STATUTORY INSTRUMENTS.

S.I. No. 272 of 2008

EUROPEAN COMMUNITIES (CLASSIFICATION, PACKAGING, LABELLING AND NOTIFICATION OF DANGEROUS SUBSTANCES) REGULATIONS 2008

(Prn. A8/1053)

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I, MARY COUGHLAN, Minister for Enterprise, Trade and Employment, in exercise of the powers conferred on me by section 3 of the European Communities Act 1972 (No. 27 of 1972) and for the purpose of giving effect to Directive 2006/121/EC of the European Parliament and of the Council of 18 December 2006[1] and for the purpose of giving further effect to Regulation (EC) No. 1907/2006 of the European Parliament and of the Council of 18 December 2006[2], hereby make the following regulations:

1. (1) These Regulations may be cited as the European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) (Amendment) Regulations 2008.

(2) The European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) Regulations 2003 and 2006 and these Regulations may be cited together as the European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) Regulations 2003 to 2008.

2. The European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) Regulations 2003 (S.I. No. 116 of 2003) are amended—

(*a*) in Regulation 2—

(i) paragraph (1)—

(I) by deleting the following definitions:

(A) "Annex V";

(B) "Annex VII.A";

(C) "Annex VII.B";

(D) "Annex VII.C";

(E) "Annex VII.D";

(F) "Annex VIII";

[1] OJ No. L396, 30.12.2006, p. 850 and Corrigendum OJ No. L136, 29.5.2007, p. 281.
[2] OJ No. L 136, 29.05.2007, p. 3.

Notice of the making of this Statutory Instrument was published in "Iris Oifigiúil" of 18*th July*, 2008.

(G) "notification";

(H) "polymer";

(I) "process-orientated research and development";

(J) "scientific research and development;",

(II) by substituting for the definition of "Annex VI" the following:

" 'Annex VI' means Annex VI to Council Directive 67/548/EEC[3], as lastly amended by Council Directive 2006/121/EC of 18 December 2006, as set out in Schedule 5;",

and

(III) in the definition of "Directives", by substituting for "2001/58/EC of 27 July 2001[40] and 2001/59/EC of 6 August 2001[41]" the following:

"2001/58/EC of 27 July 2001[40], 2001/59/EC of 6 August 2001[41] and 2006/121/EC of 18 December 2006[41A]",

(IV) by inserting after the definition of "preparations" the following:

" 'REACH Regulation' means Regulation (EC) No. 1907/2006 of the European Parliament and of the Council of 18 December 2006[2]",

and

(ii) by inserting after paragraph (3) the following:

"(4) References in these Regulations to Annexes VII A, VII B, VII C, VII D and VIII of Council Directive 67/548/EEC shall be construed as references to the corresponding Annexes VI, VII, VIII, IX, X and XI of the REACH Regulation.",

(*b*) in Regulation 3—

(i) paragraph (2), by substituting "Regulation 4 or 22" for "Regulation 4, 15 or 22", and

(ii) paragraph (5), by substituting "packaging and labelling

[3] OJ No. L196, 16.8.1967, p. 1.
[40] OJ. No. L 212, 7.8.2001, p.24.
[41] OJ. No. L 225, 21.8.2001, p.1.
[41A] OJ No. L396,30.12.2006, p.850 and Corrigendum OJ No. L136, 29.05.2007, p. 281.
[2] OJ No. L136,29.05.2007, p.3.

requirements" for "packaging, labelling and safety data sheet requirements",

(*c*) by substituting for Regulation 5 the following:

"5. The competent authority shall be the Health and Safety Authority.",

(*d*) by substituting for Regulation 6 the following:

"6. (1) A person shall not place on the market a substance, on its own or in a preparation, unless it has been packaged and labelled in accordance with Regulations 19 to 22 and with the criteria in Schedule 5, and for registered substances, in accordance with the information obtained through the application of Articles 12 and 13 of the REACH Regulation, save in the case of preparations where provisions exist in other Directives.

(2) The measures referred to in paragraph (1) shall apply until the substance is listed in Schedule 1 or until a decision not to list it is taken in accordance with the procedure laid down in Article 29 of Council Directive 67/548/EEC.",

(*e*) by substituting for Regulation 7 the following:

"Testing and assessment of properties of substances

7. For the purposes of these Regulations tests on substances shall be conducted according to the requirements of Article 13 of the REACH Regulation.",

(*f*) in Regulation 20(12), by substituting for subparagraph (*b*) the following:

"(*b*) the information regarding effects on human health is transmitted to professional or industrial users, distributors, wholesalers, retailers and consumers by the person placing the propane, butane or liquefied petroleum gas on the market, and",

(*g*) in Regulation 29(1)—

(i) by substituting for subparagraph (*a*) the following:

"(*a*) contravenes Regulation 6, 9, 19, 20, 21, 23 or 28(3),",

(ii) in subparagraph (*b*), by substituting "Regulations, or" for "Regulations,", and

(iii) by deleting subparagraphs (*c*) and (*d*),

(*h*) by revoking Regulations 10 to 18, 24, 25 and 27, and Schedules 6, 8 and 9, and

(*i*) by substituting for Schedule 5 the following:

"SCHEDULE 5

ANNEX VI

GENERAL CLASSIFICATION AND LABELLING REQUIREMENTS FOR DANGEROUS SUBSTANCES AND PREPARATIONS

CONTENTS

COMMISSION STATEMENT

1. GENERAL 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. This Annex sets out the general principles governing the classification and labelling of substances and preparations referred to in Article 4[64] of Directive 67/548/EEC and in Article 4 of Directive 1999/45/EC and other relevant Directives on dangerous preparations.

It is addressed to all those concerned (manufacturers, importers, national authorities) with methods of classifying and labelling dangerous substances and preparations.

1.3. The requirements of Directive 67/548/EEC and of Directive 1999/45/EC are intended to provide a primary means by which the general public and persons at work are given essential information about dangerous substances and preparations. The label draws the attention of persons handling or using substances and preparations to the inherent danger of certain such materials.

[64] This Article corresponds to Regulation 8.

The label may also serve to draw attention to more comprehensive product information on safety and use available in other forms.

1.4. The label takes account of all potential hazards which are likely to be faced in the normal handling and use of dangerous substances and preparations when in the form in which they are placed on the market, but not necessarily in any different form in which they may finally be used, e.g. diluted. The most severe hazards are highlighted by symbols, such hazards and those arising from other dangerous properties are specified in standard risk phrases, and safety phrases give advice on necessary precautions.

In the case of substances, the information is completed by the name of the substance under an internationally recognised chemical nomenclature, the preferred name being the one used in the European Inventory of Existing Commercial Chemical Substances (Einecs), or in the European List of Notified Chemical Substances (ELINCS), the EC number and the name, address and telephone number of the person established in the Community who is responsible for placing the substance on the market.

In the case of preparations, the information in accordance with Article 10.2. of Directive 1999/45/EC, is completed by:

— the trade name or the designation of the preparation;

— the chemical name of the substance or substances present in the preparation; and

— the name, full address and telephone number of the person established in the Community who is responsible for placing the preparation on the market.

1.5. Article 6[65] of Directive 67/548/EEC requires that manufacturers, distributors and importers of dangerous substances which appear in the Einecs but which have not yet been introduced into Annex I shall be obliged to carry out an investigation to make themselves aware of the relevant and accessible data which exist concerning the properties of such substances. On the basis of this information, they shall package and provisionally label

[65] This Article corresponds to Regulation 9.

these substances according to the rules laid down in Articles 22 to 25[66] and the criteria in this Annex.

1.6. **Data required for classification and labelling**

1.6.1. For substances the data required for classification and labelling may be obtained:

(*a*) as regards substances for which the information specified in Annexes VI, VII and VIII of the REACH Regulation is required, most of the necessary data for classification and labelling appear in the base set. This classification and labelling must be reviewed, if necessary, when further information is available (Annexes IX and X of the REACH Regulation).

(*b*) as regards other substances (e.g. those referred to in section 1.5 above), the data required for classification and labelling may, if necessary, be obtained from a number of different sources, for example:

— the results of previous tests;

— information required by international rules on the transport of dangerous substances;

— information taken from reference works and the literature; or

— information derived from practical experience.

The results of validated structure-activity relationships and expert judgement may also be taken into account where appropriate.

1.6.2. For preparations, normally the data required for classification and labelling may be obtained:

(*a*) if it concerns physicochemical data, by the application of the methods specified in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation. This applies also to preparations covered by Directive 91/414/EEC unless other internationally recognised methods are acceptable in accordance with the provisions of Annexes II and III to Directive 91/414/EEC

[66]These Articles correspond to Regulations 19, 20 and 21.

(Article 5. 5. of Directive 1999/45/EC). For gaseous preparations a calculation method may be used for flammable and oxidising properties (see 9.1.1.1 and 9.1.1.2). For non-gaseous preparations containing organic peroxides a calculation method may be used for oxidising properties (see 2.2.2.1).

(*b*) if it concerns data on health effects:

— by the application of the methods specified in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation, unless, in the case of plant protection products, other internationally recognised methods are acceptable in accordance with the provisions of Annexes II and III to Directive 91/414/EEC (Article 6. 1. (*b*) of Directive 1999/45/EC),

— and/or by the application of a conventional method referred to in Article 6 and Annex II, Parts A 1 - 6 and B 1 - 5 of Directive 1999/45/EC, or,

— in the case of R65, by the application of the rules under 3.2.3

— however, if it concerns the evaluation of the carcinogenic, mutagenic and reproductive toxicity properties, by the application of a conventional method referred to in Article 6 and Annex II, Parts A 7 - 9 and B 6 of Directive 1999/45/EC.

(*c*) if it concerns data on ecotoxicological properties

(i) for aquatic toxicity only:

— by the application of the methods specified in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation, subject to the conditions referred to in Annex III Part C of Directive 1999/45/EC, unless, in the case of plant protection products, other internationally recognised methods are acceptable in accordance with the provisions of Annexes II and III to Directive 91/414/EEC

(Article 7. 1. (*b*) of Directive 1999/45/EC), or

— by application of a conventional method referred to in Article 7 and Annex III, Parts A and B, of Directive 1999/45/EC.

(ii) for the evaluation of the potential for (or actual) bioaccumulation through the determination of log Pow (or BCF), or the evaluation of degradability, by application of a conventional method referred to in Article 7 and Annex III, Parts A and B, of Directive 1999/45/EC.

(iii) for dangers of the ozone layer by application of a conventional method referred to in Article 7 and Annex III, Parts A and B, of Directive 1999/45/EC.

Note concerning the performance of animal tests:

The performance of animal tests to establish experimental data is subject to the provisions of Directive 86/609/EEC regarding the protection of animals used for experimental purposes.

Note concerning physicochemical properties:

For organic peroxides and organic peroxide preparations data may be derived from the calculation method set out in Chapter 9.5. For gaseous preparations a calculation method may be used for flammable and oxidising properties (see chapter 9).

1.7. **Application of the guide criteria**

Classification must cover the physicochemical, toxicological and ecotoxicological properties of substances and preparations.

Classification of substances and preparations is made according to Chapter 1.6, on the basis of the criteria in Chapters 2 to 5 (substances) and Chapters 2, 3, 4.2.4 and 5 of this Annex. All types of hazard must be considered. For instance, classification under 3.2.1 does not imply that the sections such as 3.2.2 or 3.2.4 can be ignored.

The choice of symbol(*s*) and risk phrase(*s*) is made on the basis of the classification in order to ensure that the

specific nature of the potential dangers identified in classification is expressed on the label.

Notwithstanding the criteria given under 2.2.3, 2.2.4 and 2.2.5, substances and preparations in the form of aerosols shall be subject to the provisions of Directive 75/324/EEC as amended and adapted to technical progress.

1.7.1. Definitions

'Substances' means chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the product, and any impurity deriving from the production process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.

A substance may be chemically very well defined (e.g. acetone) or a complex mixture of constituents of variable composition (e.g. aromatic distillates). For certain complex substances, some individual constituents have been identified.

'Preparations' means mixtures or solutions composed of two or more substances.

1.7.2. Application of the guide criteria for substances

The guidance criteria set out in this Annex are directly applicable when the data in question have been obtained from test methods comparable with those described in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation. In other cases, the available data must be evaluated by comparing the test methods employed with those indicated in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation and the rules specified in this Annex for determining the appropriate classification and labelling.

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 on the basis of an assessment of the evidence by a competent person.

Without prejudice to Article 6, where the above procedure has been followed and there is concern over possible inconsistencies then a proposal may be submitted for the entry of the provisional classification into Annex I. The proposal should be made to one of the Member States and should be accompanied by appropriate scientific data (see also section 4.1).

A similar procedure may be followed when information is identified which gives cause for concern over the accuracy of an existing entry in Annex I.

1.7.2.1. Classification of substances containing impurities, additives or individual constituents

Where impurities, additives or individual constituents of substances have been identified, they shall be taken into account if their concentration is greater than or equal to the limits specified

— 0.1 % for substances classified as very toxic, toxic, carcinogenic (category 1 or 2), mutagenic (category 1 or 2), toxic to reproduction (category 1 or 2), or dangerous for the environment (assigned the symbol 'N' for the aquatic environment, dangerous for the ozone layer)

— 1% for substances classified as harmful, corrosive, irritant sensitising, carcinogenic (category 3), mutagenic (category 3), toxic to reproduction (category 3), or dangerous for the environment (not assigned the symbol 'N', i.e. harmful to aquatic organisms, may cause long-term adverse effects)

unless lower values have been specified in Annex I.

With the exception of substances listed specifically in Annex I, classification should be carried out according to the requirements of Articles 5, 6 and 7 of Council Directive 1999/45/EC.

In the case of asbestos (650-013-00-6) this general rule does not apply until a concentration limit has been fixed in Annex I. Substances in which asbestos is present must be classified and labelled according to the principles in Article 6.

1.7.3. Application of the guide criteria for preparations

The guidance criteria set out in this Annex are directly applicable when the data in question have been obtained

from test methods comparable with those described in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation with the exception of the criteria of Chapter 4 for which only the conventional method is applicable. A conventional method is also applicable in relation to the criteria of Chapter 5, with the exception of aquatic toxicity, subject to the conditions referred to in Annex III Part C of Directive 1999/45/EC. For preparations covered by Directive 91/414/EEC data for classification and labelling are also acceptable from other internationally recognised methods (see special provisions in Section 1.6 of this Annex). In other cases, the available data must be evaluated by comparing the test methods employed with those indicated in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation and the rules specified in this Annex for determining the appropriate classification and labelling.

Where the health and environmental hazards are assessed by applying a conventional method referred to in Articles 6 and 7 and Annexes II and III of Directive 1999/45/EC the individual concentration limits to be used are those set out either:

— in Annex I to Directive 67/548/EEC, or

— in Annex II Part B and/or Annex III Part B of Directive 1999/45/EC where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits.

In the case of preparations containing mixtures of gases, classification with respect to the health and environmental effects will be established by the calculation method on the basis of the individual concentration limits from Annex I to Directive 67/548/EEC or when these limits are not in Annex I on the basis of the criteria of Annexes II and III of Directive 1999/45/EC.

1.7.3.1. Preparations or substances described in Section 1.7.2.1 used as constituents of another preparation

The labelling of such preparations must be in conformity with the provisions of Article 10 according to the principles set out in Articles 3 and 4 of Directive 1999/45/EC. However, in certain cases, the information on the label of the preparation or substance described in Section

1.7.2.1 is insufficient to enable other manufacturers who wish to use it as a constituent of their own preparation(*s*) to carry out the classification and labelling of their preparation(*s*) correctly.

In these cases, the person established within the Community responsible for placing the original preparation or substance described in Section 1.7.2.1 on the market, whether it be the manufacturer, the importer or the distributor shall supply upon justified request and as soon as possible all necessary data concerning the dangerous substances present to enable correct classification and labelling of the new preparation. This data is also necessary to enable the person responsible for placing the new preparation on the market to comply with other requirements of Directive 1999/45/EC.

2. CLASSIFICATION ON THE BASIS OF PHYSICO-CHEMICAL PROPERTIES

2.1. Introduction

The test methods relating to explosive, oxidising and flammable properties included in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation serve to give specific meaning to the general definitions given in Article 2(2)(*a*) to (*e*) of Directive 67/548/EEC[68]. Criteria follow directly from the test methods in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation as far as they are mentioned.

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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation, 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.

2.2. Criteria for classification, choice of symbols, indication of danger and choice of risk phrases

In the case of preparations, the criteria referred to in Article 5 of Directive 1999/45/EC need to be taken into consideration.

[68] This Article corresponds to Regulation 2(2).

2.2.1. Explosive

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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation and in so far as the substances and preparations are explosive as placed on the market. One risk phrase is obligatory, it is to be specified on the basis of the following:

R2 Risk of explosion by shock, friction, fire or other sources of ignition

— substances and preparations except those set out below.

R3 Extreme risk of explosion by shock, friction, fire or other source of ignition

— substances and preparations which are particularly sensitive such as picric acid salts or PETN.

2.2.2. Oxidising

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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation. One risk phrase is obligatory, it 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, e.g. certain chlorates.

2.2.2.1. Remarks concerning peroxides

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 2.2.1. on the basis of tests carried out in accordance with the methods given in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

For the oxidising properties the existing methods in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation cannot be applied to organic peroxides.

For substances, organic peroxides not already classified as explosive are classified as dangerous on the basis of their structure (e.g. 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.

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.

2.2.3. Extremely flammable

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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation. 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 which are flammable in contact with air at ambient temperature and pressure.

2.2.4. Highly flammable

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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation. Risk phrases shall be assigned in accordance with the following criteria:

R11 Highly flammable

— Solid substances and preparations which 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 which may become hot and finally catch fire in contact with air at ambient temperature without any input of energy.

2.2.5. Flammable

Substances and preparations shall be classified as flammable in accordance with the results of the tests given in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH

Regulation. 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.

However, in practice 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.

2.2.6. Other physicochemical properties

Additional risk phrases shall be assigned to substances and preparations which have been classified by virtue of Sections 2.2.1 to 2.2.5 above or by Chapter 3, 4 and 5 below, in accordance with the following criteria (based on experience obtained during compilation of Annex I):

R1 Explosive when dry

For explosive substances and preparations put on the market in solution or in a wetted form, e.g. 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, e.g. picric acid, styphnic acid.

R5 Heating may cause an explosion

For thermally unstable substances and preparations not classified as explosive, e.g. perchloric acid > 50%.

R6 Explosive with or without contact with air

For substances and preparations which are unstable at ambient temperatures, e.g. acetylene.

R7 May cause fire

For reactive substances and preparations, e.g. fluorine, sodium hydrosulphite.

R14 Reacts violently with water

For substances and preparations which react violently with water, e.g. acetyl chloride, alkali metals, titanium tetrachloride.

R16 Explosive when mixed with oxidising substances

For substances and preparations which react explosively with an oxidising agent, e.g. red phosphorus.

R18 In use, may form flammable/explosive vapour-air mixture

For preparations not in themselves classified as flammable, which contain volatile components which are flammable in air.

R19 May form explosive peroxides

For substances and preparations which may form explosive peroxides during storage, e.g. 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 Section 2.2.1 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.

For other additional risk phrases see Section 3.2.8.

3. CLASSIFICATION ON THE BASIS OF TOXICOLOGICAL PROPERTIES

3.1. Introduction

3.1.1. Classification is concerned with both the acute and long-term effects of substances and preparations, whether resulting from a single instance of exposure or repeated or prolonged exposure.

Where it can be demonstrated by epidemiological studies, by scientifically valid case studies as specified in this Annex or by statistically backed experience, such as the assessment of data from poison information units or concerning occupational diseases, that toxicological effects on man differ from those suggested by the application of the methods outlined in Section 1.6 of this Annex, then the substance or preparation shall be classified according to its effects on man. However, tests on man should be discouraged and should not normally be used to negate positive animal data.

Directive 86/609/EEC seeks to protect animals used for experimental and other scientific purposes. For several endpoints there are validated *in vitro* test methods in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation and these tests should be used where appropriate.

3.1.2. The classification of substances must be made on the basis of the experimental data available in accordance with the following criteria which take into account the magnitude of these effects:

(*a*) for acute toxicity (lethal and irreversible effects after a single exposure), the criteria under Sections 3.2.1 to 3.2.3 are to be used,

(*b*) for sub-acute, sub-chronic or chronic toxicity the criteria under Sections 3.2.2 to 3.2.4 are to be used,

(*c*) for corrosive and irritant effects the criteria under Sections 3.2.5 and 3.2.6 are to be used,

(*d*) for sensitising effects the criteria under Section 3.2.7 are to be used,

(*e*) for specific effects on health (carcinogenicity, mutagenicity and reproductive toxicity), the criteria in Chapter 4 are to be used.

3.1.3. For preparations, the classification relating to dangerous for health is carried out:

(*a*) on the basis of a conventional method referred to in Article 6 and Annex II of Directive 1999/45/EC in the absence of experimental data. In this case, the classification is based on the individual concentration limits:

— either taken from Annex I to Directive 67/548/EEC, or

— from Annex II, Part B of Directive 1999/45/EC where the substance or substances do not appear in Annex I of Directive 67/548/EEC or appear in it without concentration limits.

(*b*) or when experimental data are available, according to the criteria described under Sections 3.1.2 excluding the carcinogenic, mutagenic and toxic to reproduction properties referred to under 3.1.2 (*e*) which must be evaluated by a conventional method referred to in Article 6 and Annex II, Parts A 7 - 9 and B 6 of Directive 1999/45/EC.

Note: Without prejudice to requirements of Directive 91/414/EEC, only where it can be scientifically demonstrated by the person responsible for placing the preparation on the market that the toxicological properties of the preparation cannot correctly be determined by the method outlined in paragraph 3.1.3 (*a*), or on the basis of existing test results on animals, the methods outlined in paragraph 3.1.3 (*b*) may be used, provided they are justified or specifically authorised under Article 12 of Directive 86/609/EEC.

Whichever method is used for the evaluation of the danger of a preparation, all the dangerous effects on health as defined in Annex II, Part B of Directive 1999/45/EC must be taken into consideration.

3.1.4. When the classification is to be established from experimental results obtained in animal tests the results should have validity for man in that the tests reflect, in an appropriate way, the risks to man.

3.1.5. 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).

3.1.5.1. The discriminating dose is the dose which causes evident toxicity but not mortality and must be one of the four dosage levels specified in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

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 following the fixed dose method may be either:

— less than 100% survival,

— 100% survival, but evident toxicity,

— 100% survival, but no evident toxicity.

In the criteria in sections 3.2.1, 3.2.2 and 3.2.3 only the final test result is shown. The 2 000 mg/kg dose should be used primarily to obtain information on the toxic effects of substances which are of low acute toxicity and which are not classified on the basis of acute toxicity.

The fixed dose method requires in some cases testing at higher or lower doses, if not already tested at the relevant dose level. Refer also to the evaluation table in test method B.1 *bis*.

3.1.5.2. The range of exposure where lethality is expected is derived from the observed absence or presence of substance related mortality following the acute toxic class method. For initial testing one of three fixed starting doses (25, 200 or 2000 mg per kg body weight) is used.

The acute toxic class method requires in some cases testing at higher or lower doses, if not already tested at the relevant dose level. Refer also to the test procedure flow charts in test method B.1 *tris* of Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

3.2. **Criteria for classification, choice of symbols, indication of danger, choice of risk phrases**

3.2.1. Very toxic

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.

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

R28 Very toxic if swallowed

Acute toxicity results:

— LD_{50} oral, rat $\leqslant$ 25 mg/kg,

— less than 100% survival at 5 mg/kg oral, rat by the fixed dose procedure, or

— high mortality at doses $\leqslant$ 25 mg/kg oral, rat, by the acute toxic class method (for test result interpretation see flow charts in Annex 2 of test method B.1 *tris* of Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

R27 Very toxic in contact with skin

Acute toxicity results:

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

R26 Very toxic by inhalation

Acute toxicity results:

— LC_{50} inhalation, rat, for aerosols or particulates: < 0.25 mg/litre/4hr,

— LC_{50} inhalation, rat, for gases and vapours: < 0.5 mg/litre/4hr.

R39 Danger of very serious irreversible effects

— Strong evidence that irreversible damage other than the effects referred to in Chapter 4 is likely to be caused by a single exposure by an appropriate route, generally in the above-mentioned dose range.

In order to indicate the route of administration/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.

3.2.2. Toxic

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. Risk phrases shall be assigned in accordance with the following criteria.

R25 Toxic if swallowed

Acute toxicity results:

— LD_{50} oral, rat: $25 < LD_{50} \leqslant 200$ mg/kg,

— Discriminating dose, oral, rat, 5 mg/kg: 100 % survival but evident toxicity, or

— high mortality in the dose range > 25 to $\leqslant$ 200 mg/kg oral, rat, by the acute toxic class method (for test result interpretation see flow charts in Annex 2 of test method B.1 *tris* of Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

R24 Toxic in contact with skin

Acute toxicity results:

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

R23 Toxic by inhalation

Acute toxicity results:

— LC_{50} inhalation, rat, for aerosols or particulates: $0.25 < LC_{50} \leqslant 1$ mg/litre/4hr,

— LC_{50} inhalation, rat, for gases and vapours: $0.5 < LC_{50} \leqslant 2$ mg/litre/4hr.

R39 Danger of very serious irreversible effects

— strong evidence that irreversible damage other than the effects referred to in Chapter 4 is likely to be caused by a single exposure by an appropriate route, generally in the above-mentioned dose range.

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.

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 when these effects are observed at levels of one order of magnitude lower (i.e. 10-fold) than those set out for R48 in Section 3.2.3.

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.

3.2.3. Harmful

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

R22 Harmful if swallowed

Acute toxicity results:

— LD_{50} per oral, rat: $200 < LD_{50} \leqslant 2000$ 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 the test method B.1 *bis* of Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation, or

— high mortality in the dose range > 200 to $\leqslant$ 2000 mg/kg oral, rat, by the acute toxic class method (for test result interpretation see flow charts in Annex 2 of test method B.1 *tris* of Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation).

R21 Harmful in contact with skin

Acute toxicity results:

— LD_{50} dermal, rat or rabbit: $400 < LD_{50} \leqslant 2000$ mg/kg.

R20 Harmful by inhalation

Acute toxicity results:

— LC_{50} inhalation, rat, for aerosols or particulates: $1 < LC_{50} \leqslant 5$ mg/litre/4hr,

— LC_{50} inhalation, rat, for gases or vapours: $2 < LC_{50} \leqslant 20$ mg/litre/4hr.

R65 Harmful: may cause lung damage if swallowed

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

(*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 3 mm 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 by the test methods shown in

Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

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

R68 Possible risk of irreversible effects

— strong evidence that irreversible damage other than the effects referred to in Chapter 4 is likely to be caused by a single exposure by an appropriate route, generally in the above-mentioned dose range.

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.

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 when these effects are observed at levels of the order of:

— oral, rat $\leqslant$ 50 mg/kg (bodyweight)/day,

— dermal, rat or rabbit $\leqslant$ 100 mg/kg (bodyweight)/day,

— inhalation, rat $\leqslant$ 0.25 mg/l, 6h/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.

3.2.3.1. Comments regarding volatile substances

For certain substances with a high saturated vapour concentration evidence may be available to indicate effects that give cause for concern. Such substances may not be classified under the criteria for health effects in this guide (3.2.3) or not covered by Section 3.2.8. However, where there is appropriate evidence that such substances may present a risk in normal handling and use then classification on a case-by-case basis in Annex I may be necessary.

3.2.4. Comments regarding the use of R48

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 which 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.

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

1. 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 (e.g. 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 (e.g. liver);

(ii) severe morphological changes that are potentially reversible but are clear evidence of marked organ dysfunction (e.g. 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 (e.g. fibrosis of the myocardium or dying back of a nerve) or in stem cell populations (e.g. aplasia or hypoplasia of the bone marrow).

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.

2. 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 which 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*) adaptative responses (e.g. 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 (e.g. specific metabolic pathways) has been demonstrated.

3.2.5. Corrosive

The substance or preparation shall be classified as corrosive and assigned the symbol 'C' and the indication of danger 'corrosive' in accordance with the following criteria:

— A substance or a preparation is considered to be corrosive if, when it is 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 cited in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation or during an equivalent method.

— Classification can be based on the results of a validated *in vitro* test, such as that cited in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation (B.40. Skin corrosion: rat skin transcutaneous electrical resistance assay and human skin model assay.)

— A substance or a preparation 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[69] may also be taken into consideration. If consideration of alkali/acid reserve suggests the substance or preparation may not be corrosive then further testing should be carried out to confirm this, preferably by use of an appropriate validated *in*

[69] 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

vitro test. Consideration of acid/alkali reserve should not be used alone to exonerate substances or preparations from classification as corrosive.

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.

Notes:

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.

3.2.6. Irritant

Substances and preparations shall be classified as irritant and assigned the symbol 'Xi' and the indication of danger 'irritant' in accordance with the criteria given below.

3.2.6.1. 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 which 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

Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation 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 e.g. hyperplasia, scaling, discoloration, fissures, scabs and alopecia should be taken into account.

Relevant data may also be available from non-acute animal studies (see comments on R48, section 2.d). These are considered significant if the effects seen are comparable to those described above.

- 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:

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

3.2.6.2. Ocular lesions

The following risk phrases shall also 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 Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation 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 in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation has been completed using three animals if the lesions, on two or more animals, are equivalent to any of the above values except that for iris lesion the value should be equal to or greater than 1 but less than 2 and for redness of the conjunctivae the value should be equal to or greater than 2.5.

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 which 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 in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation 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 which 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.

3.2.6.3. Respiratory system irritation

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

R37 Irritating to respiratory system

Substances and preparations which 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

In interpreting practical observations in humans, care should be taken to distinguish between effects which lead to classification with R48 (see section 3.2.4.) from those leading to classification with R37. Conditions normally leading to classification with R37 are reversible and usually limited to the upper airways.

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.

3.2.7. Sensitisation

3.2.7.1. Sensitisation by inhalation

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

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.

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

- the extent of exposure.

The evidence referred to above could be:

- clinical history and data from appropriate lung function tests related to exposure to the substance, confirmed by other supportive evidence which may include:

- a chemical structure related to substances known to cause respiratory hypersensitivity;

- an *in vivo* immunological test (e.g. skin prick test);

- an *in vitro* immunological test (e.g. serological analysis);

- studies indicating other specific but non-immunological mechanisms of action, e.g. 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.

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.

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.

Substances that elicit symptoms of asthma by irritation only in people with bronchial hyperreactivity should not be assigned R42.

Animal studies

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 (e.g. in mice), or

- specific pulmonary responses in guinea pigs.

3.2.7.2. Sensitisation by skin contact

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

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 contacts 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 (see also 3.1.1).

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.

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

Positive results from appropriate animal tests are:

- in the case of the adjuvant type test method for skin sensitisation detailed in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the

REACH Regulation or in the case of other adjuvant-type test methods, a response of at least 30% of the animals is considered positive;

- for any other test method a response of at least 15% of the animals is considered positive.

3.2.7.3. Immunological contact urticaria

Some substances or preparations, which meet the criteria for R42 may in addition cause immunological contact urticaria. In these cases, information concerning contact urticaria should be included by the use of appropriate S-phrases, usually S24 and S36/37, and in the Safety Data Sheet.

For substances or preparations, which produce signs of immunological contact urticaria which do not fulfil the criteria for R42, consideration should be given to classification with R43.

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

3.2.8. Other toxicological properties

Additional risk phrases shall be assigned in accordance with the following criteria (based on experience obtained during compilation of Annex I) to substances and preparations classified by virtue of 2.2.1. to 3.2.7. above and/or chapters 4 and 5:

R29 Contact with water liberates toxic gas

For substances and preparations which in contact with water or damp air, evolve very toxic/toxic gases in potentially dangerous amounts, e.g. 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, e.g. 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 which react with acids to evolve very toxic gases in dangerous amounts; e.g. 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 Section 4.2.3.3 for substances and Annex V, Part A.3. of Directive 1999/45/EC for preparations.

R64 May cause harm to breastfed babies

For substances and preparations which 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 Section 4.2.3.3 for substances and Annex V, Part A.4. of Directive 1999/45/EC for preparations.

R66 Repeated exposure may cause skin dryness or cracking

For substances and preparations which 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.

See also paragraphs 1.6 and 1.7.

R67 Vapours may cause drowsiness and dizziness

For volatile substances and preparations containing such substances which 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 $\leqslant$ 4 h to the saturated vapour concentration (SVC) at 20^0C is $\leqslant$ 1/10.

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

See also Paragraphs 1.6 and 1.7.

For other supplementary risk phrases see Section 2.2.6.

4. CLASSIFICATION ON THE BASIS OF SPECIFIC EFFECTS ON HUMAN HEALTH

4.1. Introduction

4.1.1. This Chapter sets out the procedure for the classification of substances which may have the effects mentioned below. For preparations see Section 4.2.4.

4.1.2. 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 Section 4.2.1, 4.2.2 or 4.2.3, he shall provisionally label the substance in accordance with these criteria, on the basis of the assessment of the evidence by a competent person.

4.1.3. The manufacturer, distributor or importer shall submit as soon as possible a document summarising all relevant information to one Member State in which the substance is placed on the market. Relevant information in this context comprises in particular all available published and unpublished information required for appropriate classification of the substance in question, on the basis of the intrinsic properties according to the categories laid down in Article 2 (2) and in accordance with the criteria in this Annex. The submitted summary document should include a bibliography containing all relevant references, including any relevant unpublished data.

4.1.4. Furthermore, a manufacturer, distributor or importer who has new data which are relevant to the classification and labelling of a substance in accordance with

the criteria given in Section 4.2.1., 4.2.2. or 4.2.3., shall submit this data as soon as possible to one Member State in which the substance is placed on the market.

4.1.5. To obtain as quickly as possible a harmonised classification for the Community by the procedure defined in Article 28 of Directive 67/548/EEC, Member States which have relevant information available justifying the classification of a substance in one of these categories, whether submitted by the manufacturer or not, should forward such information together with suggestions for classification and labelling, to the Commission as soon as possible.

The Commission will forward to the other Member States the classification and labelling proposal that it receives. Any Member State may ask the Commission for the information it has received.

Any Member State which has good reason to believe that the suggested classification and labelling is inappropriate as far as the carcinogenic, mutagenic or reproductive toxicity effects are concerned shall notify the Commission thereof.

4.2. **Criteria for classification, indication of danger, choice of risk phrases**

4.2.1. Carcinogenic substances

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

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

Substances which 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

Substances which 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.

4.2.1.1. The following symbols and specific risk phrases apply:

Categories 1 and 2:

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

R45 May cause cancer

However, substances and preparations which present a carcinogenic risk only when inhaled, for example, as dust, vapour or fumes, (other routes of exposure e.g. 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:

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

R40 Limited evidence of a carcinogenic effect

4.2.1.2. Comments regarding the categorisation of carcinogenic substances

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.

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.

Category 3 actually comprises 2 sub-categories:

(*a*) 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;

(*b*) substances which 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.

For a distinction between Categories 2 and 3 the arguments listed below are relevant which 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 'maximal tolerated dose'. The maximal tolerated dose is characterised by toxic effects which, although not yet reducing lifespan, go along with physical changes such as about 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 (e.g., i.p. or s.c. 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 (e.g., 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 (e.g. by specific metabolic pathways) irrelevant for man.

For a distinction between Category 3 and no classification arguments are relevant which exclude a concern for man:

- 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.

4.2.2. Mutagenic substances

4.2.2.1. 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

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

Substances which 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

Substances which 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.

4.2.2.2. The following symbols and specific risk phrases apply:

Categories 1 and 2:

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:

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

R68 Possible risk of irreversible effects

4.2.2.3. Comments regarding the categorisation of mutagenic substances

Definition of terms:

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.

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.

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

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

To place a substance in Category 2, positive results are needed from assays showing (*a*) mutagenic effects, or (*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.

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.

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

To place a substance in Category 3, positive results are needed in assays showing (*a*) mutagenic effects or (*b*) other cellular

interaction relevant to mutagenicity, in somatic cells in mammals *in vivo*. The latter especially would normally be supported by positive results from *in vitro* mutagenicity assays.

For effects in somatic cells *in vivo* at present the following methods are 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, e.g. by alkaline elution, in somatic cells.

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, e.g. 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.

4.2.3. Substances toxic to reproduction

4.2.3.1. For the purposes of classification and labelling 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

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

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 which should be regarded as if they impair fertility in humans

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 which should be regarded as if they cause developmental toxicity to humans

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

Substances which cause concern for human fertility

Generally on the basis of:

- results in appropriate animal studies which provide sufficient evidence to cause a strong suspicion of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occuring 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.

Substances which cause concern for humans owing to possible developmental toxic effects

Generally on the basis of:

- results in appropriate animal studies which 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.

4.2.3.2. The following symbols and specific risk phrases apply:

Category 1

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

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

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

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

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

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.

4.2.3.3. Comments regarding the categorisation of substances toxic to reproduction

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.

1 Effects on male or female fertility, includes 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.

2 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 embrytoxic/fetotoxic 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.

Classification of chemicals as toxic to reproduction is intended to be used for chemicals which 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 which are toxic to reproduction at exposure levels which do not produce other signs of toxicity.

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.

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.

Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation specifies a limit test in the case of substances of low toxicity. If a dose level of at least 1,000 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

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.

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

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.

Classification into Category 3 is based on similar criteria as for Category 2 but may be used where the experimental design has deficiencies which 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.

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

Substances which are classified as toxic to reproduction and which also cause concern due to their effects on lactation should in addition be labelled with R64 (see criteria in Section 3.2.8.).

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.

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 (see criteria in Section 3.2.8.). This R-phrase may also be appropriate for substances which affect the quantity or quality of the milk.

R64 would normally be assigned on the basis of:

(*a*) toxicokinetic studies that would indicate the likelihood that the substance would be present in potentially toxic levels in breast milk; and/or

(*b*) 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

(*c*) on the basis of evidence in humans indicating a risk to babies during the lactational period.

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.

4.2.4. Procedure for the classification of preparations concerning specific effects on health

If a preparation contains one or more substances classified with respect to the criteria laid out above, it must be classified according to the criteria referred to in Annex II, Part A. 7. — 9. and Part B. 6. of Directive 1999/45/EC (the concentration limits are either in Annex I of this Directive, or in Annex II, Part B. 6. of Directive 1999/45/EC where the substance or substances under consideration do not appear in Annex I or appear in it without concentration limits).

5. CLASSIFICATION ON THE BASIS OF ENVIRONMENTAL EFFECTS

5.1. Introduction

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.

The criteria set out below follow directly from the test methods set out in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation in so far as they are mentioned. The test methods required for the base set referred to in Annexes VII and VIII of the REACH Regulation are limited and the information derived from them may be insufficient for an appropriate classification. Classification may require additional data derived from Annexes IX or X of the REACH Regulation or other equivalent studies. Furthermore, classified substances may be subject to review in the light of other new data.

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.

5.1.1. 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).

5.1.2. The classification of preparations shall normally be carried out on the basis of a conventional method referred to in Article 7 and Annex III, Parts A and B of Directive 1999/45/EC. In this case, the classification is based on the individual concentration limits

- in Annex I to Directive 67/548/EEC

- or in Annex III Part B to Directive 1999/45/EC where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits.

5.1.3. Normally, the classification of a preparation is made on the basis of a conventional method. However, for the

determination of the acute aquatic toxicity, there may be cases for which it is appropriate to carry out tests on the preparation. The result of these tests on the preparation may only modify the classification concerning acute aquatic toxicity which would have been obtained by the application of a conventional method. If such tests are chosen by the person responsible for the placing on the market, it must be ensured that the quality criteria of the test methods in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation have been complied with. Furthermore, the tests are to be carried out on all three groups of species in conformity with the criteria in this Annex (algae, daphnia and fish), unless the highest hazard classification relating to acute aquatic toxicity has been assigned to the preparation after testing on one of the species or a test result was already available before Directive 1999/45/EC entered into force.

5.2. **Criteria for classification, indication of danger, choice of risk phrases**

The classification criteria for substances in Section 5.2.1. only apply to preparations where they have been tested in accordance with 5.1.3.

5.2.1. Aquatic environment

5.2.1.1. 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

Acute toxicity: 96 hr LC_{50} (for fish) $\leqslant$ 1 mg/l

or 48 hr EC_{50} (for Daphnia) $\leqslant$ 1 mg/l

or 72 hr IC_{50} (for algae) $\leqslant$ 1 mg/l

and

- the substance is not readily degradable

or

- the log Pow (log octanol/water partition coefficient) $\geqslant$ 3.0 (unless the experimentally determined BCF $\leqslant$ 100).

R50 Very toxic to aquatic organisms

Acute toxicity: 96 hr LC_{50} (for fish) $\leqslant$ 1 mg/l

or 48 hr EC_{50} (for Daphnia) $\leqslant$ 1 mg/l

or 72 hr IC_{50}(for algae) $\leqslant$ 1 mg/l

R51 Toxic to aquatic organisms

and

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

Acute toxicity: 96 hr LC_{50} (for fish) 1 mg/l < LC_{50} $\leqslant$ 10 mg/l

or 48 hr EC_{50} (for Daphnia) 1 mg/l < EC_{50} $\leqslant$ 10 mg/l

or 72 hr IC_{50} (for algae) 1 mg/l < IC_{50} $\leqslant$ 10 mg/l

and

- the substance is not readily degradable

or

- the log Pow $\geqslant$ 3.0 (unless the experimentally determined BCF $\leqslant$ 100).

5.2.1.2.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

Acute toxicity: 96 hr LC_{50} (for fish) 10 mg/l < LC_{50} $\leqslant$ 100 mg/l

or 48 hr EC_{50} (for Daphnia) 10 mg/l < EC_{50} $\leqslant$ 100 mg/l

or 72 hr IC_{50} (for algae) $10 \text{ mg/l} < IC_{50} \leqslant 100 \text{ mg/l}$

and

the substance is not readily degradable.

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 should normally be based on the studies required by Annex IX of the REACH Regulation, or studies of equivalent value, and 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, e.g. 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 chapter, 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 in this chapter, 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 1 mg/l will be covered by this criterion if:

(*a*) they are not readily degradable; and

(*b*) the log Pow $\geqslant$ 3.0 (unless the experimentally determined BCF $\leqslant$ 100).

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 should normally be based on the studies required by Annex IX of the REACH Regulation, or studies of equivalent value, and could include

(i) a proven potential to degrade rapidly in the aquatic environment;

(ii) an absence of chronic toxicity effects at the solubility limit e.g. a no-observed effect concentration of greater than the solubility limit determined in a prolonged toxicity study with fish or Daphnia.

5.2.1.3. *Comments on the determination of IC_{50} for algae and of degradability*

- 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.

- 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.

5.2.2. Non - aquatic environment

5.2.2.1. 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 5.2.1 above. Detailed criteria will be elaborated later.

5.2.2.2. 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. This includes the substances which are listed in Annex I to Council Regulation (EC) No. 2037/2000 on substances that deplete the ozone layer (OJ No. L 244, 29.9.2000, p.1) and its subsequent amendments.

Preparations shall be classified on the basis of a conventional method referred to in Article 7 and Annex III, Parts A and B of Directive 1999/45/EC.

6. CHOICE OF SAFETY ADVICE PHRASES

6.1. Introduction

Safety advice phrases (S-phrases) shall be assigned to dangerous substances and preparations in accordance with the following general criteria. In addition, for certain preparations, the safety advice listed in Annex V of Directive 1999/45/EC is mandatory.

Whenever the manufacturer is mentioned in Chapter 6 it refers to the person responsible for placing the substance or preparation on the market.

6.2. Safety phrases for substances and preparations

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 < 40° C.
- Criteria for use:

- *obligatory* for organic peroxides unless S47 is used,

- recommended for other dangerous substances and preparations having a boiling point $\leqslant$ 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 desirable 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, e.g. 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, e.g. certain organometallic 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 which may react violently with water,
  - substances and preparations which 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 which 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 which 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 which 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 feedingstuffs*

- 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, e.g. 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 which may form explosive or spontaneously flammable mixtures with combustible material.
- Criteria for use:
    - available for use in special cases, e.g. 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 which 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 (e.g. 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 which produce toxic products on combustion.
- Criteria for use:
  - normally limited to special cases (e.g. 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 which 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 (e.g. 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 which 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 used in industry. 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 which 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 which 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 which react violently with water.

- Criteria for use:

  - normally limited to special cases (e.g. 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 as 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 either 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 which 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 which 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 (e.g. 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 which 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 which become unstable at a certain temperature.
- Criteria for use:
    - normally limited to special cases (e.g. certain organic peroxides).

S48 *Keep wetted with.... (appropriate material to be specified by the manufacturer)*

- Applicability:
    - substances and preparations which may become very sensitive to sparks, friction or impact if allowed to dry out.
- Criteria for use:
    - normally limited to special cases, e.g. 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 e.g. certain organic peroxides.

S50 *Do not mix with... (to be specified by the manufacturer)*

- Applicability:
    - substances and preparations which 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 to 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 which 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/Safety data sheet*

- Applicability:
    - substances and preparations dangerous for the environment.
- Criteria for use:
    - normally used for substances and preparations which have been assigned the symbol 'N',
    - recommended for all substances and preparations classified 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 3.2.3,
    - not applicable to substances and preparations which are placed on the market in aerosol containers (or in containers fitted with a sealed spray attachment), see sections 8 and 9.
- 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 which could result in inhalation.

- Applicability:

  - corrosive or irritant substances and preparations.

- Criteria for use:

  - recommended for the above substances and preparations which are likely to be used by the general public and where the above treatment is suitable.

7. **LABELLING**

7.1. When a substance or preparation has been classified the appropriate label is determined with reference to the requirements of Article 23 and Article 10 of Directive 1999/45/EC for substances and preparations respectively. This section explains how the label is determined and, in particular, gives guidance on how to choose the appropriate risk and safety phrases.

The label contains the following information:

(*a*) for preparations the trade name or designation;

(*b*) for substances the name of the substance and for preparations the names of the substances present in the preparations in accordance with the rules set out in Article 10.2.3. of Directive 1999/45/EC;

(*c*) the name, full address and telephone number of the person responsible for placing the substance or preparation on the market, whether manufacturer, importer or distributor;

(*d*) the symbol(*s*) and indication(*s*) of danger;

(*e*) phrases indicating particular hazards (R-phrases);

(*f*) phrases indicating safety advice (S-phrases);

(*g*) for substances, the EC number, and in addition for substances appearing in Annex I, the word ‘EC label’;

(*h*) for preparations offered or sold to the general public the nominal quantity of the contents unless specified elsewhere on the package.

Note

For certain preparations there are additional labelling requirements set out in Article 10.1.2. and Annex V of Directive 1999/45/EC and in Article 20 of Directive 98/8/EC.

7.1.1. Final choice of risk and safety phrases

Although the final choice of the most appropriate risk and safety phrases is primarily governed by the need to give all necessary information, consideration should also be given in the clarity and impact of the label. With clarity in mind, the necessary information should be expressed in a minimum number of phrases.

In the case of substances which are irritant, highly flammable, flammable and oxidising, an indication of R-phrases and S-phrases need not be given where the package does not contain more than 125ml. This shall also apply in the case of the same volume of harmful substances not retailed to the general public.

For preparations, if the contents of the package do not exceed 125 ml:

- if classified as highly flammable, oxidising, irritant, with the exception of those assigned R41, or dangerous for the environment and assigned the 'N' symbol it shall not be necessary to indicate the R-phrases or the S-phrases,

- if classified as flammable or dangerous to the environment and not assigned the ‘N‘ symbol it shall be necessary to indicate the R-phrases but it shall not be necessary to indicate the S-phrases.

7.1.2. Without prejudice to Article 16.4. of Directive 91/414/EEC and to Directive 98/8/EC, indications such as ‘non-toxic’, ‘non-harmful’, ‘non-polluting’, ‘ecological’ or any other statement indicating that the substance or preparation is not dangerous or likely to lead to underestimation of the dangers of the substance or preparation in question shall not appear on the label or packaging of substances or preparations subject to this Directive or to Directive 1999/45/EC.

7.2. **Chemical name(*s*) to be displayed on the label**

7.2.1. For substances listed in Annex I the label shall show the name of the substances under one of the designations given in Annex I.

For substances not listed in Annex I, the name is established according to an internationally recognised chemical nomenclature as defined in Section 1.4 above.

7.2.2. For preparations, the choice of names to be displayed on the label follows the rules of Article 10.2.3. of Directive 1999/45/EC.

Note:

Subject to Annex V, B. 9. of Directive 1999/45/EC,

- the name of the sensitising substance must be chosen in accordance with Section 7.2.1 of this Annex,

- in the case of concentrate preparations which are intended for the perfume industry:

  - the person responsible for placing them on the market may identify merely the one sensitising substance judged by him to be primarily responsible for the sensitisation hazard,

  - in the case of a natural substance, the chemical name may be of the type: 'essential oil of...' 'extract of...', rather than the name of the constituents of that essential oil or extract.

7.3. **Choice of danger symbols**

The design of the danger symbols and the wording of the indications of danger shall comply with those laid down in Annex II[70]. The symbol shall be printed in black on an orange-yellow background.

7.3.1. For substances appearing in Annex I the danger symbols and indications of danger shall be those shown in the Annex.

7.3.2. For dangerous substances not yet appearing in Annex I and for preparations, the danger symbols and indications of danger shall be assigned according to the rules laid down in this Annex.

Where more than one danger symbol is assigned to a substance or preparation:

- the obligation to indicate the symbol 'E' makes the symbols 'F+', 'F' and 'O' optional,

[70] This Annex corresponds to Schedule 2.

- the obligation to indicate the symbol 'T+' or 'T' makes the symbols 'Xn', 'Xi' and 'C' optional,

- the obligation to indicate the symbol 'C' makes the symbols 'Xn' and 'Xi' optional,

- if the symbol 'Xn' is assigned, the symbol 'Xi' is optional.

7.4. **Choice of Risk-phrases**

The wording of the R/phrases shall comply with that laid down in Annex III[71].

The combined R-phrases in Annex III shall be used where applicable.

7.4.1. For substances appearing in Annex I, the R-phrases shall be those shown in the Annex.

7.4.2. For substances not appearing in Annex I, R-phrases will be selected according to the following criteria and priorities:

(*a*) in the case of dangers which give rise to health effects:

(i) R-phrases corresponding to the category of danger illustrated by a symbol must appear on the label;

(ii) R-phrases corresponding to other categories of danger which are not illustrated by a symbol by virtue of Article 23;

(*b*) in the case of dangers arising from physicochemical properties:

- R-phrases corresponding to the category of danger illustrated by a symbol must appear on the label;

(*c*) in the case of dangers for the environment:

- the R-phrase(*s*) corresponding to the classification category 'dangerous for the environment' must appear on the label.

7.4.3. For preparations, R-phrases will be selected according to the following criteria and priorities:

(*a*) in the case of dangers which give rise to health effects:

[71] This Annex corresponds to Schedule 3.

(i) R-phrases which correspond to the category of danger illustrated by a symbol. In certain cases the R-phrases must be adopted according to the tables of Annex II, Part B of Directive 1999/45/EC. More specifically, the R-phrases of the constituent(*s*) which are responsible for the assignment of the preparation to a danger category must appear on the label.

(ii) R-phrases which correspond to other categories of danger which have been attributed to the constituents but which are not illustrated by a symbol by virtue of Article 10.2.4. of Directive 1999/45/EC;

(*b*) in the case of dangers arising from physicochemical properties:

the criteria described under 7.4.3 (*a*) are applicable, except that the risk phrases 'extremely flammable' or 'highly flammable' need not be indicated where they repeat the wording of the indication of danger used with a symbol.

(*c*) in the case of dangers for the environment

(i) the R-phrase(*s*) corresponding to the classification category 'dangerous for the environment' must appear on the label;

(ii) where the R-phrase R50 has been assigned in addition to a combined R-phrase R51/53 or R52/53 or to the R-phrase 53 alone, the combined R-phrase R50/53 shall be used.

As a general rule, for preparations a maximum of six R-phrases shall suffice to describe the risk; for this purpose the combined phrases listed in Annex III shall be regarded as single phrases. However, if the preparation falls within more than one danger category, those standard phrases shall cover all the principal hazards associated with the preparation. In some cases, more than six R-phrases may be necessary.

7.5. **Safety phrases**

The wording of S-phrases shall comply with that laid down in Annex IV[72].3e

The combined S-phrases in Annex IV shall be used where applicable.

[72] This Annex corresponds to Schedule 4.

7.5.1. For substances appearing in Annex I, the S-phrases shall be those shown in the Annex. Where no S-phrases are shown, the manufacturer/importer may include any appropriate S-phrase(*s*). For substances not in Annex I and for preparations, the manufacturer shall include S-phrases in accordance with the criteria given in Chapter 6 of this Annex.

7.5.2. Choice of safety phrases

The final choice of safety phrases must have regard to the risk phrases indicated on the label and to the intended use of the substance or preparation:

- as a general rule, a maximum of six S-phrases shall suffice to formulate the most appropriate safety advice; for this purpose the combined phrases listed in Annex IV shall be regarded as single phrases,

- in the case of S-phrases concerning disposal, one S-phrase shall be used, unless it is clear that disposal of the material and its container does not present a danger for human health or the environment. In particular, advice on safe disposal is important for substances and preparations sold to the general public,

- some R-phrases become superfluous if a careful selection is made of S-phrases and vice versa; S-phrases which obviously correspond to R phrases will appear on the label only if it is intended to emphasise a specific warning,

- particular attention must be given, in the choice of safety phrases, to the foreseen conditions of use of certain substances and preparations, e.g. spraying or other aerosol effects. Phrases should be chosen with the intended use in view,

- the safety phrases S1, S2 and S45 are obligatory for all very toxic, toxic and corrosive substances and preparations sold to the general public,

- the safety phrases S2 and S46 are obligatory for all other dangerous substances and preparations (except those only classified as dangerous for the environment) sold to the general public.

Where the phrases selected according to the strict criteria in 6.2 result in redundancy or ambiguity or are clearly unnecessary given the specific product/package then some phrases may be deleted.

7.6. **The EC number**

If a substance named on the label is listed in the European Inventory of Existing Commercial Chemical Substances (Einecs) or in the European List of Notified Substances (ELINCS), the Einecs or ELINCS number of the substances shall be shown on the Label. This requirement does not apply to preparations.

7.7. **Dimensions of the label for preparations**

The dimensions of the label shall be as follows:

Capacity of the package	*Dimensions (in millimetres)*
- not exceeding 3 litres:	if possible, at least 52 x 74
- greater than 3 litres but not exceeding 50 litres:	at least 74 x 105
- greater than 50 litres but not exceeding 500 litres:	at least 105 x 148
- greater than 500 litres:	at least 148 x 210

Each symbol shall cover at least one-tenth of the surface area of the label but shall not be less than 1cm^2. The label shall be firmly affixed to one or more surfaces of the packaging immediately containing the preparation.

The information required on the label shall stand out clearly from its background and shall be of such size and spacing as to be easily read.

8. **SPECIAL CASES: SUBSTANCES**

8.1. **Mobile gas cylinders**

For mobile gas cylinders the requirements concerning labelling are considered to be satisfied when they are in agreement with Article 23 or Article 24(6)b[73] of Directive 67/548/EEC

However, by way of derogation from Article 24(1) and (2), one of the following alternatives can be used for gas cylinders with a water capacity of less than or equal to 150 litres:

[73] This Article corresponds to Regulation 22(2)(b).

the format and dimensions of the label can follow the prescriptions of the ISO Standard ISO/DP 7225 (1994 edition) relating to 'Gas cylinders - Precautionary labels',

the information specified in Article 23(2) may be provided on a durable information disc or label held captive on the cylinder.

8.2. **Gas containers intended for propane, butane or liquefied petroleum gas (LPG)**

These substances are classified in Annex I. Although classified in accordance with Article 2, they do not present a danger to human health when they are placed on the market in closed refillable cylinders or in non-refillable cartridges within the scope of EN 417 as fuel gases which are only released for combustion (EN 417, September 1992 edition, relating to 'Non-refillable metallic gas cartridges for liquefied petroleum gases, with or without a valve, for use with portable appliances; construction, inspection, testing and marking').

These cylinders or cartridges must be labelled with the appropriate symbol and the R- and S-phrases concerning flammability. No information concerning the effects on human health is required on the label. However, the information concerning effects on human health which should have appeared on the label shall be transmitted to the professional user by the person responsible for placing the substance on the market. For the consumer, sufficient information shall be transmitted to enable them to take all necessary measures for health and safety as foreseen in Article 1(3) of Directive 91/155/EEC, as modified by Directive 93/112/EEC and Directive 2001/58/EC.

8.3. **Metals in massive form**

These substances are classified in Annex I or shall be classified in accordance with Article 6. However, some of these substances, although classified in accordance with Article 2 do not present a danger to human health by inhalation, ingestion or contact with skin or to the aquatic environment in the form in which they are placed on the market. Such substances do not require a label according to Article 23. However, all the information which should have appeared on the label shall be transmitted to the user by the person responsible for placing the metal on the market, in a format foreseen in Article 27.

8.4. **Substances classified with R65**

Substances classified as harmful on the basis of an aspiration hazard need not be labelled as harmful with R65 when placed on the market in aerosol containers or in containers fitted with a sealed spray attachment.

9. SPECIAL CASES: PREPARATIONS

9.1. Gaseous preparations (gas mixtures)

For gaseous preparations, consideration must be given to:

- the evaluation of the physicochemical properties,
- the evaluation of health hazards,
- the evaluation of the environmental hazards.

9.1.1. Evaluation of physicochemical properties

9.1.1.1. *Flammability*

The flammable properties of these preparations are determined in accordance with Article 5 of Directive 1999/45/EC according to the methods specified in Part A of the Annex to Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation.

These preparations will be classified according to the results of the tests carried out and with respect to the criteria of Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation and to the criteria of the labelling guide.

However, by derogation, in the case where gaseous preparations are produced to order in small amounts, the flammability of these gaseous mixtures can be evaluated by the following calculation method:

the expression of the gaseous mixture

$A_1F_1 + ... + A_iF_i + ... A_nF_n + B_1I_1 + ... + B_iI_i + ... B_pI_p$

where: A_i and B_i are the molar fractions

F_i flammable gas

I_i inert gas

n number of flammable gases

p number of inert gases

can be transformed in a form where all the Ii (inert gases) are expressed by a nitrogen equivalent using a coefficient Ki and where the equivalent content of inflammable gas A'i is expressed as follows:

$A'_i = A_i \times (100 / (A_i + K_i B_i))$

By using the value of the maximum content of flammable gas which, in a mixture with nitrogen, gives a composition which is not flammable in air (Tci), the following expression can be obtained:

$\Sigma_i A'_i / Tci \leqslant 1$

The gas mixture is flammable if the value of the above expression is greater than one. The preparation is classified extremely flammable and, the phrase R12 is assigned.

Coefficients of equivalency (Ki)

The values of the coefficients of equivalency Ki, between the inert gases and nitrogen and the values of the maximum contents of flammable gas (Tci) may be found in tables 1 and 2 of the ISO Standard ISO 10156 edition 15. 12. 1990 (new: 1996 edition) relating to 'Gases and gas mixtures — Determination of fire potential and oxidising ability for the selection of cylinder valve outlets'.

Maximum content of flammable gas (Tci)

The value of the maximum content of flammable gas (Tci) may be found in table 2 of the ISO Standard ISO 10156 edition 15. 12. 1990 (new: 1996 edition) relating to 'Gases and gas mixtures — Determination of fire potential and oxidising ability for the selection of cylinder valve outlets'.

When a Tci value for a flammable gas does not appear in the above standard, the corresponding lower explosivity limit (LEL) will be used. If no LEL value exists, the value of Tci will be set at 1% by volume.

Remarks

- The expression above can be used to allow an appropriate labelling of gaseous preparations, however, it should not be regarded as a method for replacing experimentation for the determination of technical safety parameters.

- Furthermore, this expression gives no information as to whether a mixture containing oxidising gases can be prepared safely. When estimating flammability these oxidising gases are not taken into account.

- The expression above will give reliable results only if the flammable gases do not influence each other as far as their

flammability is concerned. This has to be considered, e.g. with halogenated hydrocarbons.

9.1.1.2. *Oxidising properties*

Given the fact that Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation does not contain a method to determine the oxidising properties of gaseous mixtures, the evaluation of these properties must be realised according to the following estimation method.

The principle of the method is comparison of the oxidising potential of gases in a mixture with that of the oxidising potential of oxygen in air. The concentrations of gases in the mixture are expressed in % vol.

It is considered that the gas mixture is as oxidant as or more oxidant than air, if the following condition is verified:

$\Sigma_i \, x_i C_i \geqslant 21$

where: x_i is the concentration of gas i in % vol,

C_i is the coefficient of oxygen equivalency.

In this case, the preparation is classified as oxidising and the phrase R8 will be assigned.

Coefficients of equivalency between oxidising gases and oxygen

The coefficients used in the calculation to determine the oxidising capacity of certain gases in a mixture with respect to the oxidising capacity of oxygen in air, listed under 5.2. in the ISO Standard ISO 10156 edition 15. 12. 1990 (new: 1996 edition) relating to 'Gases and gas mixtures - Determination of fire potential and oxidising ability for the selection of cylinder valve outlets', are the following.

O_2	1
N_2O	0.6

When no value for the Ci coefficient exists for a gas in the cited standard a value of 40 is attributed to this coefficient.

9.1.2. Labelling

For mobile gas containers the requirements concerning labelling are considered to be satisfied when they are in agreement with Article 11. 6.(*b*) of Directive 1999/45/EC.

However, by way of derogation from Articles 11. 1. and 11. 2., for gas containers with a water capacity of less than or equal to 150 litres, the format and dimensions of the label can follow the prescriptions of the ISO Standard 7225 (1994 edition) relating to 'Gas cylinders - Precautionary labels'. In this case, the label can bear the generic name or industrial/commercial name of the preparation provided that the dangerous component substances of the preparation are shown on the body of the gas cylinder in a clear and indelible way.

The information specified in Article 10 may be provided on a durable information disc or label held captive on the containers.

9.2. Gas containers intended for preparations containing stenched propane, butane or liquefied petroleum gas (LPG)

Propane, butane and liquefied petroleum gas are classified in Annex I. Although preparations containing these substances are classified in accordance with Articles 5, 6 and 7 of Directive 1999/45/EC, they do not present a danger to human health when they are placed on the market in closed refillable cylinders or non-refillable cartridges within the scope of EN 417 as fuel gases which are only released for combustion (EN 417, September 1992 edition, relating to 'Non-refillable metallic gas cartridges for liquefied petroleum gases, with or without a valve, for use with portable appliances; construction, inspection, testing and marking').

These cylinders and cartridges must be labelled with the appropriate symbol and the R- and S-phrases concerning flammability. No information concerning the effects on human health is required on the label. However, the information concerning effects on human health which should have appeared on the label shall be transmitted to the professional user by the person responsible for placing the substance on the market in the format foreseen in Article 14 of Directive 1999/45/EC. For the consumer, sufficient information shall be transmitted to enable them to take all necessary measures for health and safety as foreseen in Article 1(3) of Directive 91/155/EEC.

9.3. Alloys, preparations containing polymers, preparations containing elastomers

These preparations shall be classified according to the requirements of Articles 5, 6 and 7 and labelled according to the requirements of Article 10 of Directive 1999/45/EC.

However some of these preparations although classified in accordance with Articles 6 and 7 do not present a danger to

human health by inhalation, ingestion or contact with the skin or to the aquatic environment in the form in which they are placed on the market. Such preparations do not require a label according to Article 10 or according to Annex V B. 9. However, all the information which would have appeared on the label shall be transmitted to the professional user by means of an information system in a format foreseen in Article 14 of the above-mentioned Directive.

9.4. **Preparations classified with R65**

Preparations classified as harmful on the basis of an aspiration hazard need not be labelled as harmful with R65 when placed on the market in aerosol containers or in containers fitted with a sealed spray attachment.

9.5. **Organic peroxides**

Organic peroxides combine the properties of an oxidiser and a combustible substance in one molecule: when an organic peroxide decomposes, the oxidising part of the molecule reacts exothermically with the combustible (oxidisable) part. For the oxidising properties the existing methods in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation cannot be applied to the organic peroxides.

The following calculation method based on the presence of active oxygen must be used.

The available oxygen content (%) of an organic peroxide preparation is given by the formula:

$16 \times \Sigma (n_i \times c_i/m_i)$

where:

n_i = number of peroxygen groups per molecule of organic peroxide i,

c_i = concentration (mass %) of organic peroxide i,

m_i = molecular mass of organic peroxide i.

9.6. **Additional labelling requirements for certain preparations**

For certain preparations there are additional labelling requirements set out in Article 10.1.2. and Annex V of Directive 1999/45/EC and Article 20 of Directive 98/8/EC.

COMMISSION STATEMENT

With regard to Section 4.1.5. and in particular to the last paragraph of Section 4.1.5., the Commission states that, should it envisage making use of the procedure of Article 28 of Directive 67/548/EEC, it is prepared to consult in advance appropriate experts designated by Members States and having special qualifications with respect to either carcinogenicity, mutagenicity or reproductive toxicity.

This consultation will take place in the framework of the normal consultation procedure with national experts and/or in the framework of existing committees. The same will be the case when substances already included in Annex I must be reclassified in respect of their carcinogenic, mutagenic effects, or effects toxic to reproduction.".

L.S.

GIVEN under my Official Seal,
15 July 2008

MARY COUGHLAN,
Minister for Enterprise, Trade and Employment.

EXPLANATORY NOTE

(This note is not part of the Instrument and does not purport to be a legal interpretation).

These Regulations amend the European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) Regulations 2003 (S.I. No. 116 of 2003) as last previously amended by the European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) (Amendment) Regulations 2006 (S.I. No. 25 of 2006).

The Regulations transpose Directive 2006/121/EC of the European Parliament and of the Council of 18 December 2006 amending Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances in order to adapt it to Regulation (EC) No. 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and establishing a European Chemicals Agency.

The Regulations, inter alia, replace Regulations 5, 6, and 7 (relating to Competent Authority, Placing on the Market and Testing and assessment of properties of substances, respectively) and revoke Regulations 10 to 18, 24, 25 and 27 of and Schedules 6, 8 and 9 to the European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) Regulations 2003 relating to Full Notification, Reduced Notification for substances placed on the market in quantities of less than one tonne per annum, Substances Notified at least 10 years previously, Notification of Polymers, Pre-marketing Notification Period, Exemptions from the notification requirements, Follow up Information, Re-notification of the same substance and avoidance of duplicate testing in vertebrate animals, Confidentiality of data, Safety Data Sheet, Supply of Substances, Fees Payable by Notifier, Annex VIIA, Annex VIIB, Annex VIIC, Annex VIID and Annex VIII: Information required for the Technical dossier, Obligatory Headings for Safety Data Sheets and Fees Payable by Notifier, respectively. The matters covered by the revoked provisions, (other than Regulations 25 and 27 and Schedules 6 and 9 which are consequential amendments) are now provided for directly in the REACH Regulation (EC) No. 1907/2006.

The definitions of "Annex V", "Annex VII.A", "Annex VII.B", "Annex VII.C", "Annex VII.D". "Annex VIII", "notification", "polymer", "process-orientated research and development" and "scientific research and development" are deleted from the 2003 Regulations.

References in the 2003 Regulations to Annexes VII A, VII B, VII C, VII D and VIII of Council Directive 67/548/EEC shall be construed as references to the corresponding Annexes VI, VII, VIII, IX, X and XI of the REACH Regulation.

Schedule 5 to the 2003 Regulations (Annex VI of Directive 67/548/EEC as amended) is replaced in full by the provisions set out in the Schedule to these Regulations for ease of reference. The relevant changes incorporated in the

latest text of Schedule 5 are the substitution, in accordance with Article 13(2) of Regulation (EC) No. 1907/2006 and Commission Regulation (EC) No. 440/2008, of—

"(*a*) the words "Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No. 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)" for "Annex V" and "Annex V to this Directive" in each place where they occur;

(*b*) in section 1.6.1, for point (*a*) the following:

"(*a*) as regards substances for which information specified in Annexes VI, VII and VIII of Regulation (EC) No. 1907/2006 is required, most of the necessary data for classification and labelling appear in the base set. This classification and labelling must be reviewed, if necessary, when further information is available (Annexes IX and X of Regulation (EC) No. 1907/2006):";

(*c*) in section 5.1, for the second paragraph the following:

> "The criteria set out below follow directly from the test methods set out in Commission Regulation (EC) No. 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No. 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) in so far as they are mentioned. The test methods required for the base set referred to in Annexes VII and VIII of Regulation (EC) No. 1907/2006 are limited and the information derived from them may be insufficient for an appropriate classification. Classification may require additional data derived from Annexes IX or X of Regulation (EC) No. 1907/2006 or other equivalent studies. Furthermore, classified substances may be subject to review in the light of other new data."

and

(*d*) in section 5.2.1.2 for the second sentence in the second paragraph the following:

> "Such additional scientific evidence should normally be based on the studies required by Annex IX of Regulation (EC) No. 1907/2006, or studies of equivalent value and could include,".

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