APPENDIX 3

ANNEX V

(This Annex replaces the title and Part II of Annex VI to Council Directive 67/548/EEC, as last amended by Directive 79/831/EEC)

ANNEX VI

General classification and labelling requirements for dangerous substances and preparations

PART I

Save where otherwise provided in the separate Directives on dangerous preparations, the substances and preparations shall be classified as very toxic, toxic or harmful according to the following criteria:

(a) Classification as very toxic, toxic or harmful shall be effected by determining the acute toxicity of the commercial substance or preparation in animals, expressed in LD_{50} or LC_{50} values with the following parameters being taken as reference values:

Category	LD_{50} absorbed orally in rat (mg/kg)	LD_{50} percutaneous absorption in rat or rabbit (mg/kg)	LC_{50} absorbed by inhalation in rat (mg/litre per 4 hours)
Very toxic	< 25	< 50	< 0,5
Toxic	25 – 200	50 – 400	0,5 – 2
Harmful	200 – 2 000	400 – 2 000	2 – 20

(b) If facts show that for the purposes of classification it is inadvisable to use the LD_{50} or LC_{50} values as a principal basis because the substances or preparations produce other effects, the substances or preparations shall be classified according to the magnitude of these effects.

PART II

Classification and labelling of dangerous substances and preparations; criteria for the choice of phrases indicating special risks (R-phrases) and safety advice (S-phrases)

CONTENTS

1. GENERAL INTRODUCTION

1.1. The object of classification is to identify all the toxicological, physico-chemical and ecotoxicological properties of substances and toxicological and physico-chemical properties of 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 3 (3) of Directive 67/548/EEC and in Article 3 (5) of Directive 88/379/EEC 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 requirement of this Directive and of Directive 88/379/EEC 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.

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 recognized chemical nomenclature, the preferred name being the one used in the European inventory of existing commercial chemical substances (Einecs), and the name and address of the person established in the Community who is responsible for placing the substance on the market.

In the case of preparations, the information is completed by the indication of the designation or the trade name of the preparation, the indication of the chemical name of the substances present in the preparation in accordance with Article 7 (1) (c) of Directive 88/379/EEC and the indication of the name, address and telephone number of the person established in the Community who is responsible for placing the preparation on the market.

1.5. With respect to substances referred to in the second subparagraph of Article 5 (2) of Directive 67/548/EEC, the labelling applied by the manufacturer or his representative remains valid until the substance is listed in Annex I or until a decision not to list it has been taken in accordance with the procedure laid down in Article 21.

1.6. For substances, the data required for classifiction and labelling may be obtained:

(a) as regards substances for which the information specified in Annex VII 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 (Annex VIII);

(b) as regards other substances (e.g. those referred to in Article 5 (2) of Directive 67/548/EEC), 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.

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

(a) if it concerns physico-chemical data, by the application of the methods specified in Annex V to Directive 67/548/EEC. For gaseous preparations a calculation method may be used for flammable and oxidizing properties (see Chapter 9);

(b) — if it concerns data on health effects, by the application of the methods specified in Annex V to the Directive and/or by the application of the conventional method referred to in Article 3 (5) (a) to (i) of Directive 88/379/EEC,

— however if it concerns the evaluation of the carcinogenic, mutagenic and teratogenic properties, by the application of the conventional method referred to in Article 3 (5) (j) to (q) of Directive 88/379/EEC.

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.

1.7. **Application of the guide criteria**

Several possibilities may occur according to whether it concerns substances or preparations. Classification must cover the toxicological and physico-chemical properties of substances and preparations and in addition, the ecotoxicological properties of substances. The object of choosing risk phrases is to ensure that the specific nature of the potential dangers identified in classification are expressed on the label. For this purpose it is necessary to consider the criteria given for the choice of symbol(s) and risk phrases in 2.2.1 to 2.2.6, 3.2.1 to 3.2.7 and Chapters 4 and 5 for substances only. For example, classification under 3.2.1 does not imply that the sections such as 3.2.2 or 3.2.4 can be ignored.

The criteria are applicable to gaseous substances and preparations but only in so far as they may be subject to the packaging and labelling provisions of this Directive or the separate Directive on preparations.

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 flammability criteria set out in 1.8 and 2.2 (c) of the Annex to Directive 75/324/EEC.

1.7.1. **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 Annex V. In other cases, the available data must be evaluated by comparing the test methods employed with those indicated in Annex V and the rules specified in this Annex for determining the appropriate classification and labelling criteria.

Classification of substances containing impurities or additives which are classified as carcinogens

A substance containing an impurity or an additive which is classified as a carcinogen and labelled with R 45 must itself be classified as a carcinogen and labelled with R 45 if the concentration of the carcinogenic impurity or additive is equal to or exceeds:

— either the concentration of the impurity or the additive specified in Annex I, or

— the concentration of 0,1 % where the impurity or the additive appears in Annex I without a concentration limit. (However in the case of asbestos this general rule does not apply until a concentration limit has been fixed in Annex I. Substances which have asbestos impurities must be classified and labelled according to the principles in Article 5 (2)), or

— the concentration of 0,1 % where the impurity or the additive does not appear in Annex I.

NB: if a substance containing an impurity or additive which is classified as a carcinogen is used as part of a preparation, the preparation shall be classified as a carcinogen and labelled with R 45 only when the concentration of the carcinogenic impurity or additive equals or exceeds the limits shown above as a % weight of the impurity or additive in the preparation.

If the information regarding the carcinogenic impurity or additive on the label of the substance is insufficient to enable the manufacturer of a preparation to carry out the classification and labelling correctly, the person established within the Community responsible for placing the substance on the market, whether it be the manufacturer, the importer or the distributor, shall supply, upon justified request and if available, appropriate information about the impurity or additive responsible for the carcinogenic classification of the substance to enable the classification and labelling of the preparation.

1.7.2. **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 Annex V with the exception of the criteria of Chapter 4 for which only the conventional method is applicable. In other cases, the available data must be evaluated by comparing the test methods employed with those indicated in Annex V and the rules specified in this Annex for determining the appropriate classification and labelling criteria.

If the health hazards are assessed by applying the conventional method referred to in Article 3 (5) of Directive 88/379/EEC, the individual concentration limits to be used are those set out, either:

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

— in Annex I to Directive 88/379/EEC where the substance or substances do not appear in Annex I to the Directive or appear in it without concentration limits.

In the case of preparations containing mixtures of gases, classification with respect to the health effects will be established by the calculation method on the basis of the individual concentration limits from Annex I to the Directive or, when these limits are not in Annex I, on the basis of the criteria of Annex I to Directive 88/379/EEC, as amended by Directive 90/462/EEC.

Preparations used as constituents of another preparation

The labelling of such preparations must be in conformity with the provisions of Article 7 according to the conditions foreseen in Article 3 of Directive 88/379/EEC. However, in certain cases, the information on the label of the preparation 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 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 88/379/EEC.

2. CLASSIFICATION ON THE BASIS OF PHYSICO-CHEMICAL PROPERTIES

2.1. Introduction

The test methods relating to explosive, oxidizing and flammable properties included in Annex V to this Directive serve to give specific meaning to the general definitions given in Article 2 (2) (a) to (c). Criteria follow directly from the test methods in Annex V as far as they are mentioned.

If adequate information is available to demonstrate in practice that the physico-chemical properties of substances and preparations (apart from organic peroxides) are different from those revealed by the test methods given in Annex V, then such substances and preparations should be classified according to the hazard they present, if any, to those handling the substances and preparations or to other persons.

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 3 (2) of Directive 88/379/EEC need to be taken into consideration.

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 Annex V 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:

R 2 Risk of explosion by shock, friction, fire or other sources of ignition

— Substances and preparations including certain organic peroxides but excepting those set out below.

R 3 Extreme risk of explosion by shock, friction, fire or other sources of ignition

— Substances and preparations which are particularly sensitive such as picric acid salts, PETN and certain undiluted organic peroxides such as dibenzoyl peroxide.

2.2.2. Oxidizing

Substances and preparations shall be classified as oxidizing and assigned the symbol 'O' and the indication of danger 'oxidizing' in accordance with the results of the tests given in Annex V. One risk phrase is obligatory, it is to be specified on the basis of the test results but subject to the following:

R 11 Highly flammable

— Organic peroxides which have flammable properties even when not in contact with other combustible material.

R 8 Contact with combustible material may cause fire

— Other oxidizing substances and preparations which may cause fire or enhance the risk of fire when in contact with combustible material.

R 9 Explosive when mixed with combustible material

— Other substances and preparations which become explosive when mixed with combustible materials, e.g. certain chlorates.

2.2.2.1. *Remarks concerning peroxides*

Organic peroxides are classified as dangerous on the basis of their structure (e.g. R-O-O-H; R_1-O-O-R_2). In general terms, organic peroxides shall be classified as oxidizing, and labelled as under 2.2.2, unless:

— tests carried out in accordance with the methods given in Annex V show the organic peroxide, in the form in which it is placed on the market, to have explosive properties, as under 2.2.1, or

— the organic peroxide is so diluted or phlegmatized to the point where it is no longer explosive, oxidizing or flammable.

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 Annex V. The risk phrase shall be assigned in accordance with the following criteria:

R 12 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.

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

R 17 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.

R 11 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.

R 12 Extremely flammable

— Gaseous substances and preparations which are flammable in air at normal pressure.

R 13 Extremely flammable liquefied gas

— Gaseous substances and preparations which are flammable in air at normal pressure when put on the market in liquefied form.

R 15 Contact with water liberates highly flammable gases

— Substances and preparations which, in contact with water or damp air, evolve highly flammable gases in dangerous quantities, at a minimum rate of one litre per kilogram per hour.

2.2.5. Flammable

Substances and preparations shall be classified as flammable in accordance with the results of the tests given in Annex V. The risk phrase shall be assigned in accordance with the criteria mentioned below.

R 10 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 physico-chemical properties

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

R 1 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.

R 4 Forms very sensitive explosive metallic compounds

For substances and preparations which may form sensitive explosive metallic derivatives, e.g. picric acid, styphnic acid.

R 5 Heating may cause an explosion

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

R 6 Explosive with or without contact with air

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

R 7 May cause fire

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

R 14 Reacts violently with water

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

R 16 Explosive when mixed with oxidizing substances

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

R 18 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.

R 19 May form explosive peroxides

For substances and preparations which may form explosive peroxides during storage, e.g. diethyl ether, 1,4-dioxan.

R 30 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.

R 44 Risk of explosion if heated under confinement

For substances and preparations not in themselves classified as explosive in accordance with 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 3.2.7.

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 these substances and preparations, whether resulting from a single instance of exposure or repeated or prolonged exposure.

If adequate evidence is available to demonstrate in practice that the toxic effect of substances and preparations on man is, or is likely to be different from that suggested by the experimental results obtained in animal tests or by the application of the conventional method referred to in Article 3 (5) of Directive 88/379/EEC, then such substances and preparations should be classified according to their toxicity in man. However, tests on man should be discouraged and should not normally be used to negate positive animal data.

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 parameters indicated in Part I A of Annex VI and under 3.2.1 to 3.2.3 are to be used;

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

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

(d) for sensitizing effects, the criteria under 3.2.3 to 3.2.6 are to be used;

(e) for specific effects on health (carcinogenic, mutagenic and teratogenic effects), 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 the conventional method referred to in Article 3 (5) of Directive 88/379/EEC 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 I to Directive 88/379/EEC where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

(b) or when experimental data are available, according to the criteria described under 3.1.2. excluding the carcinogenic, mutagenic and teratogenic properties referred to under 3.1.2 (e) which must be evaluated by the conventional method referred to in Article 3 (5 (j) to (q) of Directive 88/379/EEC.

Whichever method is used for the evaluation of the danger of a preparation, all the dangerous effects on health as defined in Annex I to Directive 88/379/EEC 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.

3.2. **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 the indication of danger 'very toxic' in accordance with the criteria given in Part I of Annex VI, as specified below.

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

R 28 Very toxic if swallowed

— Acute toxicity results

LD_{50} oral, rat: < 25 mg/kg

R 27 Very toxic in contact with skin

— Acute toxicity results

LD_{50} dermal, rat or rabbit: < 50 mg/kg

R 26 Very toxic by inhalation

— Acute toxicity results

LC_{50} inhalation, rat: < 0,5 mg/litre per 4 hours

R 39 (*) 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 abovementioned dose range (see also 3.1.2 and 3.1.3).

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 given in Part I of Annex VI, as specified below. Risk phrases shall be assigned in accordance with the following criteria.

R 25 Toxic if swallowed

— Acute toxicity results

LD_{50} oral, rat: 25 < LD_{50} < 200 mg/kg

R 24 Toxic in contact with skin

— Acute toxicity results

LD_{50} dermal, rat or rabbit: 50 < LD_{50} < 400 mg/kg

R 23 Toxic by inhalation

— Acute toxicity results

LC_{50} inhalation, rat: 0,5 < LC_{50} < 2 mg/litre per 4 hours

R 39 (*) 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 abovementioned dose range (see also 3.1.2 and 3.1.3).

R 48 (**) 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 are classified at least as toxic when these effects are observed at levels of one order of magnitude lower (i.e. ten-fold) than those set out for R 48 in 3.2.3.

(*) In order to indicate the route of administration/exposure the following combinations should be used: R 39/26, R 39/27, R 39/28, R 39/26/27, R 39/26/28, R 39/27/28, R 39/26/27/28.

(**) In order to indicate the route of administration/exposure one of the following combinations shall be used: R 39/23, R 39/24, R 39/25, R 39/23/24, R 39/23/25, R 39/24/25, R 39/23/24/25.

(**) In order to indicate route of administration/exposure one of the following combinations shall be used: R 48/23, R 48/24, R 48/25, R 48/23/24, R 48/23/25, R 48/24/25, R 48/23/24/25.

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 given in Part I of Annex VI, as specified below. Risk phrases shall be assigned in accordance with the following criteria:

R 22 Harmful if swallowed

— Acute toxicity results

LD_{50} oral, rat: 200 < LD_{50} < 2 000 mg/kg

R 21 Harmful in contact with skin

— Acute toxicity results

LD_{50} dermal, rat or rabbit: 400 < LD_{50} < 2 000 mg/kg

R 20 Harmful by inhalation

— Acute toxicity results

LC_{50} inhalation, rat: 2 < LC_{50} < 20 mg/litre per 4 hours

R 40 (*) 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 abovementioned dose range (see also 3.1.2 and 3.1.3).

R 42 May cause sensitization by inhalation

— If practical evidence is available which shows the substances and preparations to be capable of inducing a sensitization reaction in humans by inhalation, at a greater frequency than would be expected from the response of a general population.

R 48 (*) 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 are classified at least as harmful when these effects are observed at levels of the order of:

— oral, rat < 50 mg/kg (bodyweight) per day,

— dermal, rat or rabbit < 100 mg/kg (bodyweight) per day,

— inhalation, rat < 0,25 mg/litre per 6 hours per 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.

3.2.4. **Comments regarding the use of R 48**

Use of this risk phrase refers to the specific range of biological effects within the terms described below. It should be noted that the terms are not identical to the definitions of harmful and toxic in Article 2 (2) (g) and (h) of Directive 67/548/EEC. 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 generalized 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:

(*) In order to indicate route of administration/exposure one of the following combinations shall be used: R 40/20, R 40/21, R 40/22, R 40/20/21, R 40/20/22, R 40/21/22, R 40/20/21/22.

(*) In order to indicate route of administration/exposure one of the following combinations shall be used: R 48/20, R 48/21, R 48/22, R 48/20/21, R 48/20/22, R 48/21/22, R 48/20/21/22.

1. Evidence indicating that R 48 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).

(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 R 48 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 R 48. 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 R 48, 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 whihc are more appropriately classified with R 38 'irritating to skin';

(e) where a species-specific mechanism of toxicity (e.g. specific metabolic pathways) has been demonstrated.

3.2.5. Corrosive

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 Annex V or during an equivalent method or if the results can be predicted, for example from strongly acid or alkaline reactions. Classification can be based on the results of validated *in vitro* tests.

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

R 35 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.

R 34 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.

3.2.6. Irritant

Non-corrosive 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.

1. Inflammation of the skin

Inflammation of the skin which persists for at least 24 hours after an exposure period of up to four hours and corresponds to the following values determined on the rabbit according to the cutaneous irritation test method cited in Annex V:

— the mean value of the scores for either erythema and eschar formation or oedema formation, calculated over all the animals tested, is two or more,

— or, in the case where the Annex V test has been completed using three animals, either erythema and eschar formation or oedema formation equivalent to a mean value of two 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 hours) for an effect should be used in calculating the respective mean values.

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

R 38 Irritating to skin

— If, when applied to healthy intact animal skin for up to four hours, significant inflammation is caused and which persists for 24 hours or more after the end of the exposure period.

Inflammation is significant if the mean value of the scores is two or more for either erythema and eschar formation or oedema formation. The same shall be the case where the test has been completed using three animals if the score for either erythema and eschar formation or oedema formation observed in two or more animals is equivalent to the value of two or more.

2. Ocular lesion

Ocular lesions which occur within 72 hours after exposure and which persist for at least 24 hours and correspond to the following values determined on the rabbit according to the eye irritation test method cited in Annex V:

— the mean value of the scores for each type of lesion, calculated over all the animals tested, is one of the following:

  — cornea opacitytwo or more,

  — iris lesion one or more,

  — redness of conjunctivae 2,5 or more,

  — oedema of conjunctivae (chemosis) two or more, or

— in the case where the Annex V test has been completed using three animals, either cornea opacity, iris lesion, redness of conjunctivae or oedema of conjunctivae (chemosis) equivalent to a mean value such as is quoted above, but 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, 72 hours) and for an effect should be used in calculating the respective mean values.

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

R 36 Irritating to eyes

— If, when applied to the eye of the animal, significant ocular lesions are caused and which persist for 24 hours or more after instillation of the test material.

Ocular lesions are significant if the means of the scores have any of the 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. The same shall be the case where the test has been completed using three animals if the lesions, on two or more animals, are equivalent to any of the 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 conjunctivae the value should be equal to or greater than 2,5.

R 41 (*) Risk of serious damage to eyes

— If when applied to the eye of the animal severe ocular lesions are caused and which are present 24 hours or more after instillation of the test material.

Ocular lesions are severe if the means of the scores 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.

R 43 May cause sensitization by skin contact

— If practical experience shows the substances and preparations to be capable of inducing a sensitization reaction in a substantial number of persons by skin contact, or on the basis of a positive response in experimental animals.

In the case of the adjuvent type test method for skin sensitization detailed in Annex V 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.

R 37 Irritating to respiratory system

— Substances and preparations which cause serious irritation to the respiratory system, based normally on practical observation.

3.2.7. Other toxicological properties

Additional risk phrases shall be assigned to substances and preparations classified by virtue of 2.2.1 to 3.2.6 above and/or Chapters 4 and 5, in accordance with the following criteria (based on experience obtained during compilation of Annex I):

R 29 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.

R 31 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 S 50 (do not mix with .....(to be specified by the manufacturer)) would be more suitable.

R 32 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 S 50 (do not mix with .....(to be specified by the manufacturer)) would be more suitable.

R 33 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 R 48.

Previously assigned to substances of Annex I and preparations which were likely to cause damage to health by prolonged exposure or which were likely to be retained and then accumulated within the human body. Now to be progressively replaced when appropriate by R 48.

When substances labelled with R 33 are present in preparations, R 33 shall be included in the label at all concentrations where a label is required by the Directive on dangerous preparations.

For other risk phrases see 2.2.6.

(*) The of R 34 or R 35 precludes the use of R 41.

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.

4.1.2. If a manufacturer or his representative has information available which indicates that a substance should be classified and labelled in accordance with the criteria given in 4.2.1, 4.2.2 or 4.2.3, he or his representative shall provisionally label the substance in accordance with these criteria, unless the conclusions reached by the application of the criteria mentioned in 3.2.1 to 3.2.5 indicate the need for a more severe classification.

4.1.3. The manufacturer or his representative shall submit as soon as possible a document summarizing all relevant information to one Member State in which the substance is placed on the market. This summary document should include a bibliography containing all relevant references, including any relevant unpublished data.

4.1.4. Furthermore, a manufacturer or his representative who has new data which are relevant to the classification and labelling of a substance in accordance with the criteria given in 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. In order to obtain as quickly as possible a harmonized classification for the Community by the procedure defined in Article 21 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 teratogenic effects are concerned shall notify the Commission thereof.

4.1.6. The provisional labelling applied by a manufacturer or his representative shall remain valid until the entry into force of a decision on the inclusion or non-inclusion of the substance concerned in Annex I.

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:

T; R 45 may cause cancer

However for 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), the following symbol and specific risk phrase should be used:

T; R 49 may cause cancer by inhalation

Category 3:

Xn; R 40 possible risk of irreversible effects

4.2.1.2. Comments regarding the categorization 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 effects 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 data 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 characterized 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 effets 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:

Category 1:

T; R 46 may cause heritable genetic damage

Category 2:

Xn; R 46 may cause heritable genetic damage

Category 3:

Xn; R 40 possible risk of irreversible effects

4.2.2.3. Comments regarding the categorization 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 standardized 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 recognized 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 (SCE's),
- — 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 SCE's 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. **Teratogenic substances**

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

Category 1

Substances known to be teratogenic to man.

There is sufficient evidence to establish a causal association between human exposure to a substance and subsequent non-heritable birth defects in offspring.

Category 2

Substances which should be regarded as if they are teratogenic to man.

There is sufficient evidence to provide a strong presumption that human exposure to the substance may result in non-heritable birth defects in offspring, generally on the basis of:

— appropriate animal studies,

— other relevant information.

4.2.3.2. The following symbols and specific risk phrases apply:

Category 1

T; R 47 may cause birth defects

Category 2

Xn; R 47 may cause birth defects

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 Article 3 (5) (j) to (q) of Directive 88/379/EEC (the limits of concentration are either in Annex I to this Directive, or in Annex I to Directive 88/379/EEC 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 dangerous for the environment is to alert the user to the hazards these substances present to ecosystems. Although the present criteria refer to aquatic ecosystems it is recognized that certain substances 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 Annex V, in so far as they are mentioned. The test methods required for the 'base set' referred to in Annex VII are limited and the information derived from them may be insufficient for an appropriate classification. Classification may require additional data derived from level 1 (Annex VIII) 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 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. In addition those substances classified according to the criteria set out under 5.2.1.1. and 5.2.2 will be assigned the symbol 'N' and the appropriate indication of danger after the pertinent amendment to Directive 67/548/EEC enters into force.

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

5.2.1. **Aquatic environment**

5.2.1.1. **Substances shall be classified as dangerous for the environment (*) and assigned risk phrases in accordance with the following criteria:**

R 50 Very toxic to aquatic organisms
and
R 53 May cause long-term adverse effects in the aquatic environment

Acute toxicity:	**96 hr LC_{50} (for fish)**	**< 1 mg/litre**
or	**48 hr EC_{50} (for Daphnia)**	**< 1 mg/litre**
or	**72 hr IC_{50} (**) (for algae)**	**< 1 mg/litre**
and	**the substance is not readily degradable (***)**	
or	**the log Pow (log octanol/water partition coefficient) > 3,0 (unless the experimentally determined BCF < 100)**	

R 50 Very toxic to aquatic organisms

Acute toxicity:	**96 hr LC_{50} (for fish)**	**< 1 mg/litre**
or	**48 hr EC_{50} (for Daphnia)**	**< 1 mg/litre**
or	**72 hr IC_{50} (**) (for algae)**	**< 1 mg/litre**

R 51 Toxic to aquatic organisms
and
R 53 May cause long-term adverse effects in the aquatic environment

acute toxicity:	**96 hr LC_{50} (for fish)**	**1 mg/litre**	**< LC_{50}**	**< 10 mg/litre**
or	**48 hr EC_{50} (for Daphnia)**	**1 mg/litre**	**< EC_{50}**	**< 10 mg/litre**
or	**72 hr IC_{50} (**) (for algae)**	**1 mg/litre**	**< IC_{50}**	**< 10 mg/litre**
and	**the substance is not readily degradable (***)**			
or	**the log Pow > 3.0 (unless the experimentally determined BCF < 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**

R 52 Harmful to aquatic organisms
and
R 53 May cause long-term adverse effects in the aquatic environment

acute toxicity:	**96 hr LC_{50} (for fish):**	**10 mg/litre**	**< LC_{50}**	**< 100 mg/litre**
or	**48 hr EC_{50} (for Daphnia):**	**10 mg/litre**	**< EC_{50}**	**< 100 mg/litre**
or	**72 hr IC_{50} (**) (for algae):**	**10 mg/litre**	**< IC_{50}**	**< 100 mg/litre**
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.**			

(*) After the pertinent amendment to Directive 67/548/EEC enters into force, the symbol 'N' and the appropriate indication of danger will be assigned to these substances.

(**) 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 72 h 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 BOD_5 data are available when the ration BOD_5/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.

Such additional scientific evidence should normally be based on the studies required at level 1 (Annex VIII), 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 or greater than 1,0 mg/litre determined in a prolonged toxicity study with fish or Daphnia.

At least one of the following phrases:

R 52 Harmful to aquatic organisms

R 53 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 toxicity, persistence, potential to accumulate and predicted, or observed, environmental fate and behaviour may nevertheless present a danger immediate or long-term and/or delayed, to the structure and/or functioning of aquatic ecosystems. Poorly water soluble substances i.e. substances with a solubility of less than 1 mg/litre will be covered by this criteria if:

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

(b) the log Pow > 3,0 (unless the experimentally determined BCF < 100).

This criterion applies unless there exists additional 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 at level 1 (Annex VIII), 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 a solubility limit determined in a prolonged toxicity study with fish or Daphnia.

5.2.2. Non-aquatic environment

Substances shall be classified as dangerous for the environment (*) in accordance with the criteria set out below.

At least one of the following phrases shall be assigned in accordance with the following criteria:

R 54 Toxic to flora
R 55 Toxic to fauna
R 56 Toxic to soil organisms
R 57 Toxic to bees
R 58 May cause long-term adverse effects in the environment
R 59 Dangerous for the ozone layer

} (**)

Substances 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.

(*) 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 BOD, data are available when the ration BOD_5/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.

(*) After the pertinent amendment to Directive 67/548/EEC enters into force, the symbol 'N' and the appropriate indication of danger will be assigned to these substances.

(**) Detailed criteria, along with other risk phrases will be elaborated later.

6. CHOICE OF SAFETY ADVICE PHRASES

6.1. Safety phrases for substances and preparations

Safety advice phrases (S-phrases) shall be assigned to substances and preparations in accordance with the following general criteria. In addition, for certain preparations, safety advice is listed in Annex II to Directive 88/379/EEC. Whenever the manufacturer is mentioned in Chapter 6 it refers to the person responsible for placing the substance or preparation on the market.

S 1 *Keep locked up*

— Applicability:

— Very toxic and toxic substances and preparations.

— Criteria for use:

— Recommended for very toxic and toxic substances and preparations likely to be used by members of the general public.

S 2 *Keep out of reach of children*

— Applicability:

— All dangerous substances and preparations.

— Criteria for use:

— Obligatory only for all dangerous substances and preparations likely to be used by members of the general public or likely to be used in places to which the general public have access unless there is no reason to fear any danger particularly to children.

S 3 *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 S 47 is used.

— Recommended for other dangerous substances and preparations having a boiling point < 40 °C.

S 4 *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 S 13; 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.

S 5 *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.

S 6 *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 organo-metallic compounds.

S 7 *Keep container tightly closed*

— Applicability:

— Organic peroxides.

— Substances and preparations which can give off very toxic, toxic, harmful, extremely flammable or highly flammable vapours.

— Substances and preparations which in contact with moisture give off highly flammable gases.

— Highly flammable solids.

— Criteria for use:

— Obligatory for organic peroxides in the combination of S 3/7/9.

— Recommended for the other fields of application mentioned above.

S 8 *Keep container dry*

— Applicability:

— Substances and preparations which may react violently with water.

— Substances and preparations which on contact with water liberate highly 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 R 14, R 15 in particular, and R 29.

S 9 *Keep container in a well-ventilated place*

— Applicability:

— Organic peroxides.

— Volatile substances and preparations which may give off very toxic, toxic or harmful vapours.

— Extremely flammable or highly flammable liquids and gases.

— Criteria for use:

— Obligatory for organic peroxides in the combination S 3/7/9.

— 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 gases.

S 12 *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.

S 13 *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 members of the general public.

S 14 *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.

S 15 *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 R 2, R 3 and/or R 5 have already been applied.

S 16 *Keep away from sources of ignition — no smoking*

— Applicability:

— Extremely flammable or highly flammable liquids and gases.

— Criteria for use:

— Recommended for the substances and preparations mentioned above but not assigned if risk phrases R 2, R 3 and/or R 5 have already been applied.

S 17 *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 emphasize R 8 and R 9.

S 18 *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 abovementioned cases when there is risk of damage to the eyes and/or when the substances and preparations are likely to be used by members of the general public.

S 20 *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 members of the general public.

S 21 *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).

S 22 *Do not breathe dust*

— Applicability :

— All solid dangerous substances and preparations.

— Criteria for use :

— Recommended for those substances and preparations mentioned above which are liable to form inhalable dusts, and when it is necessary to draw the attention of the user to inhalation risks not mentioned in the risk phrases which have been ascribed. However, may be used in exceptional cases to emphasize such risk phrases, in particular to emphasize R 42.

S 23 *Do not breathe gas/fumes/vapour/spray* (appropriate wording to be specified by the manufacturer)

— Applicability :

— All liquid or gaseous dangerous substances and preparations.

— Criteria for use :

— 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. However, may be used in exceptional cases to emphasize such risk phrases, in particular to emphasize R 42.

— Recommended for substances and preparations in the form of aerosols which are likely to be used by members of the general public.

S 24 *Avoid contact with skin*

— Applicability :

— All dangerous substances and preparations.

— Criteria for use :

— Recommended when it is necessary to draw the attention of the user to skin contact risks not mentioned in the risk phrases which have to be ascribed. However, may be used to emphasize such risk phrases, in particular to emphasize R 43.

S 25 *Avoid contact with eyes*

— Applicability :

— Corrosive or irritant substances and preparations.

— Criteria for use :

— Normally limited to special cases, i.e. when it is considered essential to emphasize the risk to eyes denoted by use of R 34, R 35, R 36 or R 41. Thus important if these substances and preparations are likely to be used by members of the general public and eye or face protection may not be available.

S 26 *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 R 41 has already been ascribed.

— Recommended for irritant substances to which the risk phrase R 36 has already been ascribed.

S 27 *Take off immediately all contaminated clothing*

— Applicability :

— Organic peroxides.

— Very toxic, toxic or corrosive substances and preparations.

— Criteria for use :

— Obligatory for organic peroxides.

— Recommended for very toxic and toxic substances and preparations which are easily absorbed by the skin and for corrosive substances and preparations unless safety phrase S 36 can be considered sufficient by itself.

S 28 *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 :

— Recommended for the substances and preparations mentioned above, in particular when water is not the most appropriate rinsing fluid.

S 29 *Do not empty into drains*

— Applicability :

— Extremely or highly flammable liquids.

— Criteria for use :

— Recommended for those extremely or highly flammable liquids which are immiscible with water. The intention is to avoid accidents (e.g. fire explosion) and not to emphasize general pollution problems.

S 30 *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 emphasize R 14 or as an alternative to R 14.

S 33 *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 members of the general public.

S 34 *Avoid shock and friction*

— Applicability :

— Explosive substances and preparations.

— Criteria for use :

— Obligatory for and normally limited to explosive organic peroxides.

S 35 *This material and its container must be disposed of in a safe way*

— Applicability:

— Explosive substances and preparations.

— Very toxic and toxic substances and preparations.

— Criteria for use:

— Obligatory for explosive substances and preparations other than organic peroxides.

— Recommended for very toxic and toxic substances and preparations, particularly when such substances and preparations are likely to be used by members of the general public.

S 36 *Wear suitable protective clothing*

— Applicability:

— Very toxic, toxic or harmful substances and preparations.

— Corrosive substances and preparations.

— Criteria for use:

— Recommended for substances and preparations used in industry which are:

— very toxic, toxic or corrosive, and/or

— harmful and easily absorbed by the skin, and/or

— liable to damage health by prolonged exposure.

S 37 *Wear suitable gloves*

— Applicability:

— Very toxic, toxic, harmful or corrosive substances and preparations.

— Organic peroxides.

— Substances and preparations irritating to the skin.

— Criteria for use:

— Recommended for very toxic, toxic and corrosive substances and preparations when S 36 is not used (e.g. viz general public).

— Recommended for organic peroxides as combination S 37/39.

— Recommended for substances and preparations irritating to the skin particularly when R 38 is not shown on the label.

S 38 *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.

S 39 *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:

— Recommended for organic peroxides as the combination S 37/39.

— Recommended for the corrosive substances and preparations mentioned above, in particular when there is a risk of splashing.

— 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.

S 40 *To clean the floor and all objects contaminated by this material usf...* (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.

S 41 *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.

S 42 *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.

S 43 *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 highly flammable gases.

— Recommended for extremely flammable, highly flammable and flammable substances and preparations, particularly when they are immiscible with water.

S 44 *If you feel unwell seek medical advice* (show the label where possible)

— Applicability:

— Toxic substances and preparations.

— Criteria for use:

— Obligatory for the substances and preparations mentioned above when used in industry and not likely to be used by members of the general public.

S 45 *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 substances and preparations.

— Criteria for use:

— Obligatory for the very toxic substances and preparations mentioned above.

— Obligatory for toxic substances and preparations mentioned above when likely to be used by members of the general public.

S 46 *If swallowed, seek medical advice immediately and show this container or label*

— Applicability :

— All dangerous substances and preparations other than those which are toxic or very toxic.

— Criteria for use :

— Obligatory for all dangerous substances and preparations mentioned above which are likely to be used by members of the general public, unless there is no reason to fear any danger from swallowing, particularly by children.

S 47 *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).

S 48 *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.

S 49 *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.

S 50 *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 members of the general public, when it is a better alternative to R 31 or R 32.

— Obligatory with certain peroxides which may give violent reaction with accelerators or promoters.

S 51 *Use only in wellventilated 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 S 38 would not be appropriate. Thus important when such substances and preparations are likely to be used by members of the general public.

S 52 *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 by reason of their volatilization from large treated surfaces in the home or other enclosed places where persons congregate.

S 53 *Avoid exposure — obtain special instructions before use*

— Applicability :

— Carcinogenic, mutagenic and/or teratogenic substances and preparations.

— Criteria for use :

— Obligatory for the abovementioned substances and preparations to which at least one of the following R—phrases have been assigned : R 45, R 46, R 47 or R 49.

6.2. Safety phrases assigned to substances dangerous for the environment

The complexity of the environment and the variety of uses to which chemical substances are put are such that it is not possible to specify precisely the most appropriate safety phrases. Those assigning safety phrases should consider such supplementary information as may be provided with the substances and select phrases from the following :

S 54 *Obtain the consent of pollution control authorities before discharging to wastewater treatment plants*

— Applicability and criteria for use :

— Applies to substances which may affect the functioning of sewage treatment plant processes and sludge disposal.

— Recommended for substances which are very toxic, toxic or harmful to aquatic organisms or which may cause long-term adverse effects in the aquatic environment.

— Recommended when such substances are used in industry.

S 55 *Treat using the best available techniques before discharge into drains or the aquatic environment.*

— Applicability and criteria for use :

— Recommended for substances which are very toxic, toxic or harmful to aquatic organisms or substances which may cause long-term adverse effects for which treatment techniques are available.

— Recommended when such substances are used in industry.

S 56 *Do not discharge into drains or the environment, dispose to an authorised waste collection point*

— Applicability and criteria for use :

— Recommended for substances which are very toxic or toxic to aquatic organisms or which may cause long-term adverse effects in the aquatic environment.

S 57 *Use appropriate containment to avoid environmental contamination*

— Applicability and criteria for use :

— Recommended for substances which are very toxic or toxic to aquatic organisms and particularly for substances which may cause long-term adverse effects in the aquatic or non-aquatic environment.

— Substances toxic to flora, fauna, soil or other organisms.

— Recommended when such substances are used in industry.

S 58 *To be disposed of as hazardous waste*

— Applicability and criteria for use:

— Recommended for substances which are very toxic, toxic or harmful to aquatic organisms or substances which may cause long-term adverse effects in the non-aquatic or aquatic environment.

— Recommended for substances toxic to flora, fauna, bees or other organisms.

S 59 *Refer to manufacturer/supplier for information on recovery/recycling*

— Applicability and criteria for use:

— Obligatory for substances dangerous for the ozone layer.

— Recommended for substances which are toxic to flora, fauna, soil organisms, bees or substances which may cause long-term adverse effects in the environment.

S 60 *This material and/or its container must be disposed of as hazardous waste*

— Applicability and criteria for use:

— This phrase should be used in place of S 58 in cases where contaminated containers require disposal.

— Recommended for substances which are very toxic, toxic or harmful to aquatic organisms or substances which may cause long—term adverse effects in the non—aquatic or aquatic environment.

— Recommended for substances toxic to flora, fauna, bees or other organisms.

7. LABELLING

7.1. When a substance or preparation has been classified the appropriate label is determined with reference to the requirements of Article 16 of Directive 67/548/EEC (79/831/EEC) and Article 7 of Directive 88/379/EEC 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 of a substance or a preparation should be derived from the total number of symbols, risk phrases and safety phrases assigned. It is based on:

(a) the determination of the categories of danger and indications of danger;

(b) the determination and final choice of the phrases indicating particular risks (R-phrases);

(c) the determination and final choice of the phrases indicating safety advice (S-phrases);

(d) the final choice of the name or names which will appear on the label.

7.2. Choice of R-phrases

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

(a) in the case of health effects:

(i) R-phrases corresponding to the category of danger illustrated by a symbol — these phrases 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 16 (4) of Directive 67/548/EEC;

(b) in the case of danger arising from physico-chemical properties:

— the criteria described under 7.2.1 (a) above 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 danger for the environment:

— the R-phrases corresponding to the classification category dangerous for the environment — these phrases must appear on the label.

7.2.2. 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:

(i) R-phrases which correspond to the category of danger illustrated by a symbol. In certain cases the R-phrases must be adapted according to the tables of Annex I to Directive 88/379/EEC. 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 the other categories of danger which have been attributed to the constituents but which are not illustrated by a symbol by virtue of Article 7 (d) of Directive 88/379/EEC;

(b) in the case of dangers arising from physico-chemical properties:

— the criteria described under 7.2.2 (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.

7.3. 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 to the clarity and impact of the label. With clarity in mind, the necessary information should be expressed in a minimum number of phrases.

7.3.1. Risk phrases

As a general rule, applying to substances and preparations, a maximum of four 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, the standard phrases must cover all the principal hazards associated with the preparation.

However, where there is a need to identify environmental hazards additional R-phrases shall be added as required.

7.3.2. 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:

— safety phrases which give obvious advice in relation to risk phrases are generally omitted from the label unless used to give particular emphasis to a specific warning,

— certain safety phrases, e.g. S 2, have particular relevance to substances and preparations intended to be used by the public, other phrases have particular relevance to persons at work. Phrases should be chosen with the intended use in view,

— 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,

— as a general rule, a maximum of four 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 danger to the environment a minimum of one and a maximum of four S-phrases should be used,

— 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 emphasize a specific warning.

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

(a) for substances:

the name is established according to an internationally recognized chemical nomenclature as defined in 1.4.

(b) for preparations:

the choice of the names to be displayed on the label follows the rules of Article 7 (1) (c) of Directive 88/379/EEC.

Note

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 sensitizing substance judged by him to be primarily responsible for the sensitization 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.

7.5. **Note**

It is important to remember that Annex II of Directive 88/379/EEC has special provisions concerning the labelling of certain preparations.

8. **SPECIAL CASES: SUBSTANCES**

8.1. ***Metals in massive form***

These substances are classified in Annex I to Directive 67/548/EEC or shall be classified in accordance with Article 5 (2) of Directive 67/548/EEC. However, some of these substances although classified in accordance with Article 2 of Directive 67/548/EEC do not present a danger to human health by inhalation, ingestion or contact with skin in the form in which they are placed on the market. Such substances do not require a label according to Article 16 of this Directive. 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.

9. **SPECIAL CASES: PREPARATIONS**

9.1. **Gaseous preparations (gas mixtures)**

For gaseous preparations, consideration must be given to:

— the evaluation of the physico-chemical properties,

— the evaluation of health hazards.

9.1.1. **Evaluation of physico-chemical properties**

9.1.1.1. ***Flammability***

The flammable properties of these preparations are determined in accordance with Article 3 (2) of Directive 88/379/EEC according to the methods specified in Part A of Annex V to Directive 67/548/EEC. These preparations will be classified according to the results of the tests carried out and with respect to the criteria of Annex V 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

$$A_1F_1 + \ldots + A_iF_i + \ldots A_nF_n + B_1I_1 + \ldots B_jI_j + \ldots B_pI_p$$

where: A_i and B_j are the molar fractions
F_i flammable gas
I_j inert gas
n number of inert 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:

$$A'_i = A_i \times \left(\frac{100}{(A_i + K_jB_j)}\right)$$

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:

$$\sum_i A'_i/Tci < 1$$

The gas mixture is flammable if the value of the above expression is greater than one and the preparation is classified highly flammable; furthermore, the phrase R 12 or R 13 will be assigned according to the case.

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/DIS 10156.

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/DIS 10156. 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 oxidizing gases can be prepared safely. When estimating flammability these oxidizing 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. *Oxidizing properties*

Given the fact that Annex V to Directive 67/548/EEC does not contain a method to determine the oxidizing properties of gaseous mixtures, the evaluation of these properties must be realized according to the following estimation method.

The principle of the method is comparison of the oxidizing potential of gases in a mixture with that of the oxidizing 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:

$$\sum_i x_i C_i > 21$$

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 oxidizing and the phrase R 8 will be assigned.

Coefficients of equivalency between oxidizing gases and oxygen

The coefficients used in the calculation to determine the oxidizing capacity of certain gases in a mixture with respect to the oxidizing capacity of oxygen in air, listed under 5.2 in the ISO Standard ISO/DIS 10156, are the following.

O_2	1
N_2O	0,6

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

9.1.2. **Evaluation of the health effects**

This evaluation of the dangers of a preparation for health is made according to Article 3 (3).

When the evaluation of the health hazards is made according to the conventional method described in Article 3 (5) of Directive 88/379/EEC by reference to individual concentration limits, the individual concentration limits to be used are expressed in per cent by volume and appear:

— either in Annex I to Directive 67/548/EEC for the gas(es) considered,

— or in Annex I to Directive 88/379/EEC, Tables I A to VI A, when the gas(es) considered are not in Annex I, or appear there without concentration limits.

9.1.3. **Labelling**

For mobile gas holders the requirements concerning labelling are considered to be satisfied when they are in agreement with Article 8 (5) (b).

However, by way of derogation from Article 8 (1) and (2), for gas cylinders 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 ISO/DP 7225. 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.

9.2. **Alloys, preparations containing polymers, preparations containing elastomers**

These preparations shall be classified according to the requirements of Article 3 and labelled according to the requirements of Article 7 of Directive 88/379/EEC.

However some of these preparations although classified in accordance with Article 3 (3) do not present a danger to human health by inhalation, ingestion or contact with skin in the form in which they are placed on the market. Such preparations do not require a label according to Article 7; 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 10 of the abovementioned Directive.

COMMISSION STATEMENT

With regard to 4.1.5, and in particular to the last paragraph of 4.1.5, the Commission states that, should it envisage making use of the procedure of Article 21 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 teratogenicity.

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 or teratogenic effects.
