *National Code of Practice for the Labelling of Workplace Substances*.

Products containing a substance affected by the risk phrase R33 (danger of cumulative effects)

A8.9 When a product contains at least one substance required to show the risk phrase R33, that phrase must be shown on the label of the dangerous preparation when the concentration of that substance is equal to or higher than 1%, unless a different cut-off value is shown for that substance in the List.

Products containing a substance affected by the risk phrase R64 (may cause harm to breast-fed babies)

A8.10 When a product contains at least one substance required to show the risk phrase R64, that phrase must be shown on the label of the dangerous preparation when the concentration of that substance is equal to or higher than 1%, unless a different cut-off value is shown for that substance in the List.

Paints and varnishes containing lead

A8.11 Labels of packages of paints and varnishes containing lead in quantities exceeding 0.15% (expressed as weight of lead out of the total weight of the preparation and determined in accordance with ISO Standard 6503/1984) shall show the following particulars –

"*Contains lead. Should not be used on surfaces that are liable to be chewed or sucked by children*."

A8.12 In the case of packages containing less than 125 millilitres of the preparations referred to in paragraph8.9, the particulars on the label may be –

"*Warning. Contains lead*."

Cyanoacrylate based adhesives

A8.13 The immediate packages of glues based on cyanoacrylates shall bear the following inscription –

"Cyanoacrylate. Danger. Bonds skin and eyes in seconds. Keep out of the reach of children."

A8.14 Appropriate safety advice shall accompany the package.

Preparations containing isocyanates

A8.15 The package labels of preparations containing isocyanates (whether as monomers, oligomers, prepolymers etc. or as mixtures thereof) shall bear the following inscriptions -

"*Contains isocyanates. See information supplied by the manufacturer*."

Certain preparations containing epoxy constituents

A8.16 The package labels of preparations containing epoxy constituents with an average molecular weight ≤ 700 shall bear the following inscription -

"*Contains epoxy constituents. See information supplied by the manufacturer*."

Preparations intended to be sold to the general public that contain active chlorine

A8.17 The package labels of preparations containing more than 1% of active chlorine, which are intended to be sold to the general public, shall bear the following inscription -

"Warning. Do not use with other products. May release dangerous gases (chlorine)."

Preparations containing cadmium (alloys) intended to be used for brazing or soldering

A8.18 The package labels of preparations containing cadmium (alloys) intended to be used for brazing or soldering shall bear the following inscriptions -

"Warning! Contains cadmium. Dangerous fumes are formed during use.
See information supplied by the manufacturer. Comply with the safety instructions."

Preparations not classified as sensitising but containing at least one sensitising substance

A8.19 The packaging of preparations containing at least one substance classified as sensitising and being present in a concentration ≥0.1% or in a concentration greater than or equal to that specified under a specific note for the substance in the List must bear the inscription -

"Contains (name of sensitising substance). May produce an allergic reaction."

Liquid preparations containing halogenated hydrocarbons

A8.20 For liquid preparations which show no flashpoint or a flashpoint higher than 55ºC and contain a halogenated hydrocarbon and more than 5% flammable or highly flammable substances, the packaging must bear the following inscription as appropriate -

"Can become highly flammable in use" or "Can become flammable in use".

Preparations containing a substance assigned the risk phrase R67

A8.21 When a preparation contains one or more substances assigned the risk phrase R67, the label of the preparation must bear the following inscription -

"Vapours may cause drowsiness and dizziness",

when the total concentration of such substances present in the preparation is ≥15%, unless:

- the preparation is already classified with phrases R20, R23, R26, R68/20, R39/23 or R39/26, or
- the preparation is in a package not exceeding 125 ml.

Cements and cement preparations

A8.22 The packaging of cements and cement preparations containing more than 0.0002% soluble chromium (VI) of the total dry weight of the cement must bear the inscription:

"Contains chromium (VI). May produce an allergic reaction"

unless the preparation is already classified and labelled as a sensitiser with phrase R43.

REFERENCED DOCUMENTS

1. National Occupational Health and Safety Commission, *National Model Regulations for the Control of Workplace Hazardous Substances* [NOHSC:1005(1994)], in *Control of Workplace Hazardous Substances: National Model Regulations and National Code of Practice*, AGPS, Canberra, 1994.

2. National Occupational Health and Safety Commission, *List of Designated Hazardous Substances*, NOHSC, Canberra.

3. EC Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, *Official Journal of the European Communities*, No. L196 (16 August 1967).

4. Directive 1999/45/EC of the European Parliament and of the Council concerning the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous preparations, *Official Journal of the European Communities*, No. L200 (31 May 1999).

5. Commission Directive 2001/59/EC of 6 August 2001 adapting to technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, *Official Journal of the European Communities*, No. L225 (21 August 2001).

6. Federal Office of Road Safety*, Australian Dangerous Goods Code* 6th Edition, Vol 1, Attachment 1, Road Transport Reform (Dangerous Goods) Regulations, AusInfo, Canberra, 1998.

7. Commission Directive 2001/60/EC adapting to technical progress Directive 1999/45/EC of the European Parliament and of the Council concerning the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous preparations, *Official Journal of the European Communities*, No. L226 (22 August 2001).

8. Organisation for Economic Cooperation and Development (OECD), *Guidelines for the Testing of Chemicals*, Organisation for Economic Cooperation and Development, Paris, 1992