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DETAILED REVIEW DOCUMENT ON HAZARD CLASSIFICATION SYSTEMS FOR MIXTURES

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DETAILED REVIEW DOCUMENT ON HAZARD CLASSIFICATION SYSTEMS FOR MIXTURES

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The work of the OECD related to chemical safety is carried out in the **Environment, Health and Safety Programme**. As part of its work on chemical testing, the OECD has issued several Council Decisions and Recommendations (the former legally binding on Member countries), as well as numerous Guidance Documents and technical reports. The best known of these publications, the **OECD Test Guidelines**, is a collection of methods used to assess the hazards of chemicals and of chemical preparations. These methods cover tests for physical and chemical properties, effects on human health and wildlife, and accumulation and degradation in the environment. The OECD Test Guidelines are recognised world-wide as the standard reference tool for chemical testing.

More information about the Environment, Health and Safety Programme and its publications (including the Test Guidelines) is available on the OECD's World Wide Web site (see page 8).

The Environment, Health and Safety Programme co-operates closely with other international organisations. This document was produced within the framework of the Inter-Organisation Programme for the Sound Management of Chemicals (IOMC).

The Inter-Organization Programme for the Sound Management of Chemicals (IOMC) was established in 1995 by UNEP, ILO, FAO, WHO, UNIDO and the OECD (the Participating Organisations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. UNITAR joined the IOMC in 1997 to become the seventh Participating Organisation. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWORD

The Detailed Review Document on Classification Systems for Chemical Mixtures in OECD Member Countries has been prepared by a Drafting Group lead by the USA as part of the work being carried out by the OECD's Programme on Harmonization of Classification and Labelling Systems.

This document has been produced within the framework of the Inter-Organisation Programme for the Sound Management of chemicals (IOMC).

DETAILED REVIEW DOCUMENT
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I. INTRODUCTION

GENERAL

1. The success of the Globally Harmonised System (GHS) relies upon the efforts of the countries and systems involved to work together to find a consensus. Recognition is due to many who participated in this process. Acknowledgement for providing information for this detailed review document (DRD) goes to: Australia, Austria, Brazil, Canada, the European Union, IMO, Japan, Korea, New Zealand, Norway, Slovenia, Sweden, the UN Committee of Experts on Transport of Dangerous Goods (UNCETDG), and the USA. The full text of the detailed responses received is included in an annex to this document.

2. A variety of classification regulations is used in most jurisdictions to cover all the stages of a chemical's life cycle and end uses: food, drugs, cosmetics, pesticides, consumer products, radioactive materials, explosives, workplace, environmental exposure, disposal and transportation. There are important differences in the underlying philosophy and purpose of these various classification regulations. The Drafting Group collected information about all of these sectors from the respondents in order to determine what approaches are currently used, and whether the work of the Mixtures Work Group should be focused on certain sectors where harmonisation can be achieved. For the most part, all of the major existing systems other than transport have some differentiation in approach between and among these sectors.

3. Most products in commerce are mixtures. Dissimilar mixture rules and dissimilar hazard classifications can currently result in different conclusion about the same commercial product. The harmonisation of criteria and methodology for the classification of mixtures is at the heart of the Globally Harmonised System (GHS).

4. It should be noted, however, that while there is an underlying concern about the outcome of the differing mixture rules in terms of inconsistent hazard communication, the purpose of this activity is to focus on the criteria and methodology for classification. Work concerning the warnings that will be placed on labels for mixtures, or information on material safety data sheets, is to be performed by the Hazard Communication Work Group being convened by the International Labour Organisation (ILO).

5. This Step 1 Detailed Review Document (DRD) will focus on the health and environmental hazards of mixtures. The ILO/UNCETDG joint committee has elaborated criteria for classification of Physico-Chemical Hazards which are applicable to substances or mixtures. The classification of mixtures for Physico-Chemical Hazards is not being dealt with separately. The final proposal for a harmonised system for the classification of mixtures will include the physical, the health and environmental hazards. In cases where existing systems have environmental criteria for mixtures they are included for information in an annex.

APPROACHES TO COVERING MIXTURES

6. An examination of the major existing systems indicates that the approaches to regulating mixtures can be grouped into categories based on available test data:

a) tested mixtures;
b) "bridging data" or partially tested mixtures; and
c) untested mixtures.

7. Tested mixtures are generally treated and classified in all classification systems the same way that substances are treated and classified. However, in the EU system, testing cannot be used to assess the carcinogenic, mutagenic and reproductive hazards of mixtures. In all systems whenever relevant evidence of effects on man is available on mixtures, this information generally takes precedence in classification.

8. Some systems rely upon *bridging data*/extrapolation to evaluate the effects of mixtures where there are no or incomplete data. For some mixtures, sufficient data are available for constituent ingredients to allow reliable extrapolation of the hazard of the mixture. It must be demonstrated that the new ingredient would not alter the toxicological profile for the formulation. For example, in a tested mixture one ingredient can be replaced by an analogue of similar toxicity either based on testing or SAR data. Pesticide regulations in the USA and Canada accept bridging data, particularly for acute hazards.

9. The term "untested mixtures means the mixture as a whole has not been tested. There may be data available for some/all of its constituents. Some systems cover *untested mixtures* through application of a standardised approach. These approaches are intended to ensure that all mixtures are evaluated in some fashion based on the available information, and that these evaluations are comparable for all untested mixtures under that system. It appeared to the Working Group in Ottawa that this is the area where harmonisation is most likely to be achievable. Thus standardised approaches to classification of untested mixtures are the main focus of the DRD.

10. There are several standardised approaches to the classification of untested mixtures in the existing systems. In general the workplace systems in USA and Canada use a percentage cut-off approach, i.e., the mixture is classified according to the hazards of the ingredients that are present at levels above specified percentages. The European system uses a similar concentration limit of ingredients approach to classification and applies it to preparations both in the workplace and in the consumer use setting. For certain endpoints in the EU system additivity of effects are taken into consideration and formulas are applied for this purpose. In the UN transport system classification is, in the first instance, on the basis of human experience where relevant, and in the absence of human experience, on the basis of testing. In a number of endpoints, formulae are given for a calculation method, but these are on the basis of the dilution effect and do not make any provision for synergistic or antagonistic effects. In a limited number of endpoints there is reference to structural activity relationships or comparative chemistry. All of the other sectors use either test data or bridging data in the existing systems (e.g., pesticides), or focuses on listing ingredients on product labels rather than hazard classification and labelling (e.g., cosmetics). There is further discussion of each of the sectors below to address the appropriateness of including them in the harmonisation effort.

CHEMICAL COMPOSITION

11. In the existing systems the standardised approaches to the classification of untested mixtures all rely on knowing the chemical composition down to either a percentage cut-off or a concentration limit.

PHYSICAL STATE

12. In the EU system, the percentage cut-off or concentration limits for the components of the mixture differ according to the physical state.

II. DEFINITIONS

GENERAL

13. An examination of the existing systems reveals a lack of harmonisation in terminology in a number of respects. Some specific definitions are examined in this report, and it is expected that the Step 2 document will propose harmonised definitions in these areas. However, for purposes of establishing a common understanding of the systems covered in this report, it may be helpful to review some of the areas where different terms are used, but the concept is actually the same.

14. The DRD uses the term “mixtures” to describe the coverage of the work. This is the term used in North American systems for the workplace, but it appears to be identical to the term “preparations” used in Europe. Similarly, in other parts of each country’s regulatory approach to the subject, there may be other terms used such as “products” or “formulations”. For purposes of this document, these terms are also considered to be synonymous to “mixtures” or “preparations”.

15. In the UN transport system, the word “substance” is used to cover both the terms “substance” and “mixture”. The terms “formulation” and “preparation are also sometimes used. The UN Model Regulations on the Transport of Dangerous Goods (UN MRTDG) does contain some provisions applicable to ”mixtures” or ”solutions” and there is a loose definition of retail product. Liquids and Gases are defined, and by default, solids are other goods not meeting these definitions. In the EU, this process is referred to as “hazard classification.” In the US HCS, the term is “hazard determination” or “hazard evaluation”. Another term in use is “hazard identification”. It appears that these terms are synonymous in most cases as well, and refer to the identification of relevant data regarding the hazards of a chemical or substance, and the subsequent review of that data to ascertain what hazards may be associated with it.

16. The one exception to the generally consistent approach to interpretation of these process-related terms involves consumer products in the US. Under that system, “classification” embodies a two- step process of identifying the hazard and performing an assessment of the likelihood of harm or injury for purposes of labelling. Classification under CPSC involves determination of likelihood of injury or illness, the extent of which may vary from gross/blanket determination (e.g. use of dose related cut off points for acute toxicity since a single exposure is sufficient to injure) to a detailed risk determination as appropriate. The DRD only addresses the first step of this process, i.e., identification of the hazard. It must therefore be recognised that the term “classification” when used in conjunction with the US consumer products regulations has a broader meaning than what is envisioned in this report. The report uses the terminology in the sense that it appears it is used in the majority of the systems addressed as the first step in the process or identification of the hazard. The second step - deciding what is appropriately conveyed about the chemical on the label - will be addressed in a separate forum and is not within the purview of this Work Group.

17. Another area where different terminology is used to address a similar concept is in the standardised or conventional approaches. The EU system refers to “concentration limits” for different endpoints, while the North American systems for workplace use the term “percentage cut-offs” to describe their approach. These appear to mean the same thing, although the numbers used may vary somewhat.

18. Definitions of pertinent terms (chemical/substance, mixture/preparation) from various existing classification systems are given by end use in the Appendix I tables. The tables in Appendix I include the source of the definitions, i.e., legislation, regulation, etc.

OTHER DEFINITIONS

Definitions According to the Canadian Legislation

The Workplace Hazardous Materials Information System (WHMIS)

19. "*Controlled Product*" means any product, material, or substance that meets any of the following criteria listed in Part IV of the *Controlled Products Regulations*: (A) compressed gas; (B) flammable and combustible material; (C) oxidising material; (D) poisonous and infectious material; (E) corrosive material and (F) dangerously reactive material.

20. "*Manufactured Article*" means any article that is formed to a specific shape or design during manufacture, the intended use of which when in that form is dependent in whole or in part on its shape or design, and that under normal conditions of use, will not release or otherwise cause a person to be exposed to a controlled product.

21. "*Complex Mixture*" means a mixture that is a combination of many chemicals, has a commonly known generic name and is:

a) naturally occurring;
b) a fraction of a naturally-occurring mixture that results from a separation process; or
c) a modification of a naturally-occurring mixture or a modification of a fraction of a naturally-occurring mixture that results from a chemical modification process.

Consumer products

22. *"Consumer Chemical Product"* means a chemical product that is destined for use by a consumer set out in item 1 of Part II of Schedule I to the *Hazardous Products Act* and has the properties set out in one or more of (a) Category 1, toxic products, in Part 1; (b) Category 2, corrosive products, in Part 2; (c) Category 3, flammable products, in Part 3; and (d) Category 4, quick skin-bonding adhesives, in Part 4.

23. There is no definition of article, however, for consumer products, the criteria apply only to components or generated products to which the user or others might become exposed in normal use or reasonably foreseeable use. The Regulations do not apply to a consumer chemical product if a user cannot be exposed to the product or to any of its hazardous ingredients during normal use or reasonably foreseeable use.

24. The terms "hazard identification", "hazard evaluation", "hazard determination", "hazard classification", and similar terms for purposes of comparing the various approaches are not defined in the regulation.

Pesticides

25. The Canadian *Pest Control Products Act* defines a control product as "any product, device organism, substance or thing that is manufactured, represented, sold or used as a means for directly or indirectly controlling, preventing, destroying, mitigating, attracting or repelling any pest and includes

a) any compound or substance that enhances or modifies or is intended to enhance or modify the physical or chemical characteristics of a control product to which it is added, and

b) any active ingredient used for the manufacture of a control product.

Definitions According to the European Legislation

26. Directives 67/548/EEC on dangerous substances and 88/379/EEC on dangerous preparations contain definitions for placing on the market of substances and preparations.

27. "*Placing on the market*" means the making available to third parties. Importation into the Community customs territory shall be deemed to be placing on the market for the purposes of the Directives.

28. "*Substances*" mean chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the products and any impurity deriving from the process used, but excluding any solvent which may be separated with out affecting the stability of the substance or changing its composition. A substance may be chemically very well defined (e.g. acetone) or a complex mixture of constituents of variable composition (e.g. aromatic distillates). For some complex substances, some individual constituents have been identified.

29. "*Preparations*" mean mixtures or solutions composed of two or more substances.

30. "*Chemical agent*[1]" means any chemical element or compound, on its own or admixed, as it occurs in the natural state or as produced, used or released, including release of waste, by any work activity, whether or not produced intentionally and whether or not placed on the market.

31. "Hazardous chemical agent[1]" means:

1) Any chemical agent which meets the criteria for classification as a dangerous substance according to the criteria in Annex VI to Directive 67/548/EEC, whether or not that substance is classified under that Directive, other than those substances which only meet the criteria for classification as dangerous for the environment;

2) Any chemical agent which meets the criteria for classification as a dangerous preparation within the meaning of Directive 88/379/EEC, whether or not that preparation is classified under that Directive, other than those preparations which only meet the criteria for classification as dangerous for the environment;

3) Any chemical agent, which, whilst not meeting the criteria for classification as dangerous in accordance with (1) and (2), may, because of its physico-chemical, chemical or toxicological properties and the way it is used or is present in the workplace, present a risk to the safety and health of workers, including any chemical agent assigned an occupational exposure limit value.

32. "*Article*" is defined as: an item which is formed to a specific shape, surface or design during manufacture, has end use function(s) dependent in whole or in part upon its shape or design during end

1 Definitions from Directive 98/24/EEC (OJ No L 131, 5.5.1998, p. 11)

use, and has either no change of chemical composition during its end use or only those changes of composition which have no commercial purpose separate from that of the article.

Note: The definition of an article is not included in the Directives on dangerous substances or dangerous preparations. Definition for an article is, however, specified in the document "Reporting for the EINECS Inventory".[2] This document was introduced as a guidance by Commission Decision 81/437/EEC[3] on laying down the criteria in accordance with which information relating to the inventory of chemical substances is supplied by the Member States to the Commission.

33. "Hazard identification" is the identification of the adverse effects which a substance has an inherent capacity to cause.

Note: Hazard identification" is defined in Commission Regulation 1488/94[4] and Commission Directive 93/67/EEC[5] This definition of hazard identification does not contain the element of determination of the classification on the basis of the data on adverse effects and the classification criteria. Hazard identification can be considered as a first step for classification.

Definitions According to US Legislation

US OSHA:

34. Under the Hazard Communication Standard: "Workplace" means an establishment, job site, or project, at one geographical location containing one or more work areas. "Work area" means a room or defined space in a workplace where hazardous chemicals are produced or used, and where employees are present.

US CPSC:

35. The Consumer Product Safety Act defines consumer product as any article, or component thereof, produced or distributed (i) for sale to a consumer for use in or around a permanent or temporary household or residence, a school, in recreation or otherwise, or (ii) for the personal use, consumption or enjoyment of a consumer in or around a permanent or temporary household or

2 European Commission, Constructing EINECS: Basic documents, Reporting for the EINECS In ventory, Office for Official Publications of the European Communities, L-2985 Luxembourg, ISBN 92-825-2459-0.

3 OJ No L 167, 24.6.1981, p.31.

4 Commission Regulation No 1488/94 laying down the principles for the assessment of risks to man and the environ ment of existing substances in accordance with Council Regulation No 793/93, OJ No L 161, 29.6.1994, p.3.

5 Commission Directive 93/67/EEC laying down the principles for assessment of risks to man and the environment of substances notified in accordance with Council Directive 67/548/EEC, OJ No L 227, 8.9.1993, p. 9.

residence, a school, in recreation or otherwise; but does not include foods, drugs, cosmetics, pesticides, tobacco and tobacco products, motor vehicles and motor vehicle equipment, fire arms and ammunition, aircraft and its parts and appliances, and boats that are subject to Federal Boat Safety Act.

III. SCOPE

CANADA

36. The *Hazardous Products Act* covers consumer (Part I) and workplace (Part II) chemicals, with certain exemptions. Chemicals used in the workplace are covered by the Controlled Products Regulations and the system is based on hazard classification and communication. The Workplace Hazardous Materials Information System (WHMIS) establishes uniform national requirements to ensure that information regarding health hazards, safe use, storage and handling of hazardous materials are disclosed on the MSDS. Information on toxicological properties should be provided without limiting such information to the hazards based on presumed use. WHMIS does not necessarily take into account the possibility of exposure. Information that is applicable to the product should be reported. There are no special considerations for susceptible populations in WHMIS.

37. WHMIS Exclusions: At present, the WHMIS requirements of the *Hazardous Products Act* do not apply to the following categories of products:

1. Product, material or substance packaged as a consumer product
2. Explosives
3. Cosmetic, drug, food, or device within the meaning of the Food and Drug Act
4. A pest control product within the meaning of the Pest Control Products Act
5. Radioactive materials
6. Hazardous waste
7. Wood or product made of wood
8. Manufactured articles
9. Tobacco or products made of tobacco

Note: The products excluded from WHMIS are currently under review. Tripartite sectoral committees have reached consensus agreement that explosives, cosmetics, drugs, foods, devices, pest control products, radioactive substances, hazardous waste and consumer products (Items 1 to 6) would be covered by WHMIS.

38. Consumers products are covered by Consumer Chemicals and Containers Regulations of the Hazardous Products Act. Only acute hazards are covered at this time. No environmental endpoints are covered in the Hazardous Product Act. The system applies for exposure during normal use or reasonably foreseeable use. Children are a target population in developing criteria for consumer products, as they may be more sensitive to toxic chemicals than adults, are more likely to use products inappropriately (especially with regard to ingestion), are unable to understand labels and are less able to protect themselves if exposed.

39. Consumer Product Exclusions: Components which cannot be made accessible to the user or others, by virtue of the product form or formulation, will not be subject to the criteria.

40. All pesticides are covered under the ***Pest Control Products Act***.

EUROPEAN UNION

41. The EU Directives on the classification, packaging and labelling of Dangerous Substance and Dangerous Preparations cover chemicals intended for both consumer and workplace use. The EU directive on Dangerous Substances and the proposal for a new Directive on Dangerous Preparations include the classification "dangerous to the environment" which the CPSC, the Canadian consumer chemical regulations, WHMIS and OSHA do not.

Existing Directive

42. The EU Directive 88/379 covers classification, packaging and labelling of dangerous preparations when they are placed on the market in the EU Member States. The Directive is applied to preparations which contain at least one substance classified as dangerous and which are considered to be dangerous within the meaning of the Directive. The aim is to protect both professional users and general consumers as well as the environment.

43. Some groups of preparations are exempted from the Directive; in these cases there are other specific Directives for protection of health and safety and in some cases the environment when the product is placed on the market. Preparations are excluded when intended to the final user or consumer. In cases where raw materials or intermediates to any of the exempted groups, i.e. preparations not intended for the final user, are placed on the market they are covered by the Directive.

44. The exempted groups of preparations are:

- medical and veterinary products
- cosmetic products
- mixtures of substances which in the form of waste are covered by specific legislation
- pesticides
- munitions and explosives
- foodstuffs and animal feeding stuffs in a finished stage intended for the final consumer.

45. In addition the Directive does not apply to the carriage of dangerous preparations by rail, road, inland waterway, sea or air or to preparations in transit which are under customs supervision provided they do not undergo any treatment or processing.

46. In the proposed new Directive the following changes of the scope have been proposed:

- pesticides, munitions and explosives (if in the form of chemical) shall be within the scope
- preparations containing radioactive substances shall be excluded
- those medical devices which are invasive or used in direct physical contact with the human body shall be excluded insofar as other specific legislation gives the same level of information provisions and protection.

47. In addition some provisions of the Directive shall apply to preparations which are *not* classified as dangerous but might nevertheless present a specific hazard.

Proposal for New Directive on Dangerous Preparations

48. Proposal (COM(96)347,[6] COM(97)462[7]) for the new Directive of the European Parliament and the Council on the classification, packaging and labelling of dangerous preparations is in the decision making process of the EU institutions.

49. The proposal contains the following new elements:

- Classification & labelling of preparations dangerous for the environment. (The classification principles for preparations dangerous for the environment are similar to the conventional method applied to classification for [acute lethal] health hazards. The preparations are classified as dangerous for the environment on the basis of component substances and their concentrations in the mixture);

- Classification, packaging, labelling and Safety Data Sheet requirements for pesticides (plant protection products and biocides);

- Classification of explosives;

- Extends certain specific provisions to preparations which are not classified as dangerous;

- Consolidates and updates existing EU legislation and rationalises the structure of the Directive. Consequently the key principles are in the main text. The technical detail is contained in the annexes which can be more quickly amended to take account of technical developments. A recognition that the characteristics of alloys are such that it may not be possible accurately to determine their properties using currently available conventional methods. It is therefore necessary to develop a specific method of classification which takes into account their particular chemical properties.

UNCETDG:

50. The UN Recommendations on the Transport of Dangerous Goods (UNRTDG) are not regulations in themselves, but are formatted as a model intended for adoption in international transport modal regulations and for national transport regulations, but they have also been used in some countries as a basis for supply legislation. The UNRTDG prescribe detailed requirements applicable to the transport of dangerous goods and cover all products whatever their end use is intended to be. The scope of the UN MRTDG includes radioactives and all physico-chemical hazards currently agreed for the GHS. Wastes which meet the criteria for classification in any hazard class covered by the UN MRTDG are included. Provision is also made for the transport of waste under the Basel Convention, and in some cases this may not meet the criteria for classification in the UN MRTDG. The UNRTDG do not apply to the transport of dangerous good in bulk, dangerous goods required for the propulsion of the means of transport or for the operation of its specialised equipment, dangerous goods, packaged for retails sale carried by individuals for their own use.

Endpoints covered

The UN MRTDG covers the following toxicological and eco-toxicological endpoints

6 OJ C283, 26.9.1996, p. 1.

7 OJ C.

- Acute toxic effects
- Corrosive effects to living tissue
- Infectious substances

Criteria for classification as hazardous to the aquatic environment are being addressed as part of the work programme for the current biennium. Provision is already made for the transport of goods as environmentally hazardous in the UN MRTDG

US:

51. The OSHA Hazard Communication Standard covers chemicals in the workplace. Consumer products and cosmetics in commerce and pesticides are covered by separate regulations. No environmental end points are covered.

US CPSC:

52. The classification and resultant labelling for consumer products (FHSA) is based on the determination of likelihood of injury or illness. Thus products not likely to cause injury or illness when used or foreseeably misused are not classified or labelled. The following exemptions are based on similar principle:

> Common matches, including book matches, wooden matches, and so-called "safety" matches; paper items such as newspapers, wrapping papers, toilet and cleansing tissues, and paper writing supplies; thread, string, twine, rope, cord, and similar materials; laboratory chemicals intended only for research or investigation and other laboratory uses (except those in home chemistry sets); rigid or semi-rigid ballpoint ink cartridges; the ink does not have an LD_{50} single oral dose of less than 500 milligrams per kilogram of body weight of the test animal, and the cartridge does not have a capacity of more than 2 grams of ink; porous-tip ink-marking devices; glues with a cyanoacrylate base in packages containing 3 grams or less; liquid fuels containing more than 4 percent by weight of methyl alcohol that are intended and used for operation of miniature engines for model aeroplanes, boats, cars, etc.; solid fuel pellets intended for use in miniature jet engines for propelling model jet aeroplanes, speed boats, racing cars, and similar models, kits intended for construction of model rockets and jet propelled model aeroplanes requiring the use of difluorodichloromethane as a propellant. It should be noted that these exemptions require products to meet specific conditions and may require specific labelling.

US OSHA:

53. The Hazard Communication Standard has a complicated set of exemptions that relate primarily to the standard's interface with other US laws and regulations, or to situations where exposure is so minimal that the risk is expected to be very small. The only ones that will be addressed here are those that deal with application to a specific product, rather than application in a type of workplace (such as a laboratory). It is unlikely that these exemptions would have broad enough application to be part of the GHS approach. It should be noted that these exemptions do not solely apply to mixtures; substances would also be subject to the same exemptions.

54. Additional labelling under the HCS is not required for products subject to other Federal labelling laws as follows (other requirements of the standard for MSDSs and training may be applied):

- Pesticides labelled in accordance with EPA requirements
- Chemical substances labelled in accordance with EPA requirements under the Toxic Substances Control Act
- Food, food additives, colour additives, cosmetics, or medical/veterinary devices or products, when regulated by FDA or the Department of Health
- Alcoholic beverages regulated by the Bureau of Alcohol, Tobacco and Firearms
- Consumer products or hazardous substances regulated by CPSC
- Agricultural or vegetable seed regulated by the Department of Agriculture

55. The following are totally exempted from the HCS:

- Hazardous waste when regulated by EPA
- Tobacco or tobacco products
- Wood or wood products (treatment chemicals are covered, as is wood dust that can be inhaled).
- Articles (an "article" is defined as follows: a manufactured item other than a fluid or particle: (i) which is formed to a specific shape or design during manufacture; (ii) which has end use function(s) dependent in whole or in part upon its shape or design during end use; and (iii) which under normal conditions of use does not release more than very small quantities, e.g., minute or trace amounts of a hazardous chemical (as determined by paragraph (d) of this section), and does not pose a physical hazard or a health risk to employees)
- Food or alcoholic beverages which are sold, used or prepared in a retail establishment, or food intended for personal consumption by employees while in the workplace
- Drugs that are in solid, final form for direct administration to a patient; packaged for sale to consumers in a retail establishment; and intended for personal consumption of employees while in the workplace
- Cosmetics which are packaged for sale in a retail establishment, or in the workplace for the personal consumption of employees
- Consumer products which are used in the workplace for the purpose intended by the manufacturer, and the use results in a duration and frequency of exposure which is not greater than the range of exposures that could reasonably be experienced by consumers
- Nuisance particulates
- Ionising and non-ionising radiation

- Biological hazards

US EPA:

56. Under FIFRA section 25(b) the following exclusions from the requirements of registration have been set forth:

- pheromones used only in traps and pheromone traps
- treated articles such as wood treated with preservatives
- embalming fluids
- horticultural products consisting of plant hormones, plant nutrients, inoculants, or soil amendments not intended for use on food crops and of low toxicity
- natural cedar
- foods containing no active ingredients and used to attract pests
- certain minimum risk pesticides such as castor oil, soybean oil, rosemary, sesame, etc.

IV. RATIONALE FOR EACH APPROACH

57. There are some important differences in the underlying philosophy and purpose of the existing classification systems.

BASIS FOR EXISTING SYSTEMS

58. The primary objective of chemical classification and labelling systems is to enhance protection of human health and the environment. The key principle in the USA and Canadian systems is to convey health and environmental effect information on chemicals to the user in a manner that will most appropriately meet the user's needs. They vary in where and how they provide the information and the level of detail based on knowledge of potential exposures.

59. The presence of chemicals in all economic sectors has resulted at the national level in the elaboration of sector-specific health and environmental regulations which are targeted to the chemical users in each sector (transport, workplace, agriculture, consumer products). Specific regulations are designed to protect specific populations and are based on knowledge of uses and exposures and how health effects information can be can be transmitted to those populations. Sector-specific regulations are necessitated by 1) differences in the knowledge of specific exposures available to a chemical's producer which, because of differences in the degree of uncertainty that this causes, limits to varying degrees the safety information communicated by the chemical manufacturer, and 2) the need to organise complex health and environmental knowledge in such a way that appropriate information is conveyed in a form that is easily understood and applied by chemical users, while taking into account the presence or absence of other tools (e.g., MSDSs, training). The key principle in the EU system is that hazard classification provides the foundation for a wide range of harmonised legislative processes which allow effective risk management and covering the whole life cycle of substances and preparations. The legislation facilitates the free movement of goods whilst ensuring a high level of protection of human health and the environment.

CANADA: WHMIS

60. The Workplace Hazardous Materials Information System (WHMIS) is a national information system designed to protect Canadian workers by providing safety and health information about hazardous workplace materials. WHMIS was developed through a consensus process with representation from industry, organised labour, and federal, provincial and territorial governments. WHMIS recognises the interests of workers, employers, suppliers and regulators and balances the workers right to know with industry's right to protect confidential business information.

61. The WHMIS classification system is based on cut-offs which presumes that a mixture is hazardous if it contains a hazardous ingredient at a concentration exceeding a specified cut-off. The use of cut-offs is administratively straightforward and can be applied by using available data on the toxicology of ingredients in the mixture. Since WHMIS is primarily an information system, the use of cut-off values is justifiable as a means of consistently communicating information about hazardous ingredients, as contrasted with providing a hazard evaluation of the mixture. The numerical values of cut-offs, however, are necessarily arbitrary and were chosen largely for consistency between Canada and the United States.

62. The classification of substances and mixtures is the responsibility of the supplier (or employer). There is no regulatory agency involved in classification. Hazard categorisation (i.e., sub-classifying the overall hazard classification into severity levels) is used in the Canadian system for selecting hazard symbols for hazard communication. The hazard communication audience is the worker/customer. The focus is on hazard identification and its subsequent communication.

63. The *Consumer Chemicals and Containers Regulations* are intended to ensure that consumers have ready access to the required knowledge. This is accomplished by requiring precautionary labelling to appear on containers of hazardous chemical products intended for domestic use. The labelling provides warnings about the dangers involved with the use, handling and storage of the products, the steps to take in case of an accident and recommendations for first aid treatments. Child-resistant packaging is also prescribed for some products. The *Consumer Chemicals and Containers Regulations* are intended to reduce the injuries and costs caused by accidents involving consumer chemical products.

EU

64. The philosophy of the European Union requires harmonised legislation that facilitates the free movement of goods whilst ensuring a high level of protection of human health and the environment The EU standardised approach allows that all hazard end points can be specified easily, reliably and inexpensively without animal testing.

65. The EU system for hazard classification provides the foundation for a wide range of legislative processes covering the whole life cycle of substances and preparations including e.g. hazard communication, risk assessment, worker protection, protection of the environment, prevention of major accidents and restrictions for marketing and use. Hazard classifications are scientifically defensible and robust and reflect in a credible way the real hazards of preparations.

66. Because of a number of legislative consequences it is important that the hazard classifications are scientifically defensible and robust and reflect in a credible way the real hazards of preparations.

67. Hazard classification is the responsibility of the manufacturer, importer or distributor. Classification of a mixture is based on classification of substances. The classification for a substance in Annex I to Directive 67/548/EEC has to be used, if available. If the substance is not listed in this Annex the manufacturer or importer shall classify the substance. On the basis of the classification(s) of substances the preparation is classified by applying the concentration limits for different end points.

68. Labelling and Safety Data Sheets (SDS) for professional users are consequences of classification. The information on classification is passed to the users of chemicals by the supply chain to make sure that the users are aware of the hazards so that employers or economic operators can take appropriate measures for protection of workers and the environment. The obligations set by other Community legislation may be triggered by the classification of the preparation.

69. Safety Data Sheets (SDS) submit information on dangerous components of classified preparations to the professional users. Information shall be given on components classified as dangerous to health and/or to the environment, and present at levels of 1% or greater (unless the classification limit is lower than 1%). The employer or economic operator should use this information for risk assessment purposes. This information may be needed e.g. in cases where several preparations containing similar substances are used simultaneously, or in cases where large amounts of preparations containing low concentrations of dangerous substances are used and total emissions to the environment could be significant. On the basis of the risk assessment carried out by the employer or economic operator appropriate steps should be taken for protection of health of workers and the environment.

70. An obligation to submit information by SDS also on non-classified preparations will be introduced by the new Directive on dangerous preparation. This obligation would apply to preparations that contain 1 % or more of a substance dangerous to health or to the environment, or of a substance for which a Community Exposure Limit in the work place has been defined.

71. The workers have access to the information of SDSs. The label information is available to anyone.

UNCETDG

72. The UNRTDG have been developed in light of technical progress, the advent of new substances and materials, the exigencies of modern transport systems and, above all, the requirement to ensure the safety of people, property and the environment.

73. The starting point is to classify goods for their intrinsic properties as relevant into one or more of the 9 hazard classes, or divisions of hazard classes as described in the system. The goods are then assessed for the severity of the hazard(s) that they present and are then allocated in most classes/divisions to packing groups which represent the severity of the hazard. Where substances or mixtures present more than a single hazard, the primary hazard and subsidiary hazards are determined according to a table of precedence taking into account each hazard and the severity of that hazard. The goods are allocated to a UN substance identification number (UN Number), of which there are four different types. The first type is purely for named individual substances rather than mixtures, and the other three types can be used for substances, mixtures or articles as appropriate. These entries are contained in the UN MRTDG's expertly classified database of substances and articles, the 'Dangerous Goods List' in chapter 3.2, which lists the dangerous goods most commonly carried. The classification for named substances with their own unique individual UN Number in the database can only be decided upon by the UNCETDG, but in many cases manufacturers or consignors can self classify goods to the other types of UN Numbers. This system allows the flexibility for goods which are not already identified by the system to be classified and assigned to a UN Number.

US: OSHA HCS

74. The OSHA Hazard Communication Standard provides exposed workers and employers using a chemical in their workplaces with the right to know the identities and hazards of those chemicals. The underlying philosophy is that the availability of information allows the selection and use of appropriate control measures, thus resulting in fewer illnesses and injuries based on chemical exposures. It thus is based on the premise that as complete disclosure as possible is the best approach. This desire for disclosure was balanced by concerns about trade secret claims (which are more common for chemicals in small concentrations) and the need for information about very small quantities. The percentage cut-offs were selected as a practical and pragmatic approach to addressing these concerns, while still ensuring that necessary information is readily available to employers and employees.

75. OSHA uses the term hazard determination for evaluation of the hazards. While appropriate hazard information must be provided, it is not required to name, assign, or cite a hazard category or hazard class under the OSHA HCS. No regulatory agency is involved in classification. The appropriateness of the classification may be assessed by the Agency's enforcement personnel. The hazard communication audience is the worker/customer. The focus is on hazard identification and its subsequent communication. As has already been indicated in the description in the annex, the cut-off values were based on the need for protection, ease of application, and reasonableness of approach. It did not appear to OSHA at the time this rule was promulgated that there is any specific science that indicates an appropriate cut-off for any particular endpoint. It is a policy determination rather than a scientific one.

US: FHSA

76. U.S. regulations applicable to consumer products are based on the *Federal Hazardous Substances Act* (FHSA), which covers most consumer products, with exception of some specific types of consumer products, such as pharmaceuticals and cosmetics. Due to a difference in objective, consumer product labelling regulations are based on principles that are different from workplace systems such as the Hazard Communication Standard. The purpose of U.S. consumer product regulations is to protect the public from unreasonable risk associated with consumer products by communicating the likelihood of injury that could occur as a result of use and reasonable foreseeable misuse. Therefore, the U.S. regulations under FHSA incorporate critical elements in classification that allow determination of the likelihood of injury based on available exposure data. Since there are no formal mechanisms for training consumers or distributing MSDSs to them, the consumer product manufacturer must assume the combined role of the chemical supplier who develops information on hazards for MSDSs and labels, and the employers who are to utilise information on exposures to evaluate risk to support training. The additional information taken into account provides greater differentiation among hazards, thereby capturing the consumer attention to hazards that are likely to cause injury if not managed. This improves prospects that consumers will take appropriate precautions in handling materials.

V. DESCRIPTION OF EXISTING SYSTEMS

77. Appendix II of the DRD contains tables which compare the existing systems by end use: workplace, pesticides, consumer and cosmetics. In the European system the workplace and consumer products have similar requirements. In New Zealand the systems for the workplace, pesticides and consumer products are similar for chemicals used professionally and for consumers. See Appendix II Table IV-3 for a comparison of workplace systems, Table IV-4 for pesticides, Table IV-5 for consumer products and Table IV-6 for cosmetics.

78. This section also gives a detailed description of the workplace systems which include the standardised approach to untested mixtures, the role of test data and the role of national requirements compared to state, province and territory requirements. Table IV-2 compares the health endpoint cut-off values for the major workplace and transport systems. The major workplace systems, as well as the systems responding to the questionnaire other than the CPSC, all use concentration cut-offs as part of the standardised approach to mixture classification.

79. Under the OSHA HCS the chemical manufacturer, importer or employer is responsible for determining the hazard of the mixture. The appropriateness of the classification may be assessed by the Agency's enforcement personnel. In WHMIS the responsibility for the classification of the mixture rests with the Canadian supplier, distributor or importing agent. In the EU when preparations are placed on the market of the Member States, the manufacturer, or those responsible for placing on the market (importer, distributor or any other person) shall comply with the requirements of the Directive. The employer has the obligation to identify the hazards and risks in the work place.

WORKPLACE

Canada: The Workplace Hazardous Materials Information System (WHMIS)

Standardised approach

80. Workplace Hazardous Material Information System (WHMIS) of the *Controlled Products Regulations*: Controlled products that are untested mixtures with respect to one or more applicable toxicological endpoints specified in the CPR must be evaluated on the basis of the hazards associated with each ingredient present at a reportable concentration in the mixture. In the case of a controlled product that is an untested mixture, the mixture is generally considered to have the same toxicological hazards as the ingredients subject to disclosure present at or above the cut-off concentrations. WHMIS requires the disclosure of the chemical identity and the concentration of any ingredient of which toxicological properties are not known to the supplier. Information on toxicological properties should be provided without limiting such information to the hazards based on presumed use or exposure. There are no special considerations for mixtures based on physical state in WHMIS. Information that is applicable to the product should be reported. There are no special considerations in WHMIS for mixtures that separate. There are no special considerations for impurities/contaminants. Impurities/contaminants will be treated as hazardous ingredients if they meet WHMIS criteria. The Material Safety Data Sheet (MSDS) must list any substances, materials or products which interact with the controlled product to produce a toxic effect greater than the sum of their separate effects, if this information is available. There are no criteria/rules in WHMIS when concentrations of initial ingredients are changed or when new components that have very similar or the same properties are substituted.

81. Percentage: Reportable concentrations are 0.1% w/w or more for substances which meet the classification criteria for teratogenicity, embryotoxicity, carcinogenicity, reproductive toxicity, germ cell mutagenicity, or respiratory tract sensitisation. The concentration cut-off is 1% w/w for all other

toxicological criteria in WHMIS (i.e., acute and chronic toxicity, somatic cell mutagenicity, skin and eye irritation, skin corrosion and dermal sensitisation).

82. Acute toxicity LD_{50}/LC_{50} values: Where the LD_{50} or LC_{50} of one or more ingredients of a mixture is not known, the LD_{50} or LC_{50} of the mixture is equal to the most acutely lethal ingredient that is present in the mixture at a concentration of one percent or more.

Addition rule: If LD_{50}/LC_{50} values are known for each ingredient present in the mixture at 1% w/w, the product LD_{50}/LC_{50} may be calculated using the following formulas

for a solid or a liquid:

$$\frac{1}{LD_{50}\text{ of mixture}} = \frac{\text{Proportion of Ingredient A}}{LD_{50}\text{ of Ingredient A}} + \frac{\text{Proportion of Ingredient B}}{LD_{50}\text{ of Ingredient B}} + \frac{\text{Proportion of last Ingredient}}{LD_{50}\text{ of last Ingredient}}$$

for a gas, vapour, dust, mist or fume:

$$\frac{1}{LC_{50}\text{ of mixture}} = \frac{\text{Proportion of Ingredient A}}{LC_{50}\text{ of Ingredient A}} + \frac{\text{Proportion of Ingredient B}}{LC_{50}\text{ of Ingredient B}} + \frac{\text{Proportion of last Ingredient}}{LC_{50}\text{ of last Ingredient}}$$

Role of test data:

83. Tested Mixtures: Test data, when available, are the basis for classification of mixtures. If products have been tested, it is these data that are used for classification and MSDS disclosure.

84. Section 33(1) of the *Controlled Products Regulations* (CPR) states that for the purpose of establishing that a product in included in one of the six WHMIS classes, a supplier shall use: results from testing; or evaluation and scientific judgement based on tests results with respect to the product or where appropriate, a product that has similar properties. The supplier may also use information of which he is aware or ought reasonably to be aware in place of those criteria listed above.

85. The extent to which professional judgement is used by a supplier will depend on the specific criteria being considered. The WHMIS Information Bulletin No. 8 provides guidance on the use of professional judgement in the classification of controlled products under WHMIS.

86. Neither the *Hazardous Products Act* (HPA) nor the CPR impose a requirement for the testing of materials in order to classify them for any of the WHMIS classes. If a supplier (or employer, manufacturer or importer) decides to test a mixture, data would not have to be submitted to a governmental agency for review. Therefore, it is impossible to determine if testing relates to ingredients or mixtures.

Note: However, there is one exception. In some instances an employer, supplier, importer or manufacturer may not wish to disclose the identity or concentration of an ingredient in a controlled product. In this case, a trade secret claim may be filled with the Hazardous Materials Information Commission (HMIRC) for exemption from the full requirements of WHMIS. All toxicological data that were used to prepare the MSDS would have to be submitted to the HMIRC for review. Most of the WHMIS

controlled products reviewed for trade secrets are untested mixtures with respect to toxicological properties.

87. Incomplete Data Set: When complete test data is not available on the mixture itself, one may also use human data, professional judgement and test results with a product, material or substance that has similar properties.

88. Bridging Data/Extrapolation: When all end points are not tested, ingredient data are used for toxicity end points that were not tested. Professional judgement may also be used. There are no bridging rules or criteria for extrapolation of data in the workplace legislation. On the other hand, there are no provisions per se in WHMIS that would prevent the use this approach.

Note: It is the supplier who has the legal responsibility to determine if a product meets WHMIS criteria. Therefore, as specified in CPR Section 33(2), "...the supplier may use information of which the supplier is aware or ought reasonably to be aware..." for classification. WHMIS Information Bulletin No. 12 states: Any toxicological information resulting from tests on a mixture must be disclosed if available and applicable to the mixture. Information relating to ingredients subject to disclosure must be disclosed if this information is applicable to the mixture.

Role of federal legislation

89. The federal legislation requires suppliers of hazardous workplace materials to label containers and provide MSDS as a condition of sale and importation. Since the provinces and territories have constitutional responsibility over matters relating to occupational safety and health (OSH) and Human Resources Development Canada (HRDC) is responsible for OSH matters in federally-regulated work sites, complementary and interlocking WHMIS legislation in each of these jurisdictions requires employers to classify material used in the workplace, to provide labels, MSDSs and worker education and training programs.

European Union: Dangerous Preparations Directive

Standardised approach

90. The object of classification is to identify all the toxicological, physico-chemical and ecotoxicological properties of substances and of preparations which may constitute a risk during normal handling or use.

91. Classification of substances is based on their intrinsic properties according to the categories of danger (very toxic, toxic, harmful, corrosive, irritant, sensitizing, carcinogenic, mutagenic, toxic to reproduction, explosive, oxidising, extremely flammable, highly flammable, flammable, dangerous for the environment). The general principles of classification of substances and preparations shall be applied according to the criteria in Annex VI to Directive 67/548/EEC save where contrary requirements for dangerous preparations are specified in separate Directives.

92. One or both of the following procedures cause classification of preparations

- Evaluation of test results and application of criteria of Annex VI to Directive 67/548/EEC. Testing is not allowed for preparations containing carcinogenic, mutagenic or toxic to reproduction substances.

- application of the conventional method based on classification of component substances and their concentrations in a preparation.

- if it can be demonstrated that toxicological effects on man based on epidemiological findings, by scientifically valid case studies or by statistically backed experience such as the assessment of data from poison information units or occupational diseases would differ from those deriving from the procedures of classification than the preparation must be classified according to the effects on humans.

Classification of mixtures [seen in humans] according to Directive on Dangerous Preparations/EU

93. Health hazards: The classification of mixtures can be carried out on the basis of the results of appropriate animal tests, or by applying the conventional method. Where it can be demonstrated that effects differ from those determined by either one or both methods, the classification must be based on the effects on humans.

94. The appropriate test methods are described in the Annex V to Directive 67/548/EEC.

95. The application of the conventional method according to Directive 88/379/EEC is based on a principle that the conventional method should provide a similar result of hazard assessment as testing of a preparation ensuring a high level of protection envisaged by this regulation. The method avoids using test animals and provides an inexpensive way of assessment in particular for the use by small and medium size enterprises.

96. All toxicological end points for preparations shall be assessed either on the basis of test results or by the conventional method. If the preparation has been tested for some endpoints, the test results are used for classification for those end points. All other end points have to be assessed by applying the conventional method. However, carcinogenic, mutagenic or toxic to reproduction

properties should always be determined by the conventional method rather than animal testing, because the results of such tests are not considered to be sufficiently reliable.

97. The conventional method is based on following fundamentals:

- classification of the substance
- concentration of the substance in the mixture
- concentration limit for the classification

98. The application of the conventional method requires first classification of substances present in the preparation. The substances are classified either in Annex I to Directive 67/548/EEC (harmonised classification) or provisionally by the person responsible for placing on the market of the substance or preparation on the basis of available data and application of classification criteria of Annex VI to Directive 67/548/EEC.

99. The data that are available for different end points shall be used. If the data for substances are based on tests, which have been carried out according to test guidelines the data are directly applicable for classification. If the data are not according to test guidelines the value of the data have to be assessed for the classification purposes (expert judgement).

100. By the evaluation of the dangerous properties of a preparation by the conventional method the calculation should be done by using the real concentration of the substance in the preparation. The substances are taken into account if the cut-off limits for classification are exceeded. When the additivity calculation for classification is applicable the concentrations of substances to be taken into consideration are 0.1% for very toxic and toxic substances and 1% for corrosive, irritant and harmful substances.

101. The concentration limits for classification are applied when the component substances are first classified. General concentration limits for classification of preparations are specified for all toxicological end points by Directive 88/379/EEC. In the case of substances for which individual concentrations limits are specified in Annex I of Directive 67/548/EEC, mixtures containing these substances should be classified by reference to those substance-specific limits. In these cases the substance-specific limits should be used. In any other cases the general limits laid down in the Directive 88/379 are applicable.

102. If no data are available for certain end points the preparation is not classified for those end points.

103. For some of the end points e.g. for acute toxicity decreasing ranges of concentration limits are used. The rationale behind this is that below the general concentration limit for an acute lethal effect like very toxic, the preparation can still be toxic or harmful at an even lower concentration.

104. The same principle applies to a property like corrosivity, where lower concentrations limits are also applied to take into account irritation effects.

105. A similar conventional method is proposed for the assessment of environmental hazards in the proposal for the new Directive on dangerous preparations. The applicability of test results for properties dangerous for the environment is restricted for the reason that certain tests are not suitable for mixtures.

106. Physico-chemical hazards are assessed by tests.

107. The result of the classification is the identification of the category of hazards to which the preparation is attached and which indications of special risks are associated with the preparation, for example, C, R34: Corrosive, causes burns, N, R50: dangerous to the environment, very toxic to aquatic organisms. The information on the label of a dangerous preparation is directly derived from classification

Concentration limits for classification

108. The concentration limits for the classification of a preparation for different endpoints of health effects are described in tables 1 and 2 for liquids and solids and tables 1a and 2a for gases. A similar conventional method to that described for health effects is proposed for the assessment of environmental hazards in the proposal for the new Directive on dangerous preparations. The concentration limits for the classification of preparations for the environmental effects are described in table 3 according to the new proposal for the Directive of dangerous preparations.

Table 1 Concentration limits for classification of preparations (solids and liquids) for their acute lethal effects and corrosive or irritant effects, properties for which additivity may apply

Classification of the substance	Classification of the preparation			Classification of the preparation			
	T+, R26, R27, R28 Acute lethal effects	T, R23, R24, R25 Acute lethal effects	Xn, R20, R21, R22 Acute lethal effects	C, R35 Severe burns	C, R34 Burns	Xi, R41 Serious damage to eyes	Xi, R36, R37, R38 Irritates eyes, respiratory system or skin
T+, R26, R, 27, R28 Acute lethal effects	conc. $\geq$ 7%	1% $\leq$ conc. < 7%	0.1% $\leq$ conc. < 1%	-	-	-	-
T, R23, R24, R25 Acute lethal effects	-	conc. $\geq$ 25%	3% $\leq$ conc. < 25%	-	-	-	-
Xn, R20, R21, R22 Acute lethal effects	-	-	conc. $\geq$ 25%	-	-	-	-
C, R35 Severe burns	-	-	-	conc. $\geq$ 10 %	5 % $\leq$ conc. < 10 %	conc. = 10%	1% $\leq$ conc.< 5% R36/38
Xi, R41 Serious damage to eyes	-	-	-	-	-	conc. $\geq$ 10%	5% $\leq$ conc. < 10% R36
Xi, R36, R37, R38 Irritates eyes, respiratory system or skin	-	-	-	-	-	-	conc. $\geq$ 20% R36, R37, R38
C, R34 Burns	-	-	-	-	conc. $\geq$ 10%	conc. = 10%	5% $\leq$ conc. < 10% R36/38

Notes to Table 1: Concentration limits for classification of preparations (solids and liquids) for their acute lethal effects and corrosive or irritant effects, properties for which additivity may apply

- The table shows that an acute lethal effect or a local effect (corrosive/irritant) is considered to be diluted with a diluted concentration.

- The properties of acute lethal toxicity expressed by classification of component substances as T+, T and Xn with appropriate R-phrases are considered to be additive. The same applies to corrosive and irritant properties expressed by C or Xi with appropriate phrases. This is justified by the assumption that the mechanisms causing these effects are similar.

- If the concentration of a component substance does not exceed the limits for classification given in the table the concentrations of similar substances are summarised and the sum of concentrations is compared with the classification limit. This principle can be expressed by a formula in a general form:

$$\sum \frac{p_i}{L_i} \geq 1$$

where p_i = the concentration of a dangerous substance in a preparation, L_i = the concentration limit for classification.

- The lowest concentrations to be taken into consideration are for very toxic and toxic substances 0.1 % and for harmful, corrosive and irritant substances 1 % unless lower values are given in Annex I to Directive 67/548/EEC.

- An application of the formula can be illustrated by an example:

  a preparation contains:

  - 0.5 % of a toxic substance A with T R25,
  - 1 % of a toxic substance B with T R25 and
  - 20 % of a harmful substance C with Xn R22.

- Any concentration of the components does not exceed the classification limit as toxic or harmful. The formula is then applied:

$$\frac{P_A}{L_{Xn}} + \frac{P_B}{L_{Xn}} + \frac{P_C}{L_{Xn}} =$$

$$\frac{0.5}{3} + \frac{1}{3} + \frac{20}{25} = 1.3 \geq 1$$

The sum is $\geq$ 1 which means that the preparation is classified as harmful Xn with R22.

Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply

Classification of the substance	Classification of the preparation												
	T+, R39 Non- lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. Cat. 1 or 2	Carc. Cat. 3	Muta. Cat. 1 or 2	Muta. Cat. 3	Repro tox Cat. 1 or 2	Repro tox. Cat. 3
T+, R39, Non-lethal irreversible effects	conc. ≥ 10%	1% ≤ conc. < 10%	0.1% ≤ conc. < 1%	-	-	-	-	-	-	-	-	-	-
T, R39 Non-lethal irreversible effects	-	conc. ≥ 10%	1 % ≤ conc. < 10%	-	-		-	-	-	-	-	-	-
Xn, R40 Non-lethal irreversible effects	-	-	Conc. ≥ 10%	-	-	-	-	-	-	-	-	-	-
T, R48 Severe effects after repeated or prolonged exposure	-	-	-	conc. ≥ 10%	1% ≤ conc. < 10%	-	-	-	-	-	-	-	-

Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non- lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. Cat. 1 or 2	Carc. Cat. 3	Muta Cat. 1 or 2	Muta Cat. 3	Repro tox Cat. 1 or 2	Repro tox cat. 3
Xn, R48 Severe effects after repeated or prolonged exposure	-	-	-	-	conc. ≥ 10%	-	-	-	-	-	-	-	-
Xn, R42 Sensitizing effects, inhalation	-	-	-	-	-	conc. ≥ 1%	-	-	-	-	-	-	-
Xi, R43 Sensitizing effects, skin	-	-	-	-	-	-	Conc. ≥ 1%	-	-	-	-	-	-
Carc., cat. 1 or 2	-	-	-	-	-	-	-	conc. ≥ 0.1%	-	-	-	-	-
Carc., cat. 3	-	-	-	-	-	-	-	-	Conc. ≥ 1%	-	-	-	-

Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non- lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversi ble effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitizing effects, inhalation	Xi, R43 Sensitizing effects, skin	Carc. Cat. 1 or 2	Carc. Cat. 3	Muta. Cat. 1 or 2	Muta. Cat. 3	Repro tox Cat. 1 or 2	Repro tox cat. 3
Muta. cat. 1 or 2	-	-	-	-	-	-	-	-	-	conc. ≥ 0.1%	-	-	-
Muta. cat. 3	-	-	-	-	-	-	-	-	-	-	conc. ≥ 1%	-	-
Reprotox. cat. 1 or 2	-	-	-	-	-	-	-	-	-	-	-	conc. ≥0.5%	-
Reprotox. cat. 3	-	-	-	-	-	-	-	-	-	-	-	-	conc. ≥ 5%

Notes to Table 2 Concentration limits for classification of preparations (solids and liquids) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply

- The additivity does not apply to those health effects which are listed in table 2. Concentration of a component substance is compared directly with the classification limit of table 2. If the limit is exceeded the preparation is classified, if it is not exceeded that preparation is not classified.

- The irreversible effects after single exposure and effects of long-term or repeated exposure are categorised according to the dose causing the effect. Again with diluted concentration the effects are also linearly diluted which results in milder classification in diluted concentrations.

- Both skin and respiratory sensitisers are recognised in the EU system to belong to the same category of danger and as a consequence, only one limit is applied for classification.

- The categorisation of carcinogens, mutagens and toxic to reproduction substances is based on evidence, not on severity of effects. Only one limit is applied for classification in each category of c/m/r.

Table 3 Concentration limits for classification of preparations (solids and liquids) for environmental effects
Acute aquatic toxicity and long-term adverse effects, dangerous for the ozone layer

Classification of the substance	Classification of the preparation								
	N, R50-53 Very toxic to aquatic organisms and may cause long-term adverse effects	N, R51-53 Toxic to aquatic organisms and may cause long-term adverse effects	R52-53 Harmful to aquatic organisms and may cause long-term adverse effects	N, R50 Very toxic to aquatic organisms	R52 Harmful to aquatic organisms	R53 Long term adverse effects	N, R59 Dangerous for the ozone layer	R59 Dangerous for the ozone layer	Note
1. N, R50-53 Very toxic to aquatic organisms and may cause long-term adverse effects	Conc. $\geq$ 25 %	2.5 $\leq$ conc. < 25 %	0.25 $\leq$ conc. < 2.5 %						Additivity applies
2. N, R51-53 Toxic to aquatic organisms and may cause long-term adverse effects		Conc. $\geq$ 25 %	2.5 $\leq$ conc. < 25 %						Additivity applies
3. R52-53 Harmful to aquatic organisms and may cause long term adverse effects			conc. $\geq$ 25 %						Additivity applies
4. N, R50 Very toxic to aquatic organisms				conc. $\geq$ 25%					Additivity applies

Table 3 Concentration limits for classification of preparations (solids and liquids) for environmental effects Acute aquatic toxicity and long-term adverse effects, dangerous for the ozone layer (cont.)

Classification of the substance	Classification of the preparation								
5. R52 Harmful to aquatic organisms					**Conc. ≥25 %**				**Additivity applies**
6. R53 Long term adverse effects						**Conc. ≥ 25 %**			**Additivity applies**
7. N, R59 Dangerous for the ozone layer							**Conc. ≥ 0.1 %**		**-**
8. R59 Dangerous for the ozone layer								**Conc. ≥ 0.1 %**	**-**

If the concentration of a component substance does not exceed the limits for classification given in the table the concentrations of similar substances are summarised and the sum of concentrations is compared with the classification limit.

Notes to Table 3 Concentration limits for classification of preparations (solids and liquids) for environmental effects, Acute aquatic toxicity and long-term adverse effects, dangerous for the ozone layer

- This principle can be expressed by a formula in a general form:

$$\sum \frac{p_i}{L_i} \geq 1$$

where:

P_i = the concentration of a substance dangerous for the environment in a preparation,
L_i = the concentration limit for classification.

- The additivity is restricted to certain cases. Concentrations of components of the following boxes of table 3 can be summarised:
  - boxes 1 to 3 to assess the acute aquatic toxicity in combination with long term adverse effects
  - boxes 1 and 4 to assess very toxic acute effects to the aquatic organisms
  - box 5 to assess harmful acute effects to the aquatic organisms
  - boxes 1, 2, 3 and 6 to assess adverse long term effects to the aquatic environment

  Additivy is not applied to substances which may cause dangers for the ozone layer.

- The lowest concentrations to be taken into consideration are 0.1 % for substances which are very toxic or toxic to aquatic organisms, whether or not in combination with long term adverse effects in aquatic environment. The lowest concentrations to be taken into consideration are 1 % for substances which are harmful to aquatic organisms, and/or which pose long-term adverse effects in aquatic environment, unless lower values are given in Annex 1 to Directive 67/548/EEC.

- An application of the formula can be illustrated by an example: A preparation contains:

  a substance A which is very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. The classification is N, R50-53 and concentration 0.1%

  a substance B which is toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. The classification is N, R51-53 and the concentration 2%

  a substance C which is harmful to aquatic organisms and may cause long term adverse effects in the aquatic environment. The classification is R52-53 and the concentration 20%

Any concentration of the individual components does not exceed the classification limit as dangerous for the environment. The formula is then applied:

$$\frac{P_A}{L_{R52-53}} + \frac{P_B}{L_{R52-53}} + \frac{P_C}{L_{R52-53}} > 1$$

The sum is >1 which means that the preparation is classified as harmful to aquatic organisms and may cause long-term adverse effects in the aquatic environment, R52-53.

Table 4 Concentration limits for classification of preparations (gases) for their acute lethal effects and corrosive or irritant effects, properties for which additivity may apply

Classification of the substance	**Classification of the preparation**			**Classification of the preparation**			
	T+, R26, R27, R28 Acute lethal effects	**T, R23, R24, R25 Acute lethal effects**	**Xn, R20, R21, R22 Acute lethal effects**	**C, R35 Severe burns**	**C, R34 Burns**	**Xi, R41 Serious damage to eyes**	**Xi, R36, R37, R38 Irritates eyes, respiratory system or skin**
T+, R26, R, 27, R28 Acute lethal effects	**conc. ≥ 1 %**	**0.2 % ≤ conc. < 1 %**	**0.02 % ≤ conc. < 0.2%**	**-**	**-**	**-**	**-**
T, R23, R24, R25 Acute lethal effects	**-**	**conc. ≥ 5 %**	**0.5 % ≤ conc. < 5 %**	**-**	**-**	**-**	**-**
Xn, R20, R21, R22 Acute lethal effects	**-**	**-**	**conc. ≥ 5 %**	**-**	**-**	**-**	**-**
C, R35 Severe burns	**-**	**-**	**-**	**conc. ≥ 1 %**	**0.2 % ≤ conc. < 1 %**	**conc. 0.2 %**	**0.02 % ≤ conc.< 0.2 %**
C, R34 Burns	**-**	**-**	**-**	**-**	**conc. ≥ 5 %**	**conc. 5 %**	**0.5 % ≤ conc. < 5 %**
Xi, R41 Serious damage to eyes	**-**	**-**	**-**	**-**	**-**	**conc. ≥ 5 %**	**0.5 % ≤ conc. < 5 %**
Xi, R36, R37, R38 Irritates eyes, respiratory system or skin	**-**	**-**	**-**	**-**	**-**	**-**	conc .≥ 5 %

Table 5 Concentration limits for classification of preparations (gases) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply

Classification of the substance	Classification of the preparation												
	T+, R39 Non-lethal irreversible effects	T, R39 Non-lethal irreversible effects	Xn, R40 Non-lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. cat. 1 or 2	Carc. cat. 3	Muta. cat 1 or 2	Muta. cat. 3	Repro tox cat. 1 or 2	Repro tox cat. 3
T+, R39, Non-lethal irreversible effects	**conc. ≥ 1%**	**0.2% ≤ conc. < 1%**	**0.02% ≤ conc. < 0.2%**	-	-	-	-	-	-	-	-	-	-
T, R39 Non-lethal irreversible effects	-	**Conc. ≥ 5%**	**0.5% ≤ conc. < 5%**	-	-	-	-	-	-	-	-	-	-
Xn, R40 Non-lethal irreversible effects	-	-	**conc. ≥ 5%**	-	-	-	-	-	-	-	-	-	-
T, R48 Severe effects after repeated or prolonged exposure	-	-	-	**conc. ≥ 5%**	**0.5 % ≤ conc. < 5%**	-	-	-	-	-	-	-	-

Cont. Table 5 Concentration limits for classification of preparations (gases) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non-lethal irreversible effects	T, R39 Non- lethal irreversible effects	Xn, R40 Non- lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R42/43 Sensitising effects, skin	Carc., cat. 1 or 2	Carc., cat. 3	Muta. cat. 1 or 2	Muta. cat. 3	Repro tox cat.1 or 2	Repro tox cat. 3
Xn, R48 Severe effects after repeated or prolonged exposure	-	-	-	-	conc. $\geq$ 5%	-	-	-	-	-	-	-	-
Xn, R42 Sensitising effects, inhalation	-	-	-	-	-	conc. $\geq$ 0.2%	-	-	-	-	-	-	-
Xi, R43 Sensitising effects, skin	-	-	-	-	-	-	conc. $\geq$ 0.2%	-	-	-	-	-	-

Table 5 Concentration limits for classification of preparations (gases) for other than acute lethal effects and corrosive or irritant effects, properties for which additivity does not apply (cont.)

Classification of the substance	Classification of the preparation												
	T+, R39 Non-lethal irreversible effects	T, R39 Non-lethal irreversible effects	Xn, R40 Non-lethal irreversible effects	T, R48 Severe effects after repeated or prolonged exposure	Xn, R48 Severe effects after repeated or prolonged exposure	Xn, R42 Sensitising effects, inhalation	Xi, R43 Sensitising effects, skin	Carc. cat. 1 or 2	Carc. cat. 3	Muta. cat. 1 or 2	Muta. cat. 3	Repro tox cat. 1 or 2	Repr tox cat. 3
Carc., cat. 1 or 2	-	-	-	-	-	-	-	conc. $\geq$ 0.1%	-	-	-	-	-
Carc., cat. 3	-	-	-	-	-	-	-	-	conc. $\geq$ 1%	-	-	-	-
Muta. cat. 1 or 2	-	-	-	-	-	-	-	-	-	conc. $\geq$ 0.1%	-	-	-
Muta. cat. 3	-	-	-	-	-	-	-	-	-	-	conc. $\geq$ 1%	-	-
Reprotox. cat. 1 or 2	-	-	-	-	-	-	-	-	-	-	-	conc. $\geq$0.2 %	-
Reprotox. cat. 3	-	-	-	-	-	-	-	-	-	-	-	-	conc. $\geq$ 1%

Role of test data

109. Tested Mixtures: In cases where appropriate data are available hazard classification based on test data overrule those from the conventional method (standardised approach). This does not apply to cases where the preparation contains substances which are classified as carcinogenic, mutagenic or toxic to reproduction. The test results for mixtures containing substances with carcinogenic, mutagenic and toxic to reproduction properties are not accepted for hazard classification. This is due to the way tests for a substance for these endpoints are designed. In order to explore the worst case situation and to reveal the potential effects when extrapolating the results to humans, the test system for an individual substance is optimised in different ways. For example the dose is chosen so as to be the maximal tolerated dose and the number of animals in the test groups is chosen so as to give sufficient statistical power for the test to detect an effect for an individual substance.

110. If a mixture is tested the dose of a (potentially) carcinogenic, mutagenic or reproductive toxic substance can become unacceptably low. In that case the test system will not be sufficiently sensitive and these potential toxic effects will not be revealed. It is also difficult to interpret the test results when testing a mixture; for example it may not be possible to know which component has caused a certain effect. Besides these arguments the testing of mixtures for these endpoints would lead to a big increase in the use of test animals.

111. Incomplete Data Set: The classification is carried out on the basis of test data where the test data are available for the end point. All other end points are then assessed by applying the conventional method (standardised approach).

112. Bridging Data/Extrapolation: If a preparation has been tested for its health effects, the composition of the preparation may vary according to the following table without having to carry out a new assessment. If the variation of concentration of constituents is greater, the assessment shall be carried out again either by testing or by application of the conventional method (standardised approach). A new assessment (either by testing or by conventional method) shall be carried out if any of the constituents is substituted or other components are added. This will apply unless there is valid scientific justification for considering that re-evaluation of the hazard will not result in a change of classification.

Table 6 EU Permitted Concentration Variations

Initial concentration range of the constituent (w/w %)	Permitted variation in initial concentration of the constituent
Conc. < 2.5 %	± 15 % [30 %]#)
2.5 % < Conc. = 10 %	± 10 % [20 %]#)
10 % <Conc. = 25 %	± 6 % [10 %]#)
25 % < Conc. = 50 %*)	± 5 % [5 %]#)
50 % <Conc. =100 %*)	± 2.5 % [5 %]#)

#) The concentration will be changed according to the new Directive on Dangerous Preparations.

*) The range will be changed according to the new Directive on dangerous preparations to 25-100 %.

113. Other Considerations: Where it can be demonstrated by epidemiological studies, by scientifically valid case studies or by statistically backed experience that toxicological effects differ from those

suggested by application of the conventional method or by testing then the preparation shall be classified according to its effects on man. Also effects such as potentiation and antagonism of the component substances shall be taken into consideration in the classification in cases, where application of the conventional method would not give a correct classification for the mixture.

114. Structure activity relationship (SAR) may be applied as supportive evidence in the assessment of mixtures only for component substances when the conventional method is applied for the classification of the mixtures as a whole. Application of SAR method to substances is rather limited. Advice for application of QSAR will be given by the revision of Annex VI to directive 67/548/EEC (25th ATP to Directive 67/548/EEC).

Role of regional legislation

115. The Treaties establishing the European Communities provide the overarching legislative framework for introducing more specific measures into Member State's territories in those area where the Community has competence. These measures can be introduced by various routes notably through Regulations (which are directly applicable in Member States); through Council Directives (where Member States are required to transpose the directive into national legislation): or through Commission Directives. Commission Directives provide a simpler means for addressing issues of scientific detail and adaptation to technical progress. Authority to agree Commission Directives is delegated to official level and they are not subject to political agreement through the full European Parliamentary process.

116. There are a number of Treaty base options (e.g. Article 118a worker protection, Article 100a harmonisation, Article 130 r, s and t environmental protection) for introducing regulations or directives selected on the basis of the subject matter and whether it is feasible to set minimum or harmonised standards in a particular area. Treaty articles are not mutually exclusive so for example worker protection or public health issues may be a primary consideration under a harmonisation directive. Additionally as the treaty bases are closely inter-linked legislative proposals in similar subject areas need to be consistent and compatible to support the broader Community objectives.

117. European Community legislation places obligations on Member States regulatory authorities, employers, employees and economic operators.

Information on countries or regions outside EU applying the EU system

118. Non EU blocs operating/applying the EU system for the classification, packaging and labelling of dangerous preparations include the major Eastern European states who have begun to implement the EU system in readiness for possible entry to the Union. Viz Estonia, Latvia, Lithuania, Poland, Czech Republic, Slovakia, Hungary, Slovenia, Romania, Bulgaria. Similarly Cyprus have also applied for membership of the EU.

119. Australia has adopted chemicals legislation which follows the EU system, but there is provision for testing all endpoints.

120. Norway and Iceland comply with the EU system according to the agreement on the European Economic Area with minor exemptions. Switzerland is in the process of transforming the national legislation on the basis of the EU model.

TRANSPORT: UNCETDG

121. Substances (including mixtures and solutions) and articles are assigned to one of nine classes according to the hazard or the most predominant of the hazards they present. Some of these classes are subdivided into divisions. With regard to health and environmental hazards the following classes and divisions are relevant : Division 2.3: Toxic gases Division 6.1: Toxic substances Division 6.2: Infectious substances Class 8 : Corrosive substances Class 9 : Miscellaneous dangerous substances and articles.

General

122. The UN transport system is under the responsibility of the UNCETDG and comprises of the UN Recommendations on the Transport of Dangerous Goods, which has, as an annex, the Model Regulations on the Transport of Dangerous Goods, (UNRTDG) and a supplementary publication the Manual of Tests and Criteria. The "Manual of Tests and Criteria present the United Nations schemes for the classification of certain types of dangerous goods and gives descriptions of the test methods and procedures, considered to be the most useful, for providing competent authorities with the necessary information to arrive at a proper classification of substances and articles for transport". They have also been used in some countries as a basis for supply.

123. The UN MRTDG, in chapter 3.2, contains its own expertly classified database of substances and articles. There are four types of entries in this database:

(a) Single entries for well defined substances or articles (substances).

(b) Generic entries for well defined groups of substances or articles (mainly mixtures).

(c) Specific n.o.s. (not otherwise specified) entries covering a group of substances or articles of a particular chemical or technical nature (mainly substances).

(d) General n.o.s. covering a group of substances or articles meeting the criteria of one or more classes or divisions (substances or mixtures, but mainly mixtures).

For the purposes of classification of any substance or mixture;-

a type (b) entry is only assigned if it is not already assigned to a type (a) entry
a type (c) entry is only assigned if it cannot be assigned to an entry of type (b)
a type (d) entry is only assigned if it cannot be assigned to an entry of type (c)

Dangerous goods not already classified in the expertly classified database may be classified by the consignor in conformity with the laid down procedures and rules. However in some cases classification can only be made by the competent authority of the originating country of the transport operation.

124. The nine (hazard) 'classes', or 'divisions' of classes are assigned to 'packing groups' according to the degree of hazard:

Packing Group I	Substances presenting high danger
Packing Group II	Substances presenting medium danger
Packing Group III	Substances presenting low danger

In some cases these packing groups take into account other factors such as packaging size or viscosity which affect the perceived risk during transport. These classifications and packing groups determine downstream consequences such as permitted packaging types and sizes, hazard communication etc. These downstream consequences can be further affected by the packaging size.

Gas mixtures

125. In the UN MRTDG there is no default system for the classification of all mixtures based on percentage concentration limits of substances in mixtures. However in some endpoints formulae are given for deriving the classification of mixtures based on the classification of components. In the expertly classified database, the classification of mixtures is generally based upon human experience or derived from the application of the classification criteria. Some of these entries in the database are qualified with special provisions, some of which contain additional criteria for classification. It includes entries for both substances and mixtures, including in some cases relevant concentration limits. The UN MRTDG also contain expanded lists of classifications for some endpoints where only 'n.o.s.' entries are included in the database, i.e. for self reactive substances and organic peroxides. Many of these entries relate to mixtures.

Mixtures of liquids toxic by inhalation

Health Hazards

126. Acute toxic health hazards are determined for three routes of administration, oral, dermal and inhalation and assigned to packing groups for each on the basis that in the absence of human experience the grouping shall be based on data obtained in animal experiments. Simplified threshold toxicity tests are acceptable for the inhalation toxicity of vapours. In the case of mixtures, there are formulae for calculation methods in some endpoints.

Acute Toxicity

(A) Gases – Class 2

The level of toxicity is determined either by tests to measure the LC_{50} value or by a calculation method using a formula. When LC_{50} values are unknown, the toxicity index may be determined by using the lowest LC_{50} value of substances of similar physiological and chemical effects.

(B) Liquids and Solids – Class 6; Division 6.1

Oral and Dermal Toxicity

(a) If there is only one hazardous component in a mixture, the mixture LD_{50} is taken to be the LD_{50} of the hazardous component times 100 divided by its percentage concentration.

(b) If there is more than one hazardous component, the preferred method is to obtain reliable acute oral and dermal toxicity data on the actual mixture. If reliable accurate data is not available, then the mixture LD_{50} may be taken to be the LD_{50} of the most hazardous component at the total concentration of all hazardous components; or

(c) If the LD50's of all components are known, the mixture LD50 may be calculated by formula.

The calculation is done per route of application

(ii) Inhalation toxicity of dusts and mists

There is no formula for the calculation of LC_{50} values of mixtures.

(iii) Inhalation toxicity of vapours

Where LC_{50} data is available on each toxic component, the LC_{50} value of the mixture can be determined according to a formula adjusted for volatility. In the absence of relevant data, the classification may be assigned on the basis of a simplified threshold toxicity testIf the LC_{50} data are available for each of the toxic substances, the LC_{50} of the mixture is evaluated on the basis of the LC_{50} for each substance and of its molar fraction. Otherwise a simplified threshold toxicity test (on albino rats) is allowed.

Mixtures of toxic (oral and dermal toxicity) substances

Corrosivity

127. Corrosivity is classified solely on the basis of full thickness skin destruction, but it is to be noted that in Class 2 Gases and in Division 5.2 organic peroxides, reference is made to eye damage.

Gases – Class 2

A gas mixture is classified as being toxic with a corrosive subsidiary risk either on the basis of human experience or when the LC_{50} value of the corrosive components of the mixture is calculated according to a formulaIf a mixture contain only one toxic substance, whose LD_{50} is known, the mixture is classified on the basis of the LD_{50} evaluated as: (LD_{50} of the substance) x 100/ % in mass.

Environmental hazards

128. In the UNRTDG classification for environmental effects is not directly addressed. In the IMDG Code (maritime transport) mixtures are classified as "marine pollutants" if they contain more than 10% of a marine pollutant or more than 1% of a severe marine pollutant.

129. In RID/ADR (land transport in Europe) if a mixture contain only one environmental hazardous substance, whose LC_{50} is known, the mixture is classified as environmentally hazardous on the basis of the LC_{50} (for fishes, daphnia or algae) evaluated as: (LC_{50} of the substance) x 100/% in mass.

Wastes

130. Wastes are classified according to the same rules for classification as other substances or mixtures.

Special cases

131. For some entries in the Dangerous Goods List there is a Special Provision where limits of concentration are specified for the dangerous component, so that under that limit the mixture is no more classified as dangerous (e.g. "An aqueous solution containing not more than 24 % alcohol by volume is not subject to these regulations").

US: OSHA HCS

Standardised approach

132. US OSHA Hazard Communication Standard (HCS): Where test data are not available, mixtures are assumed to have the same health hazards as do the components which comprise one percent (by weight or volume) or greater of the mixture as a whole.

133. Exceptions: Mixtures are considered carcinogenic for purposes of hazard communication when they comprise 0.1% (by weight or volume) or greater of the mixture as a whole.

134. If there is evidence that a component present in concentrations less than one percent (0.1% for carcinogens) can be released in concentrations that would exceed OSHA's established permissible exposure limits or ACGIH's recommended exposure limits, or presents a health hazard to employees in those lower concentrations, the mixture is assumed to be hazardous for purposes of hazard communication.

Role of test data

135. Tested Mixtures: If test data are available on the mixture as a whole, the classification is to be based on the data. Chemicals may have test data for some endpoints and not others. If there are no data for a particular end point, the classification for that health effect would be based on the standardised approach.

136. Incomplete Data Set: Classification is based on test data where available, and the end points where no data are available are classified based on the standardised approach. If the toxicity of components is unknown, there is no requirement to cover them. The HCS does not require testing, and structure-activity relationships are also not a required part of the evaluation process.

137. Bridging Data/Extrapolation: No. The classification is to either be based on actual test data or on the standardised approach.

138. Similar Mixtures: There is a limited exception under the HCS which does not fit neatly into the 3 categories of mixtures outlined. Where there are complex mixtures with similar contents and hazards, a single data sheet may be used to convey the hazards of more than one mixture. For example, petroleum streams may vary slightly in composition in terms of the percentage of a certain ingredient, but the hazard of the mixture would not be different because of that variation. In that situation, OSHA would allow the manufacturer to use the same data sheet even though the composition may vary. This is expected to be

applied only in very narrow circumstances. Under the HCS, negative data may never negate the finding of hazard. Chemical manufacturers and importers may report such data on the MSDS, as well as indicate their interpretations of its relevance, but the MSDS must be provided and the positive data must be reported.

Role of federal legislation

139. Under the OSH Act there is intent to pre-empt state laws in areas where federal OSHA has promulgated occupational safety and health laws. Presently, there are several states (CA, NJ, PA) which have laws promulgated for related purposes (environmental protection, drinking water safety, etc.) that have hazard communication requirements in addition to the federal requirements. The HCS applies in the workplace when employees are exposed to a chemical under normal conditions of use or in a foreseeable emergency. There are no special considerations for susceptible populations. Generally speaking, OSHA's policy has always been to protect all types of workers under its standards rather than trying to separate out certain parts of the worker population. In addition, children and the elderly are not usually part of the worker population.

140. Impurities and contaminants are treated as are any other component. There are no special considerations for synergistic and antagonistic effects of ingredients in a mixture, but it would be expected that these would be taken into account when known. As already noted, where mixtures are similar in concentration, hazard, and content, the HCS allows a single MSDS to suffice to meet the requirements. Thus slight reformulations that don't change the overall hazard should not result in new MSDSs. Exposure, potency, and seriousness of effect are not taken into consideration under the HCS. The scheme is used for hazard communication purposes only, that is, labels, MSDSs and training. There is a link to community right-to-know provisions implemented under EPA requirements. Other risk management approaches in OSHA's standards include a full range of protective measures, from engineering controls to personal protective equipment. The chemical manufacturer or importer conducting the hazard determination is responsible for interpreting and using the data available. The hazard determination is to be based on all available evidence, both animal and human data. The chemical manufacturer or importer is held responsible for identifying the required data, and for ensuring that the data meets the standard's requirements to be conducted according to scientific principles and having statistically significant results. If there is one such study that indicates an adverse health effect, the substance or mixture or component of a mixture is considered to be hazardous. Professional judgement is applied to determining the quality of the data and whether it meets the specified criteria. Otherwise, there is little professional judgement applied to untested mixtures since the percentage cut-off rule is applicable. OSHA may conduct its own hazard determination in order to ascertain whether the one performed by a chemical manufacturer or importer is appropriately done. If we find that it is not, they may be cited for non-compliance.

141. Information provided by companies may relate to the mixture as a whole or to individual components, based upon the availability of test data. OSHA does not require testing - all determinations are based on available data. MSDSs provide key information to downstream employers in designing and implementing effective employee protection programs. Before the HCS was adopted, such employers frequently had no information about the components of a mixture, or the potential hazards of products they are using. While the manufacturer or importer can provide such information about the products, it is the employer who knows how the product is used in the workplace, what other exposures there may be, and what protective measures are available. Thus the concept of risk is best introduced by the using employer with access to all of this information. That risk concept translates to selection and implementation of the protective measures best suited to the particular combination of hazards and exposure levels in the workplace.

Table 7 Workplace
Untested Mixture Classification Concentration cut-off Values (%) By Toxicity End Point

END POINT	*WHMIS*	*EU*		*OSHA HCS*	*UNCETDG*	
		solid/liquid	gas		solid/liquid	gas
Acute Toxicity (LD_{50} & LC_{50})	1	0.1, 1.0, 3, 7, 25	0.02,0.2, 0.5,1.0, 5	1	no %	no %
Carcinogenicity	0.1	0.1, 1		0.1	NA	NA
Reproductive Toxicity	0.1	0.5, 5	0.2, 1	1	NA	NA
Skin Sensitisation	1	1	0.2	1	NA	NA
Respiratory Sensitisation	0.1	1	0.2	1	NA	NA
Eye Irritation	1	20	0.02, 0.2,	1	NA	NA
Skin Irritation	1	20	0.5, 5	1	NA	NA
Corrosion to Skin	1	1, 5, 10	0.2, 1, 5	1	NA	no %
Corrosion to Eyes	1	1, 5, 10	0.2, 1, 5	1	NA	NA
Germ Cell Mutagenicity	0.1	0.1	0.1	1	NA	NA
Somatic Cell Mutagenicity	1	1	1	1	NA	NA
Target Organ -Chronic Toxicity	1	1, 10	0.5, 5	1	NA	NA

142. In the European system for classification of mixtures cut-off concentration limits for component substances are set for classification. When a preparation is classified on the basis of acute toxicity, corrosive/irritant effects or effects dangerous for the aquatic environment the concentrations of components not exceeding alone the limits for classification are summed-up and the sum is compared with the classification limit. (additivity principle). For the other end points each component substance is compared individually with respect to its end point limit to classify the mixture accordingly. However, when substance specific concentration limits exist for individual components of the mixture in Annex I to Directive 67/548/EE, these limits must be used when applying the standardised method.

143. Further more, the agreed classification criteria recognise the dilution of effects by specifying different cut-off limits for acute toxicity and for effects dangerous for the aquatic environment as well as for scores (or time dependent effects) for corrosive/irritant effects. These criteria would be followed if mixtures were tested in different concentrations of same compounds. (dilution principle)

144. The lowest concentrations of component substances that are taken into consideration are specified for application of the classification system for mixtures and in particular for the application of additivity principle.

145. In the case of acute toxic substances for instance, the value to take this end point into consideration is 0.1% whereas the cut-off limits for classification of the mixture for its acute toxicity is 3%.

146. The limits are specified for end points in the new Directive on dangerous preparations, but are included also in the present Directive. The lowest concentrations that are taken into consideration (unless

lower concentration limits are specified in Annex I to Directive 67/548/EEC or in the Annexes of preparations Directive) are presented in the following table:

Table 8

Category of danger of the substance	Concentrations to take into consideration	
	Gaseous preparations %vol/vol	Other preparations % w/w
Very toxic	0.02	0.1
Toxic	0.02	0.1
Carcinogenic,Category 1 and 2	0.02	0.1
Mutagenic,Category 1 and 2	0.02	0.1
Toxic for reproduction Category 1 and 2	0.02	0.1
Harmful	0.2	1.0
Corrosive	0.02	1.0
Irritant	0.2	1.0
Sensitising	0.2	1.0
Carcinogenic, Category 3	0.2	1.0
Mutagenic, Category 3	0.2	1.0
Toxic for reproduction, Category 3	0.2	1.0
Dangerous for the environment, N		0.1
Dangerous for the environment, Ozone	0.1	0.1
Dangerous for the environment		1.0

PESTICIDES

147. A comparison of the major classification systems for pesticides is given in Appendix II Table IV-4. In all systems, available test data on active ingredient, pesticide mixtures, formulations or marketable preparations are used to classify pesticide mixtures. Acute toxicity (oral, dermal, inhalation) end points are used for classification of mixtures in all systems. The requirement for testing skin irritation, eye irritation, sensitisation, neurotoxicity, carcinogenicity, reproductive effects and ecotoxicity vary among the systems and, in some cases, within systems depending upon the intended use of the pesticide. In the EU, if the correctness of the classification on the basis of calculation method is open to doubt, the competent authorities may require that the calculation be replaced by toxicological tests. The EU specifies the classification rules that are used by the Member State Competent Authorities for the purposes of classification. There is no standardised approach in the US or Canada for determining the hazards of an untested mixture. In Table IV-4, for example, reference is made to expert judgement, on a case-by-case basis, similarity of products and waiving of test data requirements.

Canada

148. In Canada, the *Pest Control Products Act* (PCPA) governs the registration of pesticides. Studies to identify acute hazards are performed on the active ingredient and end-use product. The active ingredient is also subjected to subchronic, chronic, reproductive and genotoxicity testing. The potential risk for the proposed use, considering risk mitigation measures such as user restrictions, education programs, protective equipment or other means determines the acceptability of the product for registration. Conditions under which the product is used are considered in the determination of risk, but foreseeable misuse is not a factor in assessing the hazard component of the risk equation.

149. In Canada, the petitioner for registration is responsible for hazard determination and proposed classification (market class designation, hazard symbols, and signal words). The regulatory authority, the Pest Management Regulatory Agency, verifies the appropriateness of the classification.

Definitions

150.

- *Substance/chemical*: chemical elements/entities and their constituents, as they occur in the natural state or produced by industry, e.g. technical grade active ingredients including impurities/contaminants resulting from the manufacturing process which can be further utilized in preparations and "chemical soups" such as creosote which may also be used in preparations. (Adapted from the EC)

- *Preparations*: a mixture or solution composed of two or more substances at least one of which is a pesticidal active ingredient; the mixture is not known to, or is not expected to chemically react (irreversibly) to form other chemical entities. (Adapted from the EC)

NB: The terms "substance" and "preparation" are not utilised in the Canadian pesticides scheme. The above two definitions represent PMRA adaptations of the EC terms. The corresponding terms used within PMRA would be "active ingredient" and "end-use product (also referred to as a formulated product), respectively.

- *Active ingredient*: that ingredient of a control product to which the effects of the control product are attributed, including a synergist, but does not include a solvent, diluent, emulsifier or component that by itself is not primarily responsible for the control effect of the control product. (Source: Regulations of the Pest Control Products Act)

- *Non-active ingredient or formulant*: a material intentionally added to a technical active ingredient during formulation of an end-use product to improve its physical characteristics, e.g., sprayability, solubility, spreadability, and stability. (Source: Registration Handbook, a PMRA document designed to provide updated information on the registration process as well as general guidance for petitioners of pesticide registration submissions.)

- *End-use product*: a product containing active ingredients(s) and usually non-active ingredients(s) that is labelled with instructions for pest control use. (Source: Registration Handbook)

Classification of pesticide mixtures

151. PMRA does not define toxicity categories/classes for classification purposes as does the United States with its four toxicity categories. But based on criteria and cut-off values (e.g. LD_{50}) a determination is made for appropriate market classification (domestic, commercial, restricted market classification). Information regarding classification of end-use products or mixtures is provided in what is known as the Registration Handbook. It contains information on market classes (for all intents and purposes representative of the Canadian classification scheme) and the associated safety criteria, cut point values for the classification of acute hazard as well as glyph or symbol usage.

Labelling

152. Regulations stipulate that pesticide labelling must contain information reflecting the nature and degree of hazard. Specific requirements for categorisation (i.e., cut-off values for toxicity classes) for acute toxicity (i.e. oral, inhalation and dermal), skin and eye irritation and sensitisation are not stated in the regulations. Identification of hazard is accomplished through the use of appropriate precautionary symbols and signal words on the label. These symbols and signal words pertain to acute toxicity and physical hazards. Consideration of factors such as the physical form of a pesticide product or the use of tamper-proof packaging can impact on the need for acute hazard labelling. It is appropriate to say, therefore, that labelling is based on a regulatory requirement to identify acute hazards, although risk considerations also play a part in some cases.

153. Products are not labelled for non-acute toxicity endpoints (carcinogenicity, reproductive toxicity, etc).

Toxicity testing

154. Acute toxicology testing is required to support registration and to provide the basis for labelling of active ingredients and mixtures. Acute oral, dermal, inhalation toxicity, skin and eye irritations, as well as skin sensitisation studies form the core battery of required tests. Acute neurotoxicity studies are required for products for which effects on the nervous system are anticipated due to chemical class (organophosphates, carbamates,) or other information. Waivers for testing are considered on a case-by-case basis taking into consideration known characteristics of the components (e.g. irritative properties), physical form (e.g. waxy or gummy resins not representing an inhalation hazard), or other scientifically sound information.

Data waivers / bridging data

155. While Canadian pesticide regulatory authorities may accept bridging data to characterise acute hazards for a mixture (formulation), the onus is on the petitioner to develop this rationale and make the necessary arrangements to use another data source (i.e., another company) for bridging purposes. PMRA must respect confidential business information when using data from one registrant's product to support a second registrant's product. It is up to the petitioner to demonstrate safety of their particular submission, thus Canadian pesticide regulatory authorities would look to the petitioner to demonstrate that the new formulant would not alter the toxicological profile of the formulation. PMRA would consider the use of existing acute toxicology data if a less toxic formulant has replaced a more toxic one or request new acute studies only for those of the studies whose results are expected to alter (e.g. irritation studies) with the new non-active ingredient. The request for the study waivers considers the fact that the properties of the new formulant may affect the overall toxicology profile, even though a comparison of the formulants may reveal that the toxicity of each is similar. Replacing a formulant to reduce eye irritation, for example, may lead to another hazard or a change in degree of an existing hazard.

156. If sufficient acute toxicity data is available for a range of concentrations of all of the ingredients in an end-use product, PMRA may be able to interpolate for toxicities of products falling within this range, providing the range of concentration falls within the same cut-off values for market classification and precautionary labelling.

157. If a petitioned product is an aqueous dilution of a product with supporting acute data, PMRA may use this data to support the petitioned product. The data would not be used as a quantitative determination of toxicity and only used in cases where there is no ambiguity with regards to the appropriate precautionary labelling. The new product would be placed in the same toxicity level as the supporting data. This approach has most merit when the well-characterised product is of low toxicity/hazard potential.

158. Where a product represents the highest hazard/toxicity level and ingredients are changed which would maintain or increase the toxicity, PMRA could use the toxicity data on the existing product keeping the new product in the highest level.

159. If a pesticide product is characterised as a dermal sensitiser, this designation will not be changed if the product is reformulated with a different concentration of the sensitising ingredient.

160. A product or active ingredient with a pH of less than 2 or greater than 11.5 should not be tested for skin or eye irritation, but will be assigned to the highest level for irritation. A product or active ingredient, which is corrosive to the skin, should not be tested for eye irritation, but will be assigned to the highest level for eye irritation.

Formulants

161. The identity and quantity of the pesticide active ingredient(s) must be disclosed on the product label according to legislation. Disclosure of formulants is not required. Information regarding the identity and quantity of formulants in pest control products is considered confidential business information and is protected from disclosure. However, any formulants which have been identified on EPA List 1 Inerts of Toxicological Concern are disclosed on the product label using the following statement: "This product contains x percent of the ingredient y which has been identified as having toxicological concerns." This disclosure is a policy and is not part of the legislation. In addition, PMRA has moved away from the use of the term "inert" or "non-toxic" ingredient in describing the non- active ingredients of a formulation as many of these may be inherently toxic.

Other issues

162. Acute toxicity testing on a mixture may give an initial indicator of possible antagonism or synergism from the combination of the ingredients.

163. There are no special considerations for mixtures that separate.

European Union

164. The legislative system of the European Community for pesticides consists of two different pieces of legislation. Firstly, provisions on the classification, packaging and labelling and secondly provisions on authorisation of pesticides for the market.

165. Specific provisions concerning placing of plant protection products (agricultural pesticides) and biocides (domestic pesticides, disinfectants, wood preservatives etc.) on the market set conditions and requirements for authorisation. They specify also testing requirements for authorisation purposes.

166. The present provisions for classification and labelling of pesticides are outdated in the European Community as they cover only a few dangerous properties. The new Directive on classification and labelling of dangerous preparations will include also pesticides in the scope allowing all dangerous properties to be taken into consideration in the classification. Biocides (domestic pesticides, disinfectants, wood preservatives etc.)are covered by the general provisions for classification and labelling.

167. Competent authorities apply the provisions for classification when specifying the classification and labelling for a plant protection product or a biocide for the authorisation. The conventional method for

classification is applicable. If the pesticides are tested for authorisation purposes then they will be classified on the basis of test results.

United States

168. US EPA: In the United States, the Federal Fungicide, Insecticide and Rodenticide Act (FIFRA) provides for classification of all pesticides with attendant labelling. The Act gives the Office of Pesticides Programs in the US the authority to regulate pesticides for any health or environmental endpoint. This includes labelling, data collection, establishment of criteria for endpoint categorisation and labelling, or establishing restrictions on use. Regulations have been promulgated which specify that all pesticides be labelled for acute toxicity (oral, inhalation, dermal), skin irritation, eye irritation, sensitisation, and toxicity to fish and wildlife and pollinating insects. In addition, pesticides have been labelled for carcinogenicity and reproductive effects. Each pesticide product is labelled for its own individual hazards as determined from data submitted for registration. Pesticides are classified and labelled for all conditions of use be they normal use, accidents, misuse, etc. System assumes a wide range of scenarios from workplace to residential use. Classification under FIFRA has consequences in addiction to hazard communication such as restricting use to certified applicators for highly toxic pesticides. Many risk management practices can be used. For example, application may be allowed only in closed cabs. Hazard assessment is done by skilled scientific experts in the pesticide program who evaluate toxicological data on pesticide active ingredients and products. Standard Evaluation Procedures have been issued for this assessment. OSHA has the authority to require MSDS's for pesticides. However, the severity of labelling language and symbols required under FIFRA affects the choice of products purchased in the marketplace. Pesticide producers often reformulate to achieve less severe warning language and symbols. In those cases, bridging logic may be applicable to reduce retesting.

Definition of substance/chemical, mixture/preparation

169. The statute, under sec. 2(a), defines pesticides, active ingredients and inerts. Most pesticide products are preparations or mixtures. Products consist of at least one active ingredient and one or more inert ingredients.

170. Under the regulations in 40CFR Part 152.3, Active Ingredient means any substance (or group of structurally similar substances if specified by the Agency) that will prevent, destroy, repel or mitigate any pest, or that functions as a plant regulator, desiccant, or defoliant within the meaning of FIFRA sec. 2(a). The technical grade of the active ingredient is the active chemical as it is produced in the factory.

171. Inert Ingredient means any substance (or group) other than an active ingredient, which is intentionally included in a pesticide product.

172. Pesticide Product means a pesticide in the particular form (including composition, packaging, and labelling) in which the pesticide is, or is intended to be, distributed or sold. The term includes any physical apparatus used to deliver or apply the pesticide if distributed or sold with the pesticide. Pesticide products can be manufacturing use products or end use products. End use products consist of the technical grade of the active ingredient and all inerts in the formulation as it is intended to be applied for pest mitigation. Manufacturing use products are products other than end use products and consist of the technical grade of the active ingredient and stabilisers or solvents.

Classification of pesticides

173. The Office of Pesticide Programs, using data and information provided by pesticide registrants classifies all pesticide products. Pesticide products can be end use products, manufacturing use products, or the technical grade of the active ingredient if the technical pesticide is a manufacturing use pesticide. (See the appendix for definitions.)

174. Applicants for pesticide registrations submit health and safety data. The Agency has promulgated regulations under 40 CFR Part 158 that describe the data required for registration.

175. Studies for acute hazards are performed on the active ingredient and each formulated product. Studies for chronic health hazards are performed on the active ingredient. Studies for aquatic hazards are performed on the active ingredient and typical products; products that are substantially similar to typical products may not require testing.

Classification for environmental hazards

176. Labelling for aquatic hazards of pesticide products is based on data for the active ingredient only. At 40 CFR.Part 156.10(h)(2)(B), regulations require that "If a pesticide intended for outdoor use contains an active ingredient with a fish acute LC_{50} of 1 ppm or less, the statement "This pesticide is Toxic to Fish" is required for the pesticide product.

Classification for acute health hazards

177. The pesticide registrant has the obligation to test each active ingredient and all pesticide products for all acute human hazard endpoints subject to hazard labelling. Pesticide products are classified for acute toxicity by the oral, dermal and inhalation routes and for skin and eye irritation and sensitisation. The regulations at 40 cfr Part 156.10 require that all pesticide products be labelled if they fall into one of 4

hazard categories for acute toxicity, sensitisation, or irritation. The Agency has a policy of accepting bridging data to characterise substantially similar products for acute human hazard.

178. Pesticides are generally biocidal in nature and classification and labelling are intended to be protective to workers and bystanders. Bridging provides a way of using existing experimental data to characterise new products, amplified only by the addition of such data that are necessary to elucidate differences among products, while conserving resources and eliminating unnecessary animal testing. Inherent in the Agency's bridging policy are incentives for registrants to reformulate for safer products in that not all endpoints always need retesting.

179. If the Agency determines that a product (pesticide active ingredient and at least one inert ingredient) is substantially similar to a registered product, experimental data may not be needed to characterise all or any of the acute hazards of the similar product. The Agency's policy and the decision logic for use of bridging data is described below.

Case A: If a product is experimentally characterised for acute toxicity, irritation and sensitisation, and an inert ingredient is changed, additional testing may not be needed if the Agency determines that the new inert is of equivalent toxicity to the original inert. However, if the new inert has the potential to be of different toxicity in one of the six acute hazards, for example skin irritation, the new product can be accepted for registration upon submission of test data for that area (skin irritation in this example). When the new and original inert ingredients are both of moderate toxicity, the Agency may use published data and information on toxicity to determine their relative toxicities. In some cases, an inert of moderate toxicity is replaced with an inert which is totally nontoxic. Such inerts are comprised of fillers such as corncob grits or foods such as vegetable oil or cookie crumbs. Nontoxic inerts are on the Agency's List D and are typically classified as Generally Recognised as Safe (GRAS) by the Food and Drug Administration.

For example, registrants may wish to reformulate a product to remove precautionary statements about eye irritation. To that end, they may replace a surfactant (surfactants are often irritants) with a non-irritating inert such as vegetable oil. The new formulation would be tested only for eye irritation and the new toxicity category would be applied to it for that hazard, i.e. the data bridged from currently registered products would cover the new formulation; in essence the data is cited or waived. The formulation would not be required to be tested for the other acute endpoints, but rather the original classifications would apply.

Case B: If two ingredients are used in two different ratios in two pesticide formulations and data are available for toxicity of both products and both products fall within the same toxicity category, the Agency can interpolate for toxicities of products with intermediate

concentrations of the two ingredients without requiring additional testing.

Case C: When a product contains more water than a registered product that is fully characterised as to its toxicity, the Agency will adjust the lethality value according to the dilution factor and assign a classification based on the adjusted lethality. However, in the absence of testing, the new product will be assigned to the irritation and sensitisation toxicology category of the original more concentrated product. Generally, this case also applies to reformulation using nontoxic (List D) inerts.

Case D: If a registered product which is in the highest toxicity category (category I) is reformulated by removing water or other non-toxic ingredients, the new formulation is also assigned to toxicity category I. If the original product is not in the highest toxicity category for lethality and it is reformulated by removing some or all of its non-toxic ingredients, and if information is provided to show that the mechanism of toxicity of the toxic ingredients is not to be subject to enhancement by concentration, then a new toxicity category may be assigned by adjusting the formulation's lethality values according to the change in concentration.

180. An example of a situation when concentration factors would not allow the original data to be bridged is as follows. Products which are corrosive could gain faster entry into the body when more concentrated. In those cases, the toxicity could be enhanced when the product is concentrated.

181. Sensitization: If a pesticide product is characterised as a sensitiser, the classification for this endpoint will not be changed if the product is reformulated to change the concentration, but not remove, the sensitiser.

182. Other considerations: A product or active ingredient with a pH of less than 2 or greater than 11.5 need not be tested for skin or eye irritation, but will be assigned to the highest class for irritation. A product or active ingredient which is corrosive to the skin need not be tested for eye irritation, but will be assigned to the highest classification for eye irritation.

CONSUMER PRODUCTS

183. A comparison of the major classification systems for consumer products is given in Appendix II Table IV-5. In the USA, classification of consumer product is not restricted to hazard, but is based on the likelihood of injury, which accounts for dose-response and exposure. The consumer product regulations in the USA do not cover consumer pesticides, food nor pharmaceuticals. The EU system for classification of consumer products, with some exceptions, is the same as the EU workplace system. In Canada and the USA the manufacturer, importer or distributor is responsible for the classification; testing is not required; and there is flexibility where there is incomplete data. Canada does have a standardised approach for consumer product mixtures, as does the EU. In the USA, there is not a standardised approach for the classification of consumer products.

Canada

184. The criteria apply only to components or generated products to which the user or others might become exposed in normal use or reasonably foreseeable use. The Regulations do not apply to a consumer chemical product if a user cannot be exposed to the product or to any of its hazardous ingredients during normal use or reasonably foreseeable use.

185. For consumer chemical products the following steps are used in the process of test data interpreted/used:

- Human experience data take precedence over data from animal experimentation in categorising products. Human experience data means data demonstrating that an injury to a person or a reversible or irreversible material impairment to the health or functional capacity of a person could result from a) exposure to a consumer chemical products; or the foreseeable use of a consumer chemical product or container by a consumer, in particular, the consumption of the product by a child.

- LD_{50} and LC_{50} values from tests conducted according to the OECD Test Guidelines for acute toxicity testing have been adopted as the core of the criteria scheme.

- When tests on animals are not appropriate or have not been conducted in accordance with the OECD Test Guidelines, results of other acute toxicity tests of the product or of its ingredients, conducted in accordance with a) a national standard or a recognised international standard, or b) a generally accepted procedure that accorded with good scientific practices at the time the tests were conducted are accepted.

186. If the product is a mixture, the LD_{50} and LC_{50} of each ingredient in the product that is present at a concentration of 1% or more, are determined using the additivity formula.

187. Results of tests conducted on or with a product, material or substance that has similar properties, in a) a national standard or a recognised international standard or b) a generally accepted procedure that accorded with good scientific practices at the time the tests were conducted, or c) other current information about the product that is known to the scientific community are accepted.

188. The use of professional judgement takes precedence over the use of a mathematical formula in estimating the toxicity hazard. Under the umbrella of professional judgement, it would be necessary to examine the human data - where it comes from and to what end-point it is being applied. For example, some epidemiological studies for chronic end-points may be biased or the human sample size too small to be acceptable, whereas, a well-conducted study for skin irritation on 1000 humans would be acceptable. There will always be different opinions or judgements on what is considered reliable data. The task of determining what data is reliable is the challenge or reality we must accept.

189. For consumer systems, the use of bridging data is not specifically required, however, may be covered under the umbrella of professional judgement.

190. If the mixture as a whole is not tested, then provisions exist for estimating the toxicity of the mixture based on the toxicity of the individual components e.g., the additivity formula.

191. If the LD_{50} or LC_{50} of one or more ingredients present in the toxic product in a concentration of 1% or more is not known, the person responsible may use an estimated LD_{50} or LC_{50} determined in accordance with good scientific practices. Where the LD_{50} or LC_{50} is unknown and cannot be estimated,

the LD_{50} or LC_{50} of the untested component be equal to the LD_{50} or LC_{50} of the most toxic known component present at over 1% w/w. (Note: This value is then used in the additivity formula to determine the LD_{50} or LC_{50} for the mixture). A cut-off is needed when using the additivity formulas because many products contain large numbers of trace components which, while not significantly affecting the toxicity, would render use of the additivity formulas prohibitively complex. The specific cut-off value, 1% w/w, is the same as that specified in the *Controlled Products Regulations* (WHMIS).

192. A list of substances of special concern have been developed for substances which are known to be toxic through human experience, test results or professional judgement, each substance is classified differently according to whatever the concentration of the toxic component is found in a mixture. For example, products containing ethylene glycol are classified as toxic when found in solutions greater than or equal to 5% w/w, where if found in concentrations less than 5% w/w but greater than or equal to 2% w/w are classified as harmful. There are 10 substances of special concern for consumer chemicals. These substances are of special concern because standard animal tests may not reflect the actual hazard posed by them to humans.

193. Some criteria e.g., flammability are based on physical state, while other e.g., toxicity are divided based on route of exposure. For the inhalation route of exposure, gases, vapours and dusts/mists have different criteria.

194. Components of consumer chemical products may separate out over time, especially in the case of emulsions of petroleum distillates. Estimation of the toxicity of the product as a whole in such cases may significantly misrepresent the hazard when the upper supernatant layer will be accessible as a distinct mixture or solution and may be so ingested by a child. Therefore, in the case of a supernatant mixture, the toxic product must be assigned the LD_{50} or LC_{50} value of the most toxic layer.

195. No consideration for impurities/contaminants less than 1% (w/w), however, if the supplier is aware that this impurity constitutes a hazard, then professional judgement would take precedence, whether the guidelines called for it or not.

196. No consideration for synergistic and antagonistic effects. There have been few systematic studies of toxicological interactions among the chemicals commonly present in consumer products. One large study of interactions determined the oral LD_{50}'s of all possible combinations of 27 industrial chemicals, including carbon tetrachloride, ethanol, ethylene glycol and toluene. The ratios of measured to predicted LD_{50}'s (predicted using the additivity formula) were mostly very close to 1, with some random variation above and below. Other studies have shown similar results. Thus the available information indicates that the acute toxicity of mixtures of such chemicals is reasonably well predicted by the additivity formulas.

197. Equivalent formulas have been adopted by regulatory agencies for calculating the occupational exposure limits of mixtures of hazardous substances in air. For example, the American Conference of Governmental Industrial Hygienists (ACGIH), which develops the Threshold Limit Values (TLVs), advises that "in the absence of information to the contrary, the effects of the different hazards should be considered as additive."

198. There are no specific criteria for mixtures that would not require new evaluations when concentrations of initial ingredients are changed or new components that have very similar or the same properties are substituted. If the product is changed, then there would be a need to reclassify to ensure that the labelling does not change too, particularly where classification would be increased.

199. Exposure (risk) and seriousness of effect are taken into consideration for consumer products. This is dealt with through the warning labels. For classification criteria, potency has not specifically been

dealt with at this point since potency, which mainly applies to chronic end- points, have not yet been developed for consumer products.

200. Risk of exposure is considered by consumer products. For example, if components are inaccessible to the user during normal use or reasonably foreseeable use, then they are not subject to the criteria.

201. Classification also determines which products will require pre-market review (permission prior to sale) and which products will require child-resistant containers.

202. In addition to labelling, the *Consumer Chemicals and Containers Regulations* requires certain products (determined by classification) be packaged in child-resistant containers to reduce the likelihood of injury and illness should a child come in contact with a product. No specific regulatory requirements exist for training or other exposure control systems. A consumer education and information program has been established, however, this does not compare to the training received by workers. In additions, engineering controls and personal protective equipment are not necessarily present in homes.

European Union

203. For consumer products the general scheme of the EU directive of preparations is followed for their hazard classification in order to make it possible to apply a hazard warning. The manufacturer has the responsibility that no health damaging products may be put into the market by applying a full risk evaluation.

204. For some categories of consumer products a full risk evaluation is done as foreseen by Community Directives and consequently a more risk based warning system is applied. These categories are therefore exempted from the substances and preparations directives. The following preparations in the finished state, intended for the user are exempted: medicinal products for human or veterinary use, cosmetic products, mixtures in the form of waste, foodstuffs, animal feeding stuffs, radioactive substances, other substances or preparations for which Community notification or approval procedures exist and for which requirements are equivalent to the substances directive 67/548/EC.

US: FHSA

205. In the USA, consumer products are generally regulated under the requirements of the *Federal Hazardous Substances Act* (FHSA). There are exceptions, however, including consumer product pesticides, food, drugs and cosmetics, all of which are addressed under the requirements of other agencies. The Consumer Product Safety Commission (CPSC) is responsible for implementing the FHSA requirements. As noted in Table IV-5, the primary objective of CPSC's regulations is to determine the likelihood of injury or illness posed by the product**.**

206. In order to accomplish this, the manufacturer, importer or distributor of a product must evaluate all available information to ascertain what the potential hazards of the product may be. This would be based on test data where available, but testing is not obligatory. The assessors may also use published data, past experience on similar products, human experience or an expert opinion. The assessment may be based on the chemical composition in some situations; SAR; extrapolation; or estimation. While there is no standardised approach using percentage cut-offs or concentration limits, formulae from the scientific literature may be used to predict the hazard when data permit. Evaluations based on extrapolation or estimation would be considered under the category of bridging data.

207. CPSC's regulations may result in a label on the product. The Agency considers the process of "classification" to include both the identification of the hazard and an assessment of the likelihood of harm to the user under normal conditions of use or foreseeable misuse. Criteria for classification and labelling for acute hazards and physical effect were derived as values that posed likelihood of injury from a single exposure and thus do not require further assessment of likelihood of injury, the Agency however require an assessment of likelihood of injury or illness to be performed when determining whether a chronic hazard is to be placed on the label. The evaluator may take into consideration the dose or exposure expected when the product is used by consumers in determining whether the hazard needs to be included on the label. The underlying assumption to this approach is that consumer exposure is often brief and intermittent, and, unlike worker exposure situations, not of a nature to lead to the development of a chronic health effect. While this is an issue that will ultimately be addressed under the work of the ILO on hazard communication, it is a basic difference in approach from the other systems' consumer products requirements that should be factored into the discussions in this area. Additional technical factors regarding the US CPSC mixtures approach in response to the questions posed:

- CPSC considers substantial personal injury or substantial illness as a result of any customary or reasonably foreseeable handling or use, including reasonably foreseeable ingestion by children. Susceptible population groups such as children or the elderly are given special consideration in the determination of likelihood of injury or illness for their increased susceptibility and special exposure conditions and other similar factors.

- If the toxicity of the components is unknown the mixture is tested. Since our system is based on the likelihood of adverse effects, if a component is not available or accessible for exposure, its contribution may not be taken into consideration. However, when a mixture is tested the values obtained are used for classification, even if the component did or did not contribute to the toxicity.

- The mixture is thoroughly mixed before test is conducted. Special consideration is not given unless there is clear impact on potential for adverse effects. Impurities and contaminants are treated in the same manner as other components.

- When the toxicity of a mixture is determined by extrapolation from toxicity of components and the synergistic or antagonistic effects of ingredients is clearly established, such an effect may be taken into account. Expert judgement that takes into account the toxicity of the components that have changed and the change in concentration provide guidance when the formulation of a mixture changes.

- With regard to bridging data, CPSC allows the use of test data, toxicity values extrapolated from the toxicity of components, human data including experience and expert opinion based on available valid and acceptable data. Extrapolation is similar to the bridging used by EPA.

Valid and acceptable human data including experience take precedence over other data.

- All relevant factors that may impact the likelihood of injury or illness from the use of a mixture are considered during the classification process. These include exposure, potency, and others.

- Classification system in itself is not used for purposes other than labelling. However, generally classification is first step in evaluation of adverse impact on health. In addition or in lieu of labelling, other appropriate regulatory steps may be taken to reduce or eliminate the adverse health impact. In order to reduce or eliminate adverse health impact from a substance or mixture, in addition to appropriate regulatory action (including labelling but independent of labelling), CPSC may prepare educational material for public distribution, or may provide public service announcements on radio and television.

COSMETICS

208. A comparison of the major classification systems for cosmetics is given in Appendix II Table IV-6. Regulation of cosmetics in Canada, the EU and the USA does not include hazard classification for cosmetics at the point of consumer use. Classification criteria will not be developed for these cosmetic mixtures. However, cosmetic mixtures are covered in some workplace systems and these product mixtures will be further considered in the classification criteria proposal. There is no standardised approach to mixtures.

ENVIRONMENTAL HAZARDS

209. The existing procedures for determining the environmental hazard of mixtures are less well-defined than the procedures for determining the hazard for human health. Appendix V presents the criteria used in the EU system based on measured or calculated toxicity.

210. It should be noted that a systematic approach to the classification of the environmental hazards for mixtures has been proposed in the EU system. Some systems use only a single aquatic toxicity cut-point to define the hazard of a mixture. For some systems, where a mixture contains a chemical with a known toxicity, the hazard of a mixture is determined by a concentration cut-off point. Moreover such cut-offs may vary (i.e., chemical specific).

211. The new GHS classification system for hazardous for the environment, which was recently approved at the OECD, depends on combinations of three levels of acute toxicity, ready biodegradation and potential for bioaccumulation. The system provides for three levels of environmental hazard. A Guidance Document concerning data interpretation and application in the classification system. This guidance will have important implications for classifying both dilute solutions of one hazardous chemical and mixtures of two or more hazardous chemicals.

212. The UNRTDG and the Canadian TDG Regulations are expected to be changed, and the EU criteria and procedures have been amended but not yet formally adopted. The IMDG Code classifies substances as ‘severe marine pollutants’ or ‘marine pollutants’ based upon the proposal of GESAMP. In addition to the adverse effects on aquatic organisms, other effects like ‘tainting’ are taken into account. It

has been proposed within IMO to delete the tainting criteria, but no formal decision has yet been made. Mixtures are classified only as marine pollutants based upon a concentration limit of 10% for marine pollutants and 1% for severe marine pollutants. No guidance is given for the classification of mixtures containing both marine pollutants and severe marine pollutants below these threshold limits

United States

Regulations under *Federal Insecticide, Fungicide and Rodenticide Act*

213. Labelling for aquatic hazards of pesticide products is based on data for the active ingredient only. Regulations require that "if a pesticide intended for outdoor use contains an active ingredient with a fish acute LC_{50} of 1ppm or less, the statement: "This pesticide is toxic to fish" is required for the pesticide product regardless of the concentration of the active ingredient. It the other components of the pesticide formulation are toxic or may affect the toxicity, i.e., by enhancing the uptake of the active ingredient, the formulation is to be tested and the lowest toxicity is used for classification.

Canada

Transport

214. The current Canadian Transport of Dangerous Goods Regulations treat Class 9 somewhat differently than the UNRTDG. The Class has three Divisions: 9.1 Miscellaneous dangerous goods; 9.2 Hazardous to the environment; and 9.3 Dangerous Wastes. Divisions 9.2 and 9.3 would be applicable to

215. All classifications of 9.2 have been assigned by the competent authority. Where a subsidiary classification of 9.2 has been assigned, that classification becomes primary in a mixture only when the cut-point of the original classification (acute toxicity, corrosivity, flammability, etc.) has been surpassed. Cut-points for environmentally hazardous substances beyond which transport regulations no longer apply are substance specific and are measured in kg of substance per package.

Pesticides

216. The Pest Management Regulatory Agency does not have an environmental hazard classification *per se* for pest control products. Testing for acute toxicity to fish, aquatic and terrestrial inverta, plants and birds is required for each active ingredient and the lowest NOEC, NOEL or EC's for plants is used directly in a risk assessment related to the planned or expected use of the product. These assessments are used to establish conditions for safe use, e.g., buffer zones, which are included on the label.

217. PMRA is proposing to use various environmental criteria (including toxicity to fish and birds, bioaccumulation potential and a leaching index) as criteria for the establishment of restricted, commercial and domestic control product categories. These criteria would supplement the existing toxicity (i.e., acute mammalian LD_{50} criteria).

HAZARDOUS WASTES

218. While the charge for the development of the GHS is contained in Chapter 19 of Agenda 21 of the UNCED Agreements, which relates to the environmentally sound management of toxic chemicals, hazardous wastes are dealt with in Chapters 20 (management of hazardous waste), 21 (management of solid waste and sewage-related issues), and 22 (management of radioactive wastes). The management of hazardous wastes internationally is the subject of extensive efforts under the Basel Convention, on the Management of Hazardous Wastes. Therefore, the classification of hazardous wastes is not included in the

scope of work the OECD Expert Group on Cassification Criteria for Mixtures and subsequently, also not in that of the ILO Working Group on Hazard Communication.

219. The Annexes to the Basel Convention include definitions of hazardous wastes and lists of wastes and waste streams within various hazard classes. Under the Basel convention, "wastes" are generally defined as substances or objects which are disposed of or are intended to be disposed of or are required to be disposed of by the provisions of national law. The hazardous characteristics covered by the convention include: explosive, flammable liquids, flammable solids, substances or wastes liable to spontaneous combustion, substances or wastes which, in contact with water emit flammable gases, oxidising, organic peroxides, poisonous (acute), infectious substances, corrosives, liberation of toxic gases in contact with air or water, toxic (delayed or chronic), ecotoxic, capable, by any means, after disposal, of yielding another material, e.g., leachate, which possesses any of the characteristics listed above.

220. Generally, hazardous wastes are classified in the same way as dangerous goods are in the UN Regulations on the Transportation of Dangerous Goods (UNRTDG). Hazardous wastes are those dangerous goods:

- that are no longer used for their original purpose, and
- that are intended for treatment and/or disposal, or
- that are recyclable materials.

221. Wastes that do not fall under the UNCETG classification criteria but fall under the Basel Convention are covered under Class 9.

222. In view of these activities within the hazardous waste sector, no summaries have been included in the Appendix to the document.

223. The answers by the major systems to the additional question on hazardous wastes from the questionnaire are given below.

Canada

224. Hazardous wastes are presently exempt from workplace (WHMIS) classification. They are classified only if they have to be transported and are classified and labelled according to the Transport of Dangerous Goods Regulations.

European Union

225. Directive 75/442/EEC on waste with a modification of Directive 91/156/EEC introduces a definition for waste:

> "any substance or object contained in Annex I (note that this is irrelevant because of entry 16 of Annex I of directive 91/156/EEC) which the holder discards, or is obliged to discard or has the intention to discard".

226. Directive 91/689/EEC on hazardous waste defines the term 'hazardous waste' by introducing lists of product types (Annexes I and II) which may be considered to be hazardous within the scope of the Directive. The waste may be in liquid, sludge or solid form.

227. The hazardous waste specified in Annexes I or II must have one or more of the properties listed in Annex III. The origin and composition of the waste and, when necessary, limit values of concentration have to be taken into consideration. All wastes fulfilling the criteria specified for substances and preparations in Annex III may be considered as hazardous.

228. The properties of wastes which render them hazardous are:

H1	Explosive
H2	Oxidizing
H3-A	Highly flammable
H3-B	Flammable
H4	Irritant
H5	Harmful
H6	Toxic
H7	Carcinogenic
H8	Corrosive
H9	Infectious
H10	Teratogenic
H11	Mutagenic
H12	Substances and preparations which release toxic or very toxic gases in contact with water, air or an acid.
H13	Substances and preparations capable by any means, after disposal, or yielding another substance, e.g. a leachate, which possesses any of the characteristics listed above
H14	Ecotoxic

229. Attribution of the hazard properties toxic, very toxic, harmful, corrosive, irritant, carcinogenic, mutagenic and teratogenic is made on the basis of the criteria laid down by Annex VI of Directive 67/548/EEC.

230. The concentration/cut off limits for mixtures are laid down by a Council Decision 94/904/EC as follows for groups H3 to H8:

- flash point $\leq$ 55 °C
- very toxic $\geq$ 0.1% (total concentration)
- toxic $\geq$ 3 % (total concentration)
- harmful $\geq$ 25 % (total concentration)
- corrosive (R35) $\geq$ 1% (total concentration)
- corrosive (R34) $\geq$ 5 % (total concentration)
- irritant (severe eye irritation, R41) $\geq$ 10 % (total concentration)
- irritant (eye, skin or respiratory irritation, R36, R37, R38) $\geq$ 20 % (total concentration)
- carcinogenic cat. 1 or 2 $\geq$ 0.1 % (total concentration)

231. These concentration limits correspond to the classification of dangerous preparations.

US

232. Hazardous wastes are regulated, classified and labelled under the Resource Conservation and Recovery Act (RCRA). RCRA's main goals are to protect human health and the environment from the potential hazards of waste disposal and recycling, to conserve energy and natural resources, to reduce the amount of waste generated, and to ensure that wastes are managed in an environmentally sound manner. Specifically, RCRA Subtitle C establishes a framework for managing hazardous wastes from generation until ultimate disposal. Hazardous wastes can be solids, liquids, gases or sludges that are either specifically listed on one of four lists ("f" hazardous wastes from non-specific sources; "k" hazardous wastes from specific sources; "p" acutely hazardous discarded commercial chemical products; and "u" toxic discarded commercial chemical products) or that exhibit at least one of four characteristics of hazardous waste: ignitability, corrosivity, reactivity; and toxicity.

233. The OSHA Hazard Communication Standard includes specific exemptions for hazardous waste as follows:

> Any hazardous waste as such term is defined by the Solid Waste Disposal Act, as amended by the Resource Conservation and Recovery Act of 1976, as amended (42 U.S.C. et seq.), when subject to regulations issued under the Environmental Protection Agency.
>
> Any hazardous substance as such term is defined by the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) (42 U.S.C. et seq.) when the hazardous substance is the focus of remedial or removal action being conducted under CERCLA in accordance with Environmental Protection Agency regulations.

VI. ANALYSIS OF SIMILARITIES AND DIFFERENCES

234. Scope: In Canada the classification of chemicals in consumer products and workplace chemicals are covered by different pieces of legislation. For the workplace physico-chemical properties and toxicological properties of the preparation are taken into account. For consumer products physico-chemical properties and only acute toxicogical hazards are taken into account. In the EU the classification of preparations is covered by a single piece of legislation, that can be applied across all product types and use categories defining clearly all end-points which need to be considered. Physico-chemical, toxicological and environmental properties are included. In the US chemicals in the workplace and in consumer products are covered by different pieces of legislation. Physico-chemical and toxicological properties are considered. Transport is covered by UN MRTDG in which physico-chemical properties and acute and corrosive effects are taken into account. Classification of pesticides is covered by separate legislation in Canada and the US, whereas in the EU it is proposed to be covered by the general legislation for preparations.

235. Exclusions/Exemptions: In Canada the exclusion of certain products under workplace regulations is under review. In the US similar exemptions are used. In addition waste and consumer products in their final form such as food or alcoholic beverages, drugs, cosmetics are also exempted. The US work place regulation has a set of exemptions for which other laws and regulations apply, for example, as in Canada, wood or wood products, manufactured articles, tobacco and tobacco products as well as medical/veterinary devices. In the EU similar exemptions apply to such products, which are governed by specific legislation. This extends in the EU also to medical devices.

236. Rationale: In the US, EU and Canada mixtures are classified for their hazards. Subsequently it is used to provide the information to workers, employers and consumers. In addition the classification is used in the EU for other purposes like restrictions for marketing and use to protect man and environment. In the US and Canada, some sectors (consumer products and pesticides) consider some elements of risk (exposure) to determine labelling requirements. The UNCETDG has a pragmatic approach to mixtures, which intends to allow the consignor to identify (without unnecessary difficulties or costs) the hazard characteristics of the mixture. Additional downstream consequences like prohibition/permission for transport and permitted packaging types and sizes can be expected.

237. For animal welfare reasons and available principles it is advocated in the EU, in cases when there are no requirements for testing, to use the standard approach for untested mixtures. Testing in order to assess the CMR hazards of mixtures is not allowed in the EU because of insufficient reliability of results.

238. Comparison of systems: The evaluation of reliable data for the mixture/preparation is used by all systems in order to classify the mixture/preparation. When one individual substance of the tested mixture/preparation is changed for another individual substance (for which the toxicity is known), all systems allow extrapolation of the test result. In the US, a standardised approach is only used for workplace chemicals. In Canada, a standardised approach is used for workplace and consumer chemicals. In the EU all kinds of preparations may be classified using the standardised approach. In the transport system a standardised approach may be used for acute toxicity.

239. When used for information purposes comparable general concentration limits in the range of 0.1% to 1% are used for safety data sheets in all systems.

240. The EU classification system allows for the determination of acute toxicity and corrosion/irritation of the non tested preparation the application of the dilution principle (extrapolation to lower hazards classes for these endpoints) in order to approach the comparable results obtained by testing.

241. For acute toxicity additivity rules are applied using a combination of all routes of exposure (EU) or one route only (Canada and the transport system).

242. In the EU a more severe general concentration limit is used for the highest hazard CMR classes than for the lowest hazard CMR class as compared to the US and Canada who have only one concentration cut-off.

243. For consumer products only acute health hazards are evaluated for hazard classification in Canada. In the US both acute and chronic health hazards are subjected to risk evaluation and a subsequent reduction in hazard labelling. In the EU however the consumer products are subject to the same classification procedures as for all other preparations placed on the market.

244. Where a specific concentration limit has been set for a substance this must be used in stead of the general limits in the standardised approach (EU). In the case of exceeding exposure levels in the workplace a hazard classification is also possible when a concentration less than the cut-off values is present for a certain component in a mixture (US).

245. The Expert Group on Classification Criteria for Mixtures held a one day workshop to illustrate conceptual, technical and practical differences between and existing systems and more importantly, to identify commonalties. A summary report of the Workshop will be provided separately.

APPENDIX I: DEFINITIONS

TABLE 9 WORKPLACE DEFINITION OF SUBSTANCE

SYSTEM	*DEFINITION*	*LEGISLATION, REGULATORY, OTHER*
USA	Chemical means any element, chemical compound, or mixture of elements/chemical compounds. Hazardous chemical means any chemical which is a physical hazard or a health hazard.	Definitions are regulatory and can be found in 29 CFR 1910.1200(c).
EUROPE	For the purposes of placing on the market **- substances** mean chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the products and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. A substance may be chemically very well defined (e.g. acetone) or a complex mixture of constituents of variable composition (e.g. aromatic distillates). For some complex substances, some individual constituents have been identified. For the protection of workers from the risks related to the exposure to chemical, physical and biological agents at work **- agent** means any **chemical, physical or biological agent present at work and likely to be harmful** present at work and likely to be harmful to health. For the protection of workers from exposure to **carcinogens** the same definition is used as in the context of Directive 67/548/EEC.	The definitions are part of the legislation. Definitions for substances and preparations have been specified in • **Article 2 of Directive 67/548/EEC**. The scope of application of Directive 88/379/EEC is specified in • **Article 1 of Directive 88/379/EEC.** Chemical agents for protection of workers have been specified in • **Article 2 of Directive 80/1107/EEC** on the protection of workers from the risks related to exposure to chemical, physical and biological agents**.**
CANADA	Controlled product: Means any product material or substance specified by the regulations to be included in any of the following class: (A) compressed gas; (B) flammable and combustible material; (C) oxidizing material; (D) poisonous and infectious material; (E) corrosive material; and (F) dangerously reactive material	The definitions **can be found in the *Hazardous Products Act* and the *Controlled Products Regulations*.**
UNCETDG	No definition	

TABLE 10: WORKPLACE DEFINITION OF MIXTURE/PREPARATION

SYSTEM	*DEFINITION*	*LEGISLATION, REGULATORY, OTHER*
USA	Mixture means any combination of two or more chemicals if the combination is not, in whole or in part, the result of a chemical reaction.	Definitions are regulatory and can be found in 29 CFR 1910.1200(c).
EUROPE	**I. For the purpose of placing on on the market** - preparations mean mixtures or solutions composed of two or more substances. The scope of Directive 88/379/EEC covers mixtures which contain at least one dangerous substance and the preparation is regarded as dangerous within the meaning of Article 3 of Directive 88/379/EEC.	The definitions are part of the legislation. Definitions for substances and preparations have been specified in • **Article 2 of Directive 67/548/EEC**. The scope of application of Directive 88/379/EEC is specified in • **Article 1 of Directive 88/379/EEC.** Chemical agents for protection of workers have been specified in • **Article 2 of Directive 80/1107/EEC** on the protection of workers from the risks related to exposure to chemical, physical and biological agents**.**
CANADA	Mixture [CPR 2(1)]: means a combination of two or more products, materials or substances that does not undergo a chemical change as a result of interaction between the products, materials or substances.	The definitions **can be found in the *Hazardous Products Act* and the *Controlled Products Regulations.***
UNCETDG	no definition	

APPENDIX II: EXISTING SYSTEMS

TABLE 11 WORKPLACE				
System Element	**U.S.**	**CANADA**	**EU**	**TRANSPORT SYSTEM**
Regulation/law	OSHA Hazard Communication Standard, 29 CFR 1910.1200	Yes . The legislative requirements for the Workplace Hazardous Material Information System or WHMIS are the *Controlled Products Regulations* (CPR) under the authority of the *Hazardous Product Act* (HPA).	<u>For placing on the market:</u> Directive 88/379/EEC on classification, packaging and labeling of dangerous preparations with technical adaptations and derived Directives (list of directives attached). Directive 67/548/EEC on classification, packaging and labeling of dangerous substances with 8 amendments and 23 adaptations to technical progress (list of directives attached). Directive 80/1107/EEC on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work (OJ No L 327, 3.12.1980, p. 8).	UN Recommendations on the Transport of Dangerous Goods. The UN Recommendations apply to all products, whatever their end use is intended to be. Exceptions from the requirements are related to quantities carried or type of packaging used rather than to the end use.

			Directive 90/394/EEC on the protection of workers from the risks related to exposure to carcinogens at work (Sixth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ No L 196, 26.7.1990, p.1). Directive 97/42/EC amending for the first time Directive 90/394/EEC on the protection of workers from the risks related to exposure to carcinogens at work (Sixth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) (OJ No L 179, 8.7.1997, p. 4).	
Which health or environmental endpoints are covered by the system?	Carcinogens; toxic or highly toxic agents; reproductive toxins; irritants; corrosives; sensitizers; hepatotoxins; nephrotoxins; neurotoxins; agents which act on the hematopoietic system; agents which damage the lungs, skin, eyes or mucous membranes. (From definition of health hazard.)	Acute toxicity (oral and dermal LD50, LC50), Skin and eye irritation, Corrosion, Skin and respiratory sensitization, Chronic toxicity, Mutagenicity, Reproductive toxicity, Teratogenicity and Embryotoxicity, Carcinogenicity No environmental endpoints covered by WHMIS	The system specified by Directive 88/379/EEC for placing on the market covers end points for health effects. These end points are specified in detail by criteria of Annex VI to Directive 67/548/EEC on classification, packaging and labelling of dangerous substances. The end points for health effects are: 1. acute lethal effects (additivity applies): • very toxic (indicated by warning symbol T+ and R-phrases 26, 27, 28) • toxic (indicated by warning symbol T and R- phrases 23, 24, 25)	Acute toxicity and corrosivity are covered; environmental endpoints are covered separately by regulations applicable to individual modes of transport.

			• harmful (indicated by warning symbol Xn and R-phrases 20, 21, 22) 2. non-lethal irreversible effects after a single exposure; • very toxic (indicated by warning symbol T+ and R-phrase 39) • toxic (indicated by warning symbol T and R- phrase 39) • harmful (indicated by warning symbol Xn and R-phrase 40) 3. severe effects after repeated or prolonged exposure; • toxic (indicated by warning symbol T and R- phrase 48) • harmful (indicated by warning symbol Xn and R-phrase 48) 4. corrosive effects, irritant effects (additivity applies); • corrorive (indicated by warning symbol C and R-phrase 35 or 34) irritant (indicated by warning symbol Xi and R-phrases 41, 36, 37 or 38)	
			5. sensitising effects; • sensitisation by inhalation (indicated by warning symbol Xn and R-phrase 42) sensitisation by skin contact (indicated by warning symbol Xi and R-phrase 43)	

			6. carcinogenic effects, mutagenic effects, toxic effects for reproduction. • carcinogen category 1 or 2 (indicated by warning symbol T and R-phrases 45 or 49) • carcinogen category 3 (indicated by warning symbol Xn and R-phrase 40) • mutagen category 1 or 2 (indicated by warning symbol T and R-phrase 46) • mutagen category 3 (indicated by warning symbol Xn and R-phrase 40) • toxic for reproduction, fertility, category 1 or 2 (indicated by warning symbol T and R-phrase 60) • toxic for reproduction, fertility, category 3 (indicated by warning symbol Xn and R-phrase 62) • toxic for reproduction, development, category 1 or 2 (indicated by warning symbol T and R-phrase 61) • toxic for reproduction, development, category 3 (indicated by warning symbol Xn and R-phrase 63).	

			The end points for environmental effects are not covered by the European legislation so far. For the protection of the health of workers from exposures to chemical agents the same end points described above are considered as a minimum requirement, however, in addition to marketed substances and preparations any agent present at work and likely to be harmful to health shall be taken into consideration by the employer.	
Definition of substance/chemical.	Chemical means any element, chemical compound, or mixture of elements/chemical compounds. Once a hazard determination is performed, the standard applies to those chemicals found to be hazardous. Hazardous chemical means any chemical which is a physical hazard or a health hazard.	Controlled product: Means any product material or substance specified by the regulations to be included in any of the following class: (A) compressed gas; (B) flammable and combustible material; (C) oxidizing material; (D) poisonous and infectious material; (E) corrosive material; and (F) dangerously reactive material.	For the purposes of placing on the market **substances** mean chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the products and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. A substance may be chemically very	There is no definition of substance.

			well defined (e.g. acetone) or a complex mixture of constituents of variable composition (e.g. aromatic destillates). For some complex substances, some individual constituents have been identified. For the protection of workers from exposure to chemicals **agent** means any **chemical** present at work and likely to be harmful to health. For the protection of workers from exposure to **carcinogens** the same definition is used as in the context of	
Definition of mixture/preparation.	Mixture means any combination of two or more chemicals if the combination is not, in whole or in part, the result of a chemical reaction.	Mixture [CPR 2(1)]: means a combination of two or more products, materials or substances that does not undergo a chemical change as a result of interaction between the products, materials or substances.	Directive 67/548/EEC. For placing on the market definition for **preparations** mean mixtures or solutions composed of two or more substances. The **scope** of Directive 88/379/EEC covers mixtures which contain at least one dangerous substance and the preparation is classified according to the rules specified by Directive 88/379/EEC.	There is no definition of preparation/mixture.

Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	Definitions are regulatory and can be found in 29 CFR 1910.1200(c).	The definitions are in the regulation and legislation.	The definitions are part of the legislation. Definitions for substances and preparations have been specified in • **Article 2 of Directive 67/548/EEC**. The scope of application of Directive 88/379/EEC is specified in • **Article 1 of Directive 88/379/EEC.** Chemical agents for protection of workers have been specified in • **Article 2 of Directive 80/1107/EEC** on the protection of workers from the risks related to exposure to chemical, physical and biological agents.	

	The chemical manufacturer, importer or employer is responsible for classifying the mixture. The appropriateness of the classification may be assessed by the Agency's enforcement personnel.	The responsibility for the classification of the mixture rests with the Canadian supplier, distributor or importing agent.	According to Article 1 of Directive 88/379/EEC the Directive is applied to classification, packaging and labeling of dangerous preparations when preparations are **placed on the market** of the Member States. The **manufacturer, or those responsible for placing on the market (importer, distributor or any other person)** shall comply with the requirements of the Directive. **The employer** has the obligation to identify the hazards and risks in the work place according to **worker protection** Directives (Directive 89/391/EEC, Directive 80/1107/EEC and Directive 90/394/EEC). The basic information on classification for this purpose is submitted via labels and Safety Data Sheets to the employer by persons placing on the market of preparations. Where a chemical is present or is produced at the work place, the employer is responsible for identification of hazards and risks.	The consignor has to certify that dangerous goods are handed over for transport are properly classified according to the transport regulations criteria, and therefore the consignor is responsible for providing the proper information. In certain instances, the classification has to be made by the appropriate competent authority (e.g., for explosives, organic peroxides, etc.)

Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	If test data are available on the mixture as a whole, the classification is to be based on that data. Chemicals may have test data for some endpoints and not others. If there are no data for a particular endpoint, the classification for that health effect would be based on the standardized approach below.	Yes.	For placing on the market according to Article 3.3 of Directive 88/379/EEC the **test data overrule** the conventional method (based on concentrations of component substances) in cases where appropriate test data are available. This **does not apply** to cases where the preparation contains **carcinogenic, mutagenic or toxic to reproduction substances**.	Normally, when relevant test data are available, they should be used for classification of mixtures. When test data are not available, calculation methods using test data on the active ingredient may be permitted in certain cases. For details see the UN Recommendations.
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	OSHA has no authority to require testing. The hazard determination is to be based on available data.	No.	Testing is obligatory to assess the following physico-chemical properties: explosive, oxidizing, extremely flammable, highly flammable and flammable properties. There are certain exemptions from these testing requirements specified in Annex VI to Directive 67/548/EEC. Exemptions: The flammability of gas mixtures need not to be tested when produced in order of small amounts. In these cases the calculation method applies (Section 9.1 of Annex VI to Directive 67/5448/EEC).	No

			The oxidizing properties of gas mixtures which cannot be tested. The method applied for classification is based on oxidizing potential of gases compared with the oxidizing potential of oxygen in air (Section 9.1 of Annex VI to Directive 67/548/EEC). Organic peroxides which cannot be tested, are classified on the basis of a calculation method based on the presence of active oxygen (Section 9.5 of Annex VI to Directive 67/548/EEC). Testing is not obligatory for assessment of health effects of preparations. However, the person placing on the market is free to choose whether to test or to apply the conventional method. Testing shall not be used in cases where the preparation contains carcinofenic, mutagenic or toxic to reproductive substances. Testing on vertebrate is not preferred because of animal welfare reasons.	

<table>
<tr>
<td>Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.</td>
<td>No. The classification is to either be based on actual test data or on the standardized approach described below.</td>
<td>Yes. You can also use:
-Professional judgement
-Test results obtained with a product, material or substance that has similar properties.
-Human data.</td>
<td>If the preparation has been tested for placing on the market for its health effects the composition of the preparation may vary according to the following table (Article 3.3 of Directive 88/379/EEC) without having an obligation to carry out a new assessment. If the variation of concentration of constituents is greater the assessment shall be carried out again either by testing or by application of the conventional method.
Table Changes of composition of the initial concentration as a w/w percentage, of one or more of the dangerous constituents are introduced by the manufacturer
<table>
<tr><th>Initial concentration range of the constituent</th><th>Permitted variation in initial concentration of the constituent</th></tr>
<tr><td>2.5%</td><td>+/-15%</td></tr>
<tr><td>> 2.5 – 10%</td><td>+/-10%</td></tr>
<tr><td>> 10 – 25%</td><td>+/-6%</td></tr>
<tr><td>> 25 – 50%</td><td>+/-5%</td></tr>
<tr><td>> 50 – 100%</td><td>+/-2.5%</td></tr>
</table>
A new assessment (either by testing or by conventional method) shall be carried out if any of the constituents is substituted, or other components are added.</td>
<td>Yes. Classification can be done by:

analogy to substance with similar properties;

consideration of human experience.</td>
</tr>
</table>

			Potentiation, antagonism and synergism of the component substances shall be taken into consideration in the classification in cases, where application of the conventional method would not give a correct classification for the mixture. Structure activity relationship (SAR) may be applied in the assessment of mixtures only for component substances when the conventional method is applied for classification of mixtures. Application of SAR method to substances is rather limited. Advice for application of SAR is given by Annex VI to Directive 67/548/EEC.	
Please describe any standardised approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	Where test data are not available, mixtures are assumed to have the same health hazards as do the components which comprise one percent (by weight or volume) or greater of the mixture as a whole. **Exceptions:** Mixutres are considered caracinogenic for purposes of hazard communication when they comprise 0.1% or greater of the mixture as a whole. If there is evidence that a component present in concentrations less than one percent (0.1% for	- Controlled products that are untested mixtures with respect to one or more applicable toxicological endpoints specified in the CPR must be evaluated on the basis of the hazards associated with each ingredient present at a reportable concentration in the mixture. In the case of a controlled product that is an untested mixture, the mixture is generally considered to have the same toxicological hazards as the ingredients subject to disclosure present at or above the cut-off concentrations. Reportable concentrations are 0.1% w/w or more for substances which meet the classification criteria for teratogenicity, embryotoxicity,	The *conventional method* based on the properties and concentrations of component substances of preparations may be applied for health effects in cases where no test data are available. The concentration limits of components for classification are specified either for individual substances in Annex I (list of dangerous substances) to Directive	An untested mixture is considered to have the same toxicological hazards as the ingredients. ACUTE TOXICITY If LC_{50} data is available for each of the toxic componants the LC_{50} value of the mixture can be estimated by the following formula: $$LC_{50}\ (\text{mixture}) = \frac{1}{\sum_{i=1}^{n} \frac{f_i}{LC_{50i}}}$$

	carcinogens) can be released in concentrations that would exceed OSHA's established permissible exposure limits or ACGIH's recommended exposure limits, or presents a health hazard to employees in those lower concentrations, the mixture is assumed to be hazardous for purposes of hazard communication	Carcinogenicity, reproductive toxicity, germ cell mutagenicity, or respiratory tract sensitisation. The concentration cut-off is 1% w/w for all other toxicological criteria in WHMIS (i.e. acute and chronic toxicity, somatic cell mutagenicity, skin and eye irritation, and dermal sensitisation). Acute toxicity LD_{50} or LC_{50} values Where the LD_{50} or LC_{50} of one or more ingredients of a mixture is not known, the LD_{50} or LC_{50} of the mixture is equal to the most acutely lethal ingredient that is present in the mixture at a concentration of one percent or more. Additional rule: If LD_{50} / LC_{50} values are known for each ingredient present in the mixture at $\geq$ 1% w/w, the product LD_{50} / LC_{50} may be calculated Using the following formulas: a) for a solic or a liquid $\frac{1}{LD_{50}\text{ of mixture}} = \frac{\text{Part Ingred A}}{LD_{50}\text{ Ingred A}} + \frac{\text{Part Ingred B}}{LD_{50}\text{ Ingred B}} + \frac{\text{Part Last Ingred}}{LD_{50}\text{ Last Ingred}}$	67/548/EEC or in Annex I to Directive 88/379/EEC generally for different end points. Where individual concentration limits have been specified for a substance in Annex I to Directive 67/548/EEC, they have to be used. The concentration limits applied generally for different end points are specified in Annex 2. The formulas apply where the properties are considered to be additive and no single component substance alone exceeds the classification limit. (see Annex 3). The classification of preparations carried out by a person responsible for marketing can be applied by the employer, but where other chemicals are present or produced at the work place, the employer has the obligation to identify the hazards and risks.	Where f_i = mole fraction of the I^{TH} component LC_{50i} = mean lethal concentration for the I^{TH} component If LD_{50} data is not available for all components of the mixture: The formulation is classified according to the most hazardous constituent of the mixture as if that constituent were in the same concentration as the total concentration of all active components; or b) apply the formula: $\frac{C_A}{T_A} + \frac{C_B}{T_B} + \ldots + \frac{C_Z}{T_Z} = \frac{100}{T_M}$ where c = percentage concentration of constituent A, B, …, Z in the mixture; T = LD_{50} values for components A, B, …, Z; T_M = LD_{50} value of the mixture

		b) for a gas, vapour, dust, mist or fume $\frac{1}{LC_{50} \text{ of mixture}} = \frac{\text{Part Ingred A}}{LC_{50} \text{ Ingred A}} + \frac{\text{Part Ingre B}}{LC_{50} \text{ Ingre B}} + \frac{\text{Part Last Ingred}}{LC_{50} \text{ Last Ingred}}$		
Please briefly describe the rationale for the standardised approach to untested mixtures.	The Hazard Communication Standard provides exposed workers and employers using a chemical in their workplaces with the right to know the identities and hazards of those chemicals. The underlying philosophy is that the availability of information allows the selection and use of appropriate control measures, thus resulting in fewer illnesses and injuries based on chemical exposures. It thus is based on the premise that as complete disclosure as possible is the best approach. This desire for disclosure was balanced by concerns about trade secret claims (which are more	• A classification system based on cut-offs presumes that a mixture is hazardous if it contains a hazardous ingredient at a concentration exceeding a specified cut-off. The use of cut-offs is administratively straightforward and can be applied by using available data on the toxicology of ingredients in the mixture. Since WHMIS is primarily an information system, the use of cut-off values is justifiable as a means of consistently communicating information about hazardous ingredients, as contrasted with providing a hazard evaluation of the mixture. • The numerical values of cutoffs, however, are necessarily arbitrary and were chosen largely for consistency between Canada and the United States.	The standardised approach, the *conventional method*, for assessment of health effects of mixtures is based on • identified classifications of component substances and • concentration limits set to identify the same classifications as for component substances. The objective of the conventional method is to discourage testing for animal welfare reasons, and to provide an easy, inexpensive and from toxicological point of view valid method for classification which offers at least the same level of protection of health as the method based on testing.	The approach is a pragmatic one, i.e., it should allow the consignor to determine, without unnecessary difficulties or costs, the hazard characteristics of the mixture (including wastes, where the exact composition is not always easy to determine) which would determine its correct identification (proper shipping name), labeling, marking and packing conditions with transport requirements.

	Common for chemicals in small concentrations) and the need for information about very small quantities. The percentage cutoffs were selected as a practical and pragmatic approach to addressing these concerns, while still ensuring that necessary information is readily available to employers and employees		A study[1] was carried out for justification of concentration limits on acute effects. The concentration limits for classification for long term effects are based on a reasonable approach taking into consideration the characteristics of the effects. Often, if data are available, individual concentration limits for classification are set for substances in Annex I to Directive 67/548/EEC For genotoxic carcinogens and mutagens normally a no-effect limit cannot be established. The conventional values of 0.1 % for category 1 and 2 carcinogens and mutagens are therefore merely set on the basis of a level of impurities and estimation of the potency of strong carcinogens. For reproductive toxic substances the values have been set taking the no-effect levels into consideration. The values of 1 % and 5 % for suspected carcinogens and mutagens, and for suspected reproductive toxic substances are established recognising the lower grade of proof that these endpoints may occur in practice.	

			For carcinogenic, mutagenic and reproductive toxic substances the establishment of specific concentration limits is more difficult. However, a system based on the potency of a carcinogenic substance is used to establish individual limits (see step 1 OECD report for carcinogenicity) in specific cases. The experience on the Community level is, however, in an early stage. The identification of toxicological end points provides the basis for the down stream legislation, like: • hazard communication by labels and Safety Data Sheets • protection of workers from the exposure to chemical agents and carcinogens, • protection of the environment from the emissions to the environment (water, air, soil)	

			• restrictions for marketing and use of dangerous substances and preparations • prevention of major accidents. Hazard communication is the immediate consequence of classification. In most cases information on the identified classifications is passed to the final user, whether it be a professional user or a consumer. Information on the names of dangerous components giving rise to the classification is passed by labels according to certain specified rules from the concentrations triggering the classification. For professional users of preparations, in addition to labels, Safety Data Sheets on classified preparations are also submitted giving even more detailed information than the labels. In the Safety Data Sheets information shall be given on components dangerous to health from 1 % on, unless the classification limit is lower. This information is intended for the employer who according to the Community legislation has the obligation to protect the workers from the exposure to chemical agents and carcinogens. The employer has to inform the workers about the potential hazards.	

	.		In the framework of downstream legislation other than hazard communication normally a risk assessment shall be carried out on the top of the hazard assessment to examine whether measures for protection of health and the environment are needed.	
How are mixtures classified when some endpoints have test data and others don't?	Classification is based on test data where available, and the endpoints where such data are not available are classified based on the standardized approach.	Test data are used when available; ingredients data are used for other toxicity endpoints that were not tested. Information relating to ingredients must be disclosed if this information is applicable to the mixture. Professional judgment can also be used.	All end points for a mixture have to be assessed on the basis of available data. Where appropriate test data exist they have a preference over the conventional method based on the concentrations of individual components, except in cases the preparation contains c/m/r-substances. The classification is carried out on the basis of test data where the test data are available for the end point. All other end points are then assessed by applying the conventional method.	Test data are used when available; ingredients data are used for other toxicity endpoints that are not tested.
Is there any other information regarding the approach to mixture classification that needs to be addressed?	As noted above, the standard includes a back-up provision to ensure that employee protection is not compromised by the percentage cutoffs. This back-up provision makes exceptions to the cutoffs when there is evidence that they don't provide sufficient protection.	Complex mixtures are exempt to disclose on a material safety data sheet the chemical identity and concentration of the ingredients if the generic name is disclosed on the material safety data sheet. Turpentine and petroleum distillates are examples of complex mixtures. A complex mixture can be comprised of a multitude of ingredients whose concentrations may vary from batch to batch. A complex mixture is classified based on its generic name rather than the		

		ingredients present in the mixture. Complex mixture means a mixture that is a combination of many chemicals, has a commonly known generic name and is : a) naturally occuring, b) a fraction of a naturally occurring mixture that results from a separation process, or c) a modification of a naturally occuring nixture or a modification of a fraction of a naturally occurring nixture that results from a chemical modification process.		
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	No. The system has worked quite well since adopted in 1983. Furthermore, OSHA has delayed consideration of any changes to this standard until the internationally harmonized system is available.	No.	The formal decision making process for revising the Directive 88/379/EEC on classification, packaging and labeling of dangerous preparations began in 1996 and is expected to be finalized by the end of 1998. The revision of Directive 88/379/EEC is necessary to comply with the commitments set by the Accession Treaties of Austria, Finland and Sweden. The following new elements have been introduced into the proposal:	

			Provisions for classification, packaging and labeling of preparations dangerous for the environment Pesticides will be covered by the new Directive, existing Directive 78/631/EEC will be repealed by the new Directive Explosives are brought in the scope of the Directive Some provisions of the Directive cover also preparations which are not classified as dangerous. Revision of Directive 80/1107/EEC on exposure to chemical agents is on the way. The revised Directive will likely be adopted in 1998.	No

[1] Regulatory Toxicology and Pharmacology, Vol. 4(1984), p.145-156.

Table 12: Pesticides

System Element	U.S.	Canada	EU	Transport System
Regulation/law	Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. 136 et seq.	Yes. However, there are no provisions per se in the Pest. Act regarding classification of mixtures. Primary consideration in classification is the use for which the pesticide is intended. Additional consideration is given to characterization of individual toxicological, environmental and packaging criteria. Mixtures are classified for domestic, commercial, or restricted use with an ascending degree of hazard associated with each class. Acute toxicity considerations are common safety criteria for assignment to all classes. Additional consideration for the domestic class include considerations of acceptable package size and methods for disposal. Additional criteria for assignment to the restricted class include consideration of environmental risk as well as whether the product is intended for use in environmentally sensitive areas (such as aquatic or forestry situations).	Directive 78/631/EEC on classification, packaging and labeling of dangerous preparations (pesticides) (OJ No L 206, 29.7.1978, p. 13) (list of directives attached). Directive 91/414/EEC on placing the plant protection products on the market (list of directives attached).	UN Recommendations on the Transport of Dangerous Goods. The UN Recommendations apply to all products, whatever their end use is intended to be. Exceptions from the requirements are related to quantities carried or type of packaging used rather than to the end use

Which health or environmental endpoints are covered by the system?	Acute toxicity (oral, inhalation, dermal), skin irritation, eye irritation, sensitization, and toxicity to fish and wildlife and pollinating insects. In addition, some pesticides have been labeled for carcinogenicity and reproductive effects. EPA has the authority to regulate pesticides for any health or environmental endpoint.	Acute oral, dermal, inhalation toxicity, skin and eye irritation, skin sensitization. Acute neurotoxicity studies are required for products for which effects on the nervous system are anticipated due to chemical class or other information.	The system specified by Directive 78/631/EEC on classification, packaging and labeling of dangerous preparations (pesticides) covers end points for acute health effects. The endpoints specified by Directive 78/631/EEC are: 1) acute lethal effects (calculation and adaptivity may apply): I. very toxic by ingestion, inhalation or percutaneous route II. toxic by ingestion, inhalation or percutaneous route III. harmful by ingestion, inhalation or percutaneous route 2) additional toxicological data may be taken into consideration in classification if : II. the facts suggest that in normal use of a pesticide involves a risk to human health III. it is shown that other than rat is more suitable test species IV. oral or percutaneous LD50-values should not be used as a basis of classification.	Acute toxicity and corrosivity are covered; environmental endpoints are covered separately by regulations applicable to individual modes of transport.

			The acute oral and dermal toxicity has been specified separately for solids and liquids. The cut-off limits for acute toxicity are different from the cut-off limits for general chemicals (see Annex 1 to this document). The end points for other health effects are not specified in detail by the European legislation for the time being. The environmental effects are not covered by Directive 78/631/EEC. Although the detailed criteria for classification of Directive 78/631/EEC cover only acute lethal effects the labeling requirements indicate that other end points may be taken into consideration (reference to Directive 67/548/EEC is made).	
Definition of substance/chemical.	Neither substance/chemical nor mixture are defined. See below for other definitions that apply.	**Substances**: chemical elements/entitles and their constituents, as they occur in the natural state or produced by industry. Eg. Technical grade active ingredients including impurities/contaminants resulting from the manufacturing process; can be further utilized in preparations Eg. Chemical soups, such as creosote; may also be utilized in preparations	For placing on the market the term of **II.** **active substances** is used within Directive 78/631/EEC on classification, packaging and labeling of dangerous preparations without definition. **III.** **active substances** according to Directive 91/414/EEC (on placing plant protection products on the market) mean substances or micro-organisms including viruses, having general or specific action	There is no definition of substance.

			IV. **substances** according to Directive 91/414/EEC (on placing plant protection products on the market) mean chemical elements and their compounds, as they occur naturally or by manufacture, including any impurity inevitable resulting from the manufacturing process.	
Definition of mixture/preparation.	N/A	**Preparation**: a mixture or solution composed of two or more substances*; the mixture is not known to, or is not expected to chemically react (irreversibly) with each other to form other chemical entities. e.g. End-use formulations (market-ready) e.g. Manufacturing use concentrates; these products may subsequently be formulated into preparations e.g. 2,4-D dimethylamine salt preparation resulting from the combining of 2,4-D acid, dimethylamine and water; although representing a chemical reaction, the reaction is easily reversible by manipulation of pH * at least one of which is a pesticidal active ingredient -otherwise would not be subject to PCPA	For placing on the market of pesticides the term of a **II.** **mixture/preparation** is used within Directive 78/631/EEC on classification, packaging and labeling of dangerous preparations without definition. **III.** **preparations** according to Directive 91/414/EEC (on placing plant protection products on the market) mean mixtures or solutions composed of two or more substances of which at least one is an active substance intended for use as plant protection products.	There is no definition of preparation/ mixture.
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	N/A	No. There are no definitions in regulation or legislation. The above definitions have been developed to reflect the working practice.	For placing on the market definitions of substances and preparations are presented in II. **Article 2 of Directive 91/414/EEC** on placing the plant protection products on the market.	

Who is responsible for the classification of the mixture?	All pesticides and pesticide products are classified by EPA's Office of Pesticide Programs, using data and information provided by pesticide registrants.	Not sure if this question refers to the legislative authority - if so, it would be the Pest Control Products Act, although as indicated above, there are no provisions, per se, in the Act.	According to Article 6.3 of Directive 78/631/EEC on classification, packaging and labeling of pesticides, the indications of special risks for the pesticides which are subject to authorization shall be specified by the **competent authority**. This specification of classification and labeling is carried out in the context of authorization, following the submission of an application. The application contains all the data needed for classification and normally a proposal of the applicant for the classification.	The consignor has to certify that dangerous goods are handed over for transport are properly classified according to the transport regulations criteria, and therefore the consignor is responsible for providing the proper information. In certain instances, the classification has to be made by the appropriate competent authority (e.g., for explosives, organic peroxides, etc.)
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Available test data are used to classify mixtures.	Yes. Please consider the answer to this question together with those for the next three questions.	Test data are used as a basis of classification, and in most cases tests are required for identification of hazards of pesticide preparations **for marketing** purposes. Exceptions may be considered case by case in the context of national authorizations. Little or no experience is yet available on the application of Directive 91/414/EEC on	Normally, when relevant test data are available, they should be used for classification of mixtures.

			authorization of plant protection products on the Community level as the transitional period for entering into force of Directive 91/414/EEC has not yet expired.	When test data are not available, calculation methods using test data on the active ingredient may be permitted in certain cases. For details see the UN Recommendations
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	Health and safety data are required to be submitted by applicants for pesticide registrations. The Agency has promulgated regulations under 40 CFR Part 158 describing the data and the fact that data required for characterization of pesticides as acutely hazardous to humans are to be developed and submitted for each active ingredient and each pesticide product. Studies for chronic health hazards are performed on the active ingredient, and studies for aquatic hazards are performed on the active ingredient or typical products. The choice of typical product for aquatic testing involves expert judgement about substantial similarity of products, but obviates the need to test every product for these endpoints.	Yes. Acute toxicity testing (i.e. acute oral, dermal, inhalation toxicity, skin and eye irritation, skin sensitization and in some cases acute neurotoxicity) is required to support registration of preparations. Waivers for testing are considered on a case-by-case basis on the basis of known characteristics of the components (e.g., irritative properties), physical form (e.g., waxy or gummy resins not representing an inhalation hazard), or other scientifically sound information (see also next question).	Directive 91/414/EEC on placing the plant protection products on the market sets requirements for testing of products for authorization purposes. These test results are used for classification of individual products. The calculation method may be applicable in the case of acute lethal effects. According to Article 3.4 of Directive 78/631/EEC, if facts appear which leave the correctness of the classification on the basis of the calculation method open to doubt, the competent authorities may require that the calculation be replaced by toxicological tests.	No.

Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	EPA accepts bridging data to characterize substantially similar products for acute human hazards. If the Agency determines that a product (pesticide active ingredient and at least one inert ingredient) is substantially similar to a registered product, experimental data may not be needed to characterize all or any of the acute hazards of the similar product.	Yes. A hazard may be predicted on the basis of available information on one or several of the constituents, e.g., in some cases involving ingredients of known sensitization, irritative/corrosive properties, pH extremes (acidity or alkalinity), other test data for similar mixtures (respecting proprietary rights to data), See also next question.	According to Article 3.2 of Directive 78/631/EEC, instead of determination of toxicological properties a pesticide containing one active substance may be classified by means of a calculation, if it is shown that the composition of a pesticide closely resembles that of another pesticide which has already been classified and the toxicological data relating to the latter are sufficiently well established. In such cases there must be valid grounds for assuming that the classification resulting from a calculation would not vary substantially from those obtainable by biological testing in accordance with paragraph 1.	Yes. Acute LD_{50} values for mixtures. The formulation is classified according to the most hazardous constituent of the mixture.
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	N/A	There are no standardized approaches, per se, when test data are not available such as the use of formulae or percentage cutoffs. Each is considered on a case-by- case basis. See also above responses.	*A calculation method* based on acute toxicity values of active substances and concentrations of component substances in preparations may be applied for classification of pesticides in certain cases. The calculation method is presented in Annexes 4 and 5.	No
Please briefly describe the rationale for the standardized approach to untested mixtures.	N/A	Not applicable	The objective of the classification of pesticides is to assess the toxicological end points of pesticide preparations. Testing requirements for classification are specified for authorization by Directive 91/414/EEC (or by Directive on Biocides) or by national provisions. The criteria for classification are specified only for acute effects, for which also *a calculation method* is available. The	The approach is a pragmatic one, i.e., it should allow the consignor to determine, without unnecessary difficulties or costs, the hazard characteristics of

			calculation method is intended to assess the acute toxicity equally with the test methods.	the mixture (including wastes, where the exact composition is not always easy to determine) which would determine its correct identification (proper shipping name), labeling, marking and packing conditions with transport requirements.
How are mixtures classified when some endpoints have test data and others don't?	As described above, the pesticide registrant generally has an obligation to test for all acute human hazard endpoints subject to hazard labeling. Data for other endpoints are based on the intended use pattern.	See responses above	Directive 91/414/EEC sets the requirements for placing plant protection products on the market. This Directive specifies the testing requirements to assess the hazards. The calculation method can be used for classification on the basis of acute lethal toxicity.	See responses above.
Is there any other information regarding the approach to mixture classification that needs to be addressed?	The technical grade of the active ingredient is the form that is tested for hazard potential. Most technical grade chemicals have residual impurities which are fully identified to the Agency. If the impurity profile changes significantly from one product to another, the agency may require testing.	The above responses reflect the PMRA definition of classification as pertaining primarily to market classes. This definition may not be consistent with other regulatory agencies.		

Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	No.	Agreement on the definition of mixture will be required to establish a common basis for development of classification criteria. In addition, discussions of the scope of application of the criteria and subsequent labeling may have an impact. The degree to which harmonization may constitute disharmony within national authorities (ie. the impact on regulatory sectors within each national body) may also have an impact.	A new Directive on Biocides (non-agricultural pesticides) was adopted on 14th January 1998. This Directive specifies conditions for authorization of Biocides on the market. Directive 88/379/EEC will be applied to classification, packaging and labeling of Biocides. When the new Directive on dangerous preparations is adopted that Directive will be applicable to Biocides.	

Table 13: Consumer Products

System Element	U.S.	Canada	EU	Transport System
Regulation/law.	Federal Hazardous Substances Act 15 USC 1261 et seq. and regulations 16 CFR 1500 et seq.	Yes. New regulations are being currently drafted (CCCR).	The same provisions apply as for placing on the market of preparations intended for professional users.	Recommendations on the Transport of Dangerous Goods. The UN Recommendations apply to all products, whatever their end use is intended to be. Exceptions from the requirements are related to quantities carried or type of packaging used rather than to the end use
Which health or environmental endpoints are covered by the system?	Acute oral, dermal and inhalation toxicity; eye and skin irritation and corrosion; sensitization, carcinogenicity (including mutagenicity and germ cell mutagenicity), reproductive toxicity, neurotoxicity, and other organ toxicity.	Acute oral, dermal, and inhalation toxicity endpoints , skin and eye irritation, aspiration hazards and quick skin-bonding adhesives.	The same provisions apply as for placing on the market of preparations intended for professional users.	Acute toxicity and corrosivity are covered; environmental endpoints are covered separately by regulations applicable to individual modes of transport.
Definition of substance/chemical.	Any substance or mixture of substances which is toxic, corrosive, an irritant, a strong sensitizer, flammable or combustible, or generates pressure through decomposition, heat, or other means, if such substance or mixture of substances may cause substantial personal injury or substantial illness during or as a proximate result of any customary or reasonably foreseeable handling or use, including reasonably fore-seeable ingestion by children.16 CFR 1500.3	*Consumer chemical product* means a chemical product that is destined for use by a consumer that is set out in item 1 of Part II of schedule I to the Act, and that has the properties set out in one or more of A) Category 1, toxic products, in Part 1, B) Category 2, corrosive products in Part 2, C) Category 3, flammable products in Part 3,and D) Category 4, quick skin-bonding adhesives in Part 4.	The same definitions are used for placing on the market of preparations for consumer uses as for workplace uses.	There is no definition of substance.

Definition of mixture/preparation.	16 CFR 1500.3 (above)	mixture: means a combination of two or more products, materials or substances that do not undergo a chemical change as a result of their interaction.	The same definitions are used for placing on the market of preparations for consumer uses as for workplace uses.	There is no definition of preparation/mixture.
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	Statute and regulations 15 USC 1261 et seq. and regulations 16 CFR 1500 et seq.	The definition appears in the proposed legislation	The same definitions for placing on the market apply to consumer products as to products intended for workplace uses.	
Who is responsible for the classification of the mixture?	Primarily manufacturer, importer or distributor and the agency monitors compliance	The manufacturer or importer is responsible for the classification of the mixture.	The provisions apply to consumer products as to products intended for workplace use.	The consignor has to certify that dangerous goods are handed over for transport are properly classified according to the transport regulations criteria, and therefore the consignor is responsible for providing the proper information. In certain instances, the classification has to be made by the appropriate competent authority (e.g., for explosives, organic peroxides, etc.)

Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Test data, if available on the mixture are used as the basis for classification of the mixture. Human experience takes precedence and there are certain circumstances when chemical composition is sufficient to classify and label.	Yes.	The same provisions apply to consumer products as to products intended for workplace use.	Normally, when relevant test data are available, they should be used for classification of mixtures. When test data are not available, calculation methods using test data on the active ingredient may be permitted in certain cases. For details see the UN Recommendations.
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	Testing in animals is not obligatory, one can use published data, past experience on similar products, human experience or an expert opinion. The manufacturer has the responsibility not to over or under estimate the hazard	No.	The same provisions apply to consumer products as to products intended for workplace uses.	No
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	Yes, one can use all available information to determine the right classification by SAR, extrapolation, estimation or human experience. One should not over or under classify.	Professional judgement can be used.	The same provisions apply to consumer products as to products intended for workplace use.	
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	N/A	- You can evaluate and classified the hazards of the mixture based on the properties and concentrations of components. - For Acute Toxicity - *Additivity Formulas* The use of additivity formulas are to be considered acceptable in the absence of expertise or data on the complete formulation. The formulas are:	The same provisions are applied to consumer products as to products intended for workplace use.	The same provisions apply to consumer products as to other Dangerous Goods.

		a) for a solid or a liquid $\frac{1}{LD_{50}\ \text{mixture}} =$ $\frac{\text{Part Ingredient A}}{LD_{50}\ \text{Ingredient A}} +$ $\frac{\text{Part Ingredient B}}{LD_{50}\ \text{Ingredient B}} +$ $\frac{\text{Part Last Ingredient}}{LD_{50}\ \text{Last Ingredient}}$ b) for a gas, vapour, dust, mist or fume $\frac{1}{LC_{50}\ \text{mixture}} =$ $\frac{\text{Part Ingredient A}}{LC_{50}\ \text{Ingredient A}} +$ $\frac{\text{Part Ingredient B}}{LC_{50}\ \text{Ingredient B}} +$ $\frac{\text{Part Last Ingredient}}{LC_{50}\ \text{Last Ingredient}}$ (part = the weight of the ingredient divided by the weight of the mixture); - Percentage cut-offs are used for some chemicals, as specified in Annex 1.		

Please briefly describe the rationale for the standardised approach to untested mixtures.	N/A	Additional Rationale:- *Components of Unknown Toxicity* The additivity formula can be adapted to situations where information about the LD_{50} or LC_{50} of a component of a mixture is limited or not available. Some of these situations are the following: 1) LD_{50} or LC_{50} has been estimated in an alternative test, such as the Fixed Dose Method. The LD_{50} or LC_{50} is known to exceed one of the fixed doses. The calculation can be performed as an inequality. For example, component A (40%) has LD_{50} = 300 mg/kg and component B (60%) has LD_{50} 2000 mg/kg. $1/LD_{50} = 0.4/300 + 0.6/(\geq 2000)$ $= 0.00133 + < 0.00035$ $= < 0.00168$ LD_{50} >595 mg/kg	The same rational applies to consumer products as to products intended for workplace use.	The approach is a pragmatic one, i.e., it should allow the consignor to determine, without unnecessary difficulties or costs, the hazard characteristics of the mixture (including wastes, where the exact composition is not always easy to determine) which would determine its correct identification (proper shipping name), labeling, marking and packing conditions with transport requirements.

		2) The LD_{50} or LC_{50} can be estimated by comparison to similar substances. By professional judgement it is often possible to estimate that the LD_{50} or LC_{50} exceeds a certain value. For example, if the known LC_{50}'s of several members of a family of solvents all exceed 6000 ppm, then one may judge that an untested member of the family with similar properties has an LC_{50} exceeding 6000 ppm. This value can be used in the formula as in the above example. 3) Testing shows that serious non-lethal effects occur at a significantly lower dose than the LD_{50}. By professional judgement, the lower dose could be substituted into the formula. 4)The LD_{50} or LC_{50} is unknown and cannot be estimated. Two alternatives to deal with this situation were considered:		

		i) Whole Product Premise: In the Controlled Products Regulations (WHMIS), if no information is available about a component present at over 1%, then the LD_{50} or LC_{50} of the product is taken to be the LD_{50} or LC_{50} of the most toxic known component over 1%. This approach tends to over-classify the majority of mixtures in order to avoid the occasional under-classification. ii) Untested Component Premise: The recommended alternative is to assume that the LD_{50} or LC_{50} of the untested component is equal to the LD_{50} or LC_{50} of the most toxic component present in the mixture at a concentration of 1% or more. This avoids extreme over-classifications at the cost of more frequent under-classification. For example, a product consists of components A (10%, LD_{50} unknown), B (10%, LD_{50} = 200 mg/kg) and water (80%). In WHMIS, the assumed LD_{50} of the product is 200 mg/kg, whereas in the recommended approach, the LD_{50} is calculated to be 1000 mg/kg.		

		It should rarely occur that the toxicity of a major component of a consumer product is completely unknown. Normally it is possible to use professional judgement and qualitative and quantitative structure-activity relations (SARs) to estimate the toxicity of a material, however approximately. Nevertheless, many dealers may lack the expertise, resources or confidence to make estimates.		
How are mixtures classified when some endpoints have test data and others don't?	For some end points such as eye irritation/corrosion one may use skin irritation/corrosion data, if appropriate. For others may use published data, past experience, and expert opinion.	Test data are used when available; ingredients data are used for other toxicity endpoints that were not tested..	The same provisions apply to consumer products as to products intended for workplace use.	
Is there any other information regarding the approach to mixture classification that needs to be addressed?	The primary objective is to determine the hazard posed by the product for non-chronic end points and risk posed by the product for chronic hazards. While there is no standardized approach that applies across the board, formulae from the scientific literature may be used to predict the hazard when data permit. The manufacturer or the agency provides the rationale for the formula used.			

Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	No	New regulations are being currently drafted.	The same provisions apply to consumer products as to products intended for workplace use.	No

Table 14: Cosmetics

System	U.S.	Canada	EU	Transport System
Regulation/law.	Regulation of cosmetics in the United States does not include hazard classification and labeling such as that being addressed in this process. Cosmetics produced or distributed for retail sale to consumers for their personal care are required to bear a full declaration of ingredients (21 CFR 701.3). See note below.	Yes. There are no provisions for classification of mixtures. Cosmetics are not classified.	<u>For placing on the market of cosmetic products:</u> Directive 76/768/EEC on cosmetic products with 6 amendments and 22 adaptations to technical progress (list of directives attached) known as the Cosmetics Directive. There is no requirement for hazard communication and labelling such as is being considered in this process. Recently, (6th Amendment to the Cosmetic Products Directive) a requirement has been introduced for ingredient labelling. <u>For protection of workers:</u> the same legislation as applicable to all chemicals (as it refers to handling of chemical raw materials).	Recommendations on the Transport of Dangerous Goods. The UN Recommendations apply to all products, whatever their end use is intended to be. Exceptions from the requirements are related to quantities carried or type of packaging used rather than to the end use
Which health or environmental endpoints are covered by the system?			The system controlling cosmetic products is different from the system that controls chemicals. The Cosmetics Directive requires that a cosmetic product put on the market be safe when applied under normal or reasonably foreseeable conditions of use. The safety of cosmetic products is evaluated based on risk, before they are placed on the market. Cosmetic ingredients are covered by the chemical legislation (the Dangerous Substances Directive, the	Acute toxicity and corrosivity are covered; environmental endpoints are covered separately by regulations applicable to individual modes of transport.

			Existing Chemicals Reg., etc.) but are subject to risk assessment - as opposed to hazard evaluation - when added to a cosmetic product (risk = hazard x exposure). For cosmetic ingredients on the annexes of the Cosmetics Directive, the same endpoints are taken into account as for chemicals when carrying out the risk assessment.	
Definition of substance/chemical.			A cosmetic ingredient is any chemical substance or preparation of synthetic or natural origin used in the composition of cosmetic products.	There is no definition of substance.
Definition of mixture/preparation.			A cosmetic product is defined in the Cosmetics Directive, Art.1: any substance or preparation intended to be placed in contact with various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition.	There is no definition of preparation/mixture.
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.			Definition of a cosmetic product is specified by Directive 76/768/EEC.	

Who is responsible for the classification of the mixture?			There is no classification system for cosmetic products. The person placing cosmetic products on the EU market is responsible for ensuring that cosmetics do not cause damage to human health when applied under normal or reasonably foreseeable conditions of use (Article 2 of the Cosmetics Directive). The Cosmetics Directive also requires that for each product the person responsible for placing it on the market has to keep a Product Information which includes a safety assessment that is based on the toxicological profile of ingredients, their chemical structure and their level of exposure. In addition, a series of cosmetic ingredients is controlled through: - a negative list (Annex II) - a restrictive list (Annex III) - 3 positive lists (Annexes IV, VI and VII). Addition of a substance to a positive/restrictive list is based on the submission of a comprehensive safety file that is examined by SCCNFP. Where appropriate, warnings for use (which have to be printed on the finished product's label) are given in the annexes.	The consignor has to certify that dangerous goods are handed over for transport are properly classified according to the transport regulations criteria, and therefore the consignor is responsible for providing the proper information. In certain instances, the classification has to be made by the appropriate competent authority (e.g., for explosives, organic peroxides, etc.)
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?			Not applicable as there is no classification of cosmetic products**.**	

Is testing obligatory? Are there any exceptions to the obligatory testing requirements?		No.	There are no obligatory testing requirements for cosmetic products. However, the Cosmetics Directive requires that a safety assessment be carried out for each cosmetic product, based on risk. Guidelines are available on the tests that are to be carried out for the safety assessment.	
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.			Not applicable to cosmetic products (mixtures), only to cosmetic ingredients (chemicals).	
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.			There is no standardized approach for classifying cosmetic products.	
Please briefly describe the rationale for the standardized approach to untested mixtures.			No standardized approach exists on cosmetic products.	
How are mixtures classified when some endpoints have test data and others don't?			No standardised approach exists for classification of cosmetic products.	

Is there any other information regarding the approach to mixture classification that needs to be addressed?			No	
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?			There is no pending or future work on classification of cosmetic products. However, efforts are in progress between many countries/economic blocks around the world for the international harmonization of cosmetic regulations. This is one more reason why cosmetics should be excluded from the project on global harmonization of hazard classification.	

APPENDIX III: RATIONALE

TABLE 15 RATIONALE FOR WORKPLACE SYSTEMS	
SYSTEM	*RATIONALE*
USA	The Hazard Communication Standard provides exposed workers and employers using a chemical in their workplaces with the right to know the identities and hazards of those chemicals. The underlying philosophy is that the availability of information allows the selection and use of appropriate control measures, thus resulting in fewer illnesses and injuries based on chemical exposures. It thus is based on the premise that as complete disclosure as possible is the best approach. This desire for disclosure was balanced by concerns about trade secret claims (which are more common for chemicals in small concentrations) and the need for information about very small quantities. The percentage cutoffs were selected as a practical and pragmatic approach to addressing these concerns, while still ensuring that necessary information is readily available to employers and employees.
EUROPE	The standarised approach, the *conventional method,* for assessment of health effects of mixtures is based on - identified classifications of component substances and - concentration limits set to identify the same classifications as for component substances.
	The objective of the conventional method is to discourage testing for animal welfare reasons, and to provide an easy, inexpensive and from toxicological point of view valid method for classification which offers at least the same level of protection of health as the method based on testing.
	A study[8] was carried out for justification of concentration limits on acute effects. The concentration limits for classification for long term effects are based on a reasonable approach taking into consideration the characteristics of the effects.
	Often, if data are available, individual concentration limits for classification are set for substances in Annex I to Directive 67/548/EEC.

Regulatory Toxicology and Pharmacology, Vol 4 (1984), p. 145 - 156.

	For genotoxic carcinogens and mutagens normally a no-effect limit cannot be established. The conventional values of 0,1 % for category 1 and 2 carcinogens and mutagens are therefore merely set on the basis of a level of impurities and estimation of the potency of strong carcinogens.
	For reproductive toxic substances the values have been set taking the no-effect levels into consideration. The values of 1 % and 5 % for suspected carcinogens and mutagens, and for suspected reproductive toxic substances are established recognizing the lower grade of proof that these endpoints may occur in practice.
	For carcinogenic, mutagenic and reproductive toxic substances the establishment of specific concentration limits is more difficult. However, a system based on the potency of a carcinogenic substance is used to establish individual limits (see step 1 OECD report for carcinogenicity) in specific cases. The experience on the Community level is, however, in an early stage.
	The identification of toxicological end points provides the basis for the down stream legislation, like: • hazard communication by labels and Safety Data Sheets • protection of workers from the exposure to chemical agents and carcinogens, • protection of the environment from the emissions to the environment (water, air, soil) • restrictions for marketing and use of dangerous substances and preparations
	• prevention of major accidents. Hazard communication is the immediate consequence of classification. In most cases information on the identified classifications is passed to the final user, whether it be a professional user or a consumer. Information on the names of dangerous components giving rise to the classification is passed by labels according to certain specified rules from the concentrations triggering the classification.

	For professional users of preparations, in addition to labels, Safety Data Sheets on classified preparations are also submitted giving even more detailed information than the labels. In the Safety Data Sheets information shall be given on components dangerous to health from 1 % on, unless the classification limit is lower. This information is intended for the employer who according to the Community legislation has the obligation to protect the workers from the exposure to chemical agents and carcinogens. The employer has to inform the workers about the potential hazards.
	In the framework of downstream legislation other than hazard communication normally a risk assessment shall be carried out on the top of the hazard assessment to examine whether measures for protection of health and the environment are needed.
CANADA	A classification system based on cut-offs presumes that a mixture is hazardous if it contains a hazardous ingredient at a concentration exceeding a specified cut-off. The use of cut-offs is administratively straightforward and can be applied by using available data on the toxicology of ingredients in the mixture. Since WHMIS is primarily an information system, the use of cut-off values is justifiable as a means of consistently communicating information about hazardous ingredients, as contrasted with providing a hazard evaluation of the mixture. The numerical values of cut-offs, however, are necessarily arbitrary and were chosen largely for consistency between Canada and the United States.
UNCETDG	The UNCETDG regulations cover all products, whatever their end use is intended to be. Exceptions from the regulations are related to quantities carried or type of packaging used rather than to the end use. The UNCETDG approach to mixtures is a pragmatic one, i.e., it should allow the consignor to determine, without unnecessary difficulties or costs, the hazard characteristics of the mixture (including wastes, where the exact composition is not always easy to determine) which would determine its correct identification (proper shipping name), labeling, marking and packing conditions in accordance with transport requirements. Adoption of the UN Recommendations in national regulations for the transport of dangerous good is intended to address safety concerns, to facilitate the transport of products and to provide a uniform global system which minimizes or eliminates discrepancies among jurisdictions and transport modes. Classification under this system provides specific requirements for packaging container size, type, labeling and specific recommendations for substance or categories

APPENDIX IV: OTHER SYSTEMS

AUSTRALIA					
System Element	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	The National Occupational Health and Safety Commission's *Approved Criteria for Classifying Hazardous Substances* [1008(1994)] is the national standard for the classification in the workplace of hazardous substances, including mixtures. National standards are advisory becoming law after adoption by Australian Commonwealth, State, or Territory governments. Industrial Chemicals (Notification and Assessment Act) 1989 and Amendment Bill 1997. This bill governs notifications and assessment of new industrial chemicals in the Australian workplace.	The registration of end use products (EUPs) containing pesticides is by the *Agricultural and Veterinary Chemicals Code Act, the Agricultural and Veterinary Chemicals Regulation Act and the Agricultural and Veterinary Chemicals Administration Act.* There are controls on the access to chemicals in poisons legislation of the separate States of Australia, and there are also State controls on packaging and labelling.			
Which health or environmental endpoints are covered by the system?	Health effect endpoints are subdivided into: • acute lethal effects; • corrosivity • irritancy a) oral b) dermal c) inhalation • sensitisation; • carcinogenicity; • mutagenicity; • reproductive toxicity. Positive results to many of these endpoints is the basis for classification into the following categories: a) very toxic	In the health consideration of a chemical, there is consideration of all acute endpoints, as well as short-term repeat dose, subchronic, chronic, reproduction and development effects, genotoxicity and special studies (including any human poisoning incidents). Endpoints are considered on a case-by-case basis, particularly for long-term studies. A weight-of-evidence approach is used for regulatory decisions. Any evidence of abnormality (including neurotoxicity and immunotoxicity) is considered in the determination of the regulation of a chemical. Data is supplied on all endpoints for the active constituent in a pesticide. The only information generally supplied for a product (or mixture) is information relating to the acute toxicity of the mixture.			

	b) toxic c) harmful				
Definition of substance/ chemical.	**Substance:** any natural or artificial entity, composite material, mixture or formulation, other than an article. **Chemical:** any element compound or complex present as an entity or contained in a mixture.	**Definition of substance/chemical and definition of mixture/preparation.** The following definitions are present in *The Agricultural and Veterinary Chemicals Code Act, 1994*. In addition, there are working definitions which apply in the assessment of chemicals. A chemical is generally considered to be the active constituent, while the product which is to be registered is generally considered a mixture, since it normally contains active constituents and excipients or non-actives. An "agricultural chemical product" is defined as a: Substance or mixture of substances that is represented, imported, manufactured, supplied or used as a means of directly or indirectly: (a) destroying, stupefying, repelling, inhibiting the feeding of, or preventing infestation by or attacks of, any pest in relation to a plant, a place or a thing; or (b) destroying a plant; or (c) modifying the physiology of a plant or pest so as to alter its natural development, productivity, quality or reproductive capacity; or (d) modifying an effect of another agricultural chemical product; or (e) attracting a pest for the purposes of destroying it. An "agricultural chemical product" does not include: (a) a veterinary chemical product; (b) a substance or mixture of substances declared by the regulations not to be an agricultural chemical product. A "veterinary chemical product" is defined as: a substance or mixture of substances that is			

		represented as being suitable for, or is manufactured, supplied or used for, administration or application to an animal by any means, or consumption by an animal, as a way of directly or indirectly: (a) preventing, diagnosing, curing or alleviating a disease or condition in the animal or an infestation of the animal by a pest; or (b) curing or alleviating an injury suffered by the animal; or (c) modifying the physiology of the animal: (i) so as to alter its natural development, productivity, quality or reproductive capacity; or (ii) so as to make it more manageable; or (d) modifying the effect of another veterinary chemical product. A veterinary chemical product does not include: (a) a substance or mixture of substances that is: (i) prepared by a pharmacist in accordance with the instructions of a veterinary surgeon; or (ii) prepared by a veterinary surgeon; in the course of the practice, by the person preparing the substance or mixture of substance, of his or her profession as permitted by or under a law of this jurisdiction; or (b) a substance or mixture of substances declared by the regulations not to be a veterinary chemical product. All 'active constituents' used in agricultural or veterinary chemical products must be approved prior to use.			
Definition of mixture/ preparation.	**Mixture:** a physical combination of chemicals resulting from the deliberate mixing of those chemicals or from a chemical	**See above**			

	reaction.				
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	These are definitions are from the National Commission's *Approved Criteria for Classifying Hazardous Substances* [1008(1994)] or the Industrial Chemicals (Notification and Assessment Act) 1989 and Amendment Bill 1997				
Who is responsible for the classification of the mixture?	The responsibility for determining whether a substance is hazardous and for identifying its health hazards belongs to the manufacturer or importer. New industrial chemicals are assessed by the National Occupational Health and Safety Commission as individual isolated chemicals except where isolation is unfeasible because of the nature of production and/or use of the chemical.	The National Drugs and Poisons Scheduling Committee (NDPSC) recommends which Schedule the pesticide is to be placed in. This Committee is established under the auspices of the Australian Health Ministers' Advisory council, and decisions are based on the evaluation carded out in the Chemicals Unit of the TGA, within the Department of Health and Family Services. Recommendations contained in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) are published with a view to promoting uniform scheduling of substances and uniform labelling and packaging requirements throughout Australia. It has no legal standing other than that given to it by relevant legislation. Mixtures of AgVet chemicals are not necessarily classified separately from their components. An AgVet chemical product which contains one or more actives or non-actives, which are classified by the NDPSC as scheduled poisons assume the poisons schedule classification of the most toxic ingredient, unless exemptions or cut-offs are applied to low concentrations (as often happens). While particular combinations of substances in therapeutic goods (eg combination analgesics) for human use may have a poisons schedule allocated on the basis of the specific hazards of that combination, this approach is extremely rare for AgVet chemical combination products.			

		Where individual AgVet products are combined as mixtures during use (eg in tank mixtures), there is no formal mechanism for classifying the hazard of such combinations.			
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Data is used from mixtures tested as a whole or not tested as a whole. For those not tested as a whole each ingredient in the mixture is considered separately against the health effects criteria.	Where available, test data on the mixture are used for classification, with information assessed on the active constituent used to determine long term hazards relating to the use of the product. Where no information is available on the mixture, extrapolations are made based on the assessment of individual components of the formulation.			
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	Not obligatory for mixtures	Testing of active constituents is required prior to approval of that source of active and product registration. The data required must cover acute, short-term, sub-chronic and long-term toxicity studies, and investigations of reproductive and development toxicity, genotoxicity, carcinogenicity and other toxicology studies. Any available human data should also be presented. Where a product is based on an approved active constituent, it may be possible to estimate the toxicity of a formulation by extrapolation from data on the active constituent. Data on the product to be registered is always preferable, and should address the acute toxicity considerations.			
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	No specific policy applies to mixtures. As stated above data is used from mixtures tested as a whole or not tested as a whole. For those not tested as a whole each ingredient in the mixture is considered separately against the health effects criteria. Information on health effects for a substance can be obtained from existing classifications for substances which have similar structural relationships. For new industrial chemicals analogue data for specific chemicals is only accepted when	Extrapolation from the hazards of individual components is used when information on the acute or chronic hazards of the mixture is not available. There is generally no information on the effects of chronic exposure to mixtures of chemicals, or where more than one active constituent is used in combination.			

	specific data is unobtainable and the structural relationship is close.				
Please describe any standardised approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	Concentration cut-off levels are used to determine whether or not a mixture is hazardous on the basis of its ingredients, and to classify the mixture on the basis of its health effects. Formula as applied to the calculation of cut-offs for mixtures are taken from EC methodology. Currently being updated to reflect the amendments of EC directive 93/18/EC.	Not done			
Please briefly describe the rationale for the standardized approach to untested mixtures.	No specific mixtures rationale is applied but if the mixture has not been tested as a whole the health effects data of each ingredient in the mixture are considered. Mixtures do not require additional animal testing will need to be carried out if individual chemical data is available.				
How are mixtures classified when some endpoints have test data and others don't?	No specific mixtures policy but, as mentioned above, information on health effects for a substance can be obtained from existing classifications for substances which have similar structural relationships.	Consideration of all data available is made, and a conservative approach, involving the use of the most toxic endpoint is used. In some cases, additional safety factors may be used to limit exposure where the information available is limited.			
Is there any other information regarding the	No.	The difficulty in determining the risks posed by exposure to more than one chemical; particularly over a long period is of concern for public health			

approach to mixture classification that needs to be addressed?		risk assessment. It has been noted that the matrices for determining risks from multiple exposure are extremely complex, and the matter is currently under consideration. In Australia, we have been noting with interest the research on this matter being carried out, and await the outcome of this work.			
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	No				

Additional Questions Regarding Mixture Classifications:

1. How are hazardous liquid or solid hazardous wastes (mixtures) classified as hazardous to health and the environment for purposes of classification and labelling? In what circumstances?

2. How are articles classified under your system? How is article defined? Are articles exempted? Under what circumstances?

Workplace:

Article: An item which is formed to a specific shape, surface or design during production, has an end function dependent in whole or in part on its shape or design, and which undergoes no change in chemical composition and physical state during the end use except as an intrinsic aspect of that end use. Fluids and particles are not considered articles, regardless of the shape or design.

Department of Health:

In the system of classifying poisons, a chemical is defined as being a poison if it is a substance listed in the schedules, or if it contains a substance listed in the schedules. Rather than making a general exemption for articles, the decision was made to specifically list items which are exempted, even though they may contain scheduled materials. These are listed as a separate Appendix in the SUSDP. Examples of exempted products which may contain poisons include ceramics, batteries, electronic components, explosives, food, matches, glass, timber, paper, porcelain etc. Some items (such as food) are controlled under specific legislation; other are controlled only by the provisions of the Trade Practices Act. New articles can be added to the exempt list as required.

3. How are alloys treated under your system? Are they considered mixtures? Is there any special consideration?

Workplace: Alloys are not distinguished.

4. Are there any other products that receive special treatment, e.g., elastomers? What are they, and how are they classified?

5. Are there any products that are addressed under special sectors, but are also covered in the workplace (e.g., pharmaceuticals)? What accommodations are made in the general use/workplace approach to address these types of products?

6. Please indicate any key definitions from your system that will help those unfamiliar with it to understand the scope and substance of the approach.

7. Is your system patterned after another existing system? Which one? Are you aware of your system being applied somewhere outside your own country or region?

Workplace: the National Commission has adopted the classification criteria of the European Communities.

Department of Health:

The Australian system has historically developed within Australia, rather than being patterned on any external system. Recently, there have been moves for Australia and New Zealand to harmonize the controls on poisons. The two systems were already similar, and moves are underway to attempt to harmonize fully.

8. Are there any lessons you have learned in implementing your system that would help us in considering a proposed approach? Anything you would do differently now having that knowledge?

9. Are there any other aspects of your system that you would like to describe to ensure we have a complete picture of your approach.

AUSTRIA					
System Element	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	Chemicals Act 1996 (FLG 53/1997) 67/548/EEC 88/379/EEC	Plant Protection Products Act 1997 (FLG 60/1997)	Same as referring entries for general use/workplace.		
Which health or environmental endpoints are covered by the system?	see Section 3 – Paragraph 1 Chemicals Act 1996 or Section 2 – Paragraph 2 67/548/EEC	see Section 3 Paragraph 1 Chemicals Act 1996			
Definition of substance/chemical.	see Section 2 - Paragraph 1 Chemicals Act	see §2 Plant Protection Products Act 1997			
Definition of mixture/preparation.	see Section 2 - Paragraph 5 Chemicals Act	see §2 (5) Plant Protection Products Act 1997			
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	legislation	legislation			
Who is responsible for the classification of the mixture?	see Section 27 Chemicals Act	see §§ 37(3) and 40 Plant Protection Products Act 1997			
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Yes, existing data complying with GLP; there also exist calculation methods	test data on Pesticides are used as basis for classification.			
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	only for new substances, Section 7 Chemicals Act	testing obligatory			

Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	see Chemicals Ordinance FLG No 208/1989, Section 3 Paragraph 2 such methods are not allowed	for Pesticides authorised according to the Plant Protection Act 1948 without re-evaluation according to the Plant Protection Acts 1990 or 1997 extrapolation of hazards according to Chemicals Act 1997 ordinance FLG 620/1993			
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	calculation methods based on concentration limits of ingredients as outlined in Directive 88/379/EEC				

BRAZIL					
System Element	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	Brazil approved the ILO convention 170, 1990, concerning safety in the use of chemicals at work, by legislatiive law. This convention and the recommendatiom177 establishes general guidelines to chemical classification but this have not regulated in ordinary law.	To agriculture use	include home use insecticides, rat poison, insect repellent regulation 321 07/28/1997	include personal hygiene, cosmetocs, perfumes	transport of dangerous goods mercosul accord law 1797 01/25/1996
Which health or environmental endpoints are covered by the system?		Toxicity in superior animals; mutagenicity, embryotoxicity and carcinogenicity in animals; toxicity to microorganisms, microcrustaceans, fish, algae, soil and plant organisms, bioaccumulation, persistence, biodegradation.	Toxicity in superior animals, reproductive effects, teratogenicity, acute and chronic neurotoxicity, genetic effects, NOEL, NOAEL, IDA, TLV, RD, ETC. Carcinogenic reppelent isn't authorized. Deactivation and discard methods are necessary, stability	the law regulates that the chemicals which can participate in cosmetics and other mixtures composition need to be harmless and they are present in a list of ministry of health. There isn't reference to environment.	The basis for the classification are similar to those in recommendation for transport of dangerous goods by un
Definition of substance/chemical.		Don't have	don't have	don't have	
Definition of mixture/preparation.		Don't have	formulation is an association of active ingredients, solvents, diluents, additives, inert substances and other components to obtain an efficient and useful end product to its purpose	don't have	

Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.			yes		
Who is responsible for the classification of the mixture?		Ministry of health; ministry of environment and ministry of agriculture	ministry of health	ministry of health	the basis for the classification are elaborated by the ministry of transport of the countries, but the classification is done by the dangerous chemicals transporter.
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?		yes	yes	no	yes
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?			No, the mixture is not authorized in this case	normally, there isn't obligation of tests when the formulation is made with authorized chemicals. On the other hand, the ministry of health need emit an opinion about the mixture harmless	
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.		no		Only are accepted mixtures with authorized ingredients.	
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-		There are lists with authorized substances with its % cut-offs. But even in this case , tests in the mixture are	There are lists with authorized substances with its % cut-offs. But even in this case , tests in the mixture are	The classification is done in comparison with the list of authorized substances	

offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.		required.	required		
Please briefly describe the rationale for the standardized approach to untested mixtures.					
How are mixtures classified when some endpoints have test data and others don't?					
Is there any other information regarding the approach to mixture classification that needs to be addressed?					

Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?					

JAPAN						
System Element	**General Use 1**	**General Use 2**	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**
Regulation/law	Poisonous and Deleterious Substances Control Law	The Law concerning the Examination & Regulation of Manufacture, etc. of Chemical Substances	Industrial Safety & Health Law	Agricultural Chemicals Law	Food Sanitation Law	Pharmaceutical Affairs Law
Which health or environmental endpoints are covered by the system?	Acute toxicity & irritancy (not specified in the law)	biodegradability, bioaccumulation, chronic toxicity, reproductive toxicity, teratogenicity, mutagenicity, carcinogenicity, toxicokinetics, pharmacological tests	mutagenicity, carcinogenicity	human health and environmental safety (not specified)	health end point (not specified)	health end point (not specified)
Definition of substance/chemical.	All substances except pharmaceuticals	compound obtained by causing a chemical reaction to occur in elements, a compound and/or compounds, excluding in the following: specified poisons, stimulants ,stimulants' ??? materials, narcotics, & psychotropics, radioactive substances.	chemical substance means element and compound (article 2)	agricultural chemicals: substances for control of fungi, ?, mites, insects or other animals and plants or viruses which are injurious to crops including natural enemies and for plant growth regulators	substances to be used in or on food, in the process of manufacturing food or for the purpose of processing or preserving food, by adding, mixing, ? or other means	article intended to be used by means of rubbing, sprinkling or by similar application to the human body or cleaning, beautifying, promoting effectiveness, altering the appearance of the human body, and for keeping the skin and hair healthy.

Definition of mixture/preparation.	No definition in the law. Toxic mixtures and preparations are listed in the same way as toxic pure substances.	No definition (a mixture whose components cannot be separated is handled in the same way as pure substances)	No definition	formulation: the combination of various ingredients	no definition	no definition
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	Definition by the law and the Cabinet Order	Chemical: By the law Mixture: The interpretation in above is mentioned by notice	N/A	by the law	N/A	N/A
Who is responsible for the classification of the mixture?	The Government of Japan	The Government of Japan	N/A	The Government of Japan	N/A	N/A
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Yes. If human experience is available, test data will not be ?	yes	N/A	yes	N/A	N/A
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	no	obligatory testing: new chemicals exceptions: new chemicals to be produced or imported in less 1 l/year	N/A	yes, no exceptions	N/A	N/A
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	Based on expert judgment	if there is scientific knowledge, it can be used	N/A	N/A	N/A	N/A

Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	No standardized methodology is established	No standardized methodology is established	No standardized methodology is established	No standardized methodology is established	No standardized methodology is established	No standardized methodology is established
Please briefly describe the rationale for the standardized approach to untested mixtures.	N/A	N/A	N/A	N/A	N/A	N/A
How are mixtures classified when some endpoints have test data and others don't?	only available data are examined	mixtures are classified by available data	N/A	N/A	all data are required	all data are required
Is there any other information regarding the approach to mixture classification that needs to be addressed?	No	no	no	no	no	no
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	nothing special for the moment	nothing special for the moment	no	no	no	no

KOREA						
System Element	**General Use**	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	Toxic Chemicals Control Act (TCCA)	industrial safety and health act/ presidential decree/ ministerial ordinance/ public notice of the ministry of labor(mol)	agrochemicals management act (ama)			
Which health or environmental endpoints are covered by the system?	A. Health endpoints: acute toxicity,(oral, dermal, inhalation) irritation(skin, eye, respiratory) corrosion(skin, eye) sensitization(skin, respiratory) mutagenicity carcinogenicity reproductive toxin long-term systemic toxicity B. Environmental endpoints: aquatic toxicity(fish, daphnia, algae) degradation octanol-water partition coefficient bioaccumulation.	Classification standards are regulated in the standards for preparing and keeping on file the msds, etc.(mol public notice no. 97-27) substances hazardous to health: highly toxic, toxic, corrosive, irritating, sensitizing, carcinogenic, mutagenic, toxic for reproduction. Hazardous substances environment: physically hazardous substances: explosive, oxidizing, extremely, water prohibiting (refer to annex for details)	both			
Definition of substance/chemical.	chemical substances: materials created by an artificial chemical reaction of elements or any combination thereof or a material extracted and purified from substances occurring in	"chemical substances" refers to any element or substance created as a result of a chemical reaction in such elements.	pesticides			

	nature					
Definition of mixture/preparation.	Mixture: a product which is processed by advertently adding chemical to other chemical substances for the purpose of efficient use thereof.	"mixture" refers to any substance in which two or more chemical substances commingled without a chemical reaction "preparation" refers to any product manufactured by adding vehicle, solvent, stabilizer, etc. to the main component of chemical substances	Combined pesticides			
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	A. both definitions are provided in the relevant regulations. . regulatory citations: (a) chemical substances: TCCA, Article 3 (b) mixture: national institute of environmental research's (NIER) Public Notice No. 1997-3	definitions for each term are included in the standards for preparing and keeping on file the msds, etc. (mol public notice no. 97-3 give regulatory citation where available: workplace in the nation.	Definitions are in the ama			
Who is responsible for the classification of the mixture?	Suppliers, handlers, and transporters of toxic chemicals the recommended classifications for toxic chemicals are provided by NIER	A business owner who is classified to manufacture, import, use, transport or store the mixture	Rural development administration (rda)			
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Partly, yes classification of mixtures, which is provided by NIER public notice no. 1997-2 and no. 1997-3, is only based on the most hazardous components, but a person who is responsible for classification can reclassify	no	Yes, test should be done for all the combined pesticides before registration			

	the mixture if someone knows the hazard of mixture itself or has test data.					
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	Testing is not obligatorily required	testing of a mixture is not an obligation	Testing is obligatory. There is no exception.			
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	There are not any provisions in the regulations. However, it would be possible if the use of either data is applied on the side of precaution.	No other data is used	There are complete testing data for all the mixtures.			
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	There are not overall standardized concentration cut-off values to classify mixtures. However, the lowest percentage cut-off values are used as follows: (there are some exceptions) for carcinogenicity and reproductive toxicity: 0.1% for other endpoints:1.0%	methods for classifying mixtures when test data is not available, are as follows: in the case of physically dangerous substances, the data on the individual chemicals that compose the mixture is used for the assessment in the case of health hazardous substances, the substance in question is considered to be similarly health hazardous as the individual chemicals, if the individual	No standardized approach to classifying mixtures.			

		chemicals that compose the mixture constitute more than 1% of the chemical(over 0.1%, by weight ratio, for carcinogenic chemicals)				
Please briefly describe the rationale for the standardized approach to untested mixtures.	NIER public notice provides the appropriate classifications of any mixtures based on the most hazardous component which is toxic chemical. TCCA's mixture classification scheme covers only the toxic chemical. Thus, any mixture not designated as toxic chemicals is not necessarily classified by the NIER's recommendation.	The classification point of the mixture in question is determined from the data on the individual components that constitute the mixture	none			
How are mixtures classified when some endpoints have test data and others don't?	Our mixture classifications are only based on available test dataat the time of classification. Available test data would be very valuable because some substances are extensively tested and others not.	In case where test results of hazardness mixtures exist, sucg data is preferentially used to decide whether or not the mixture is hazardous. In case where test results of hazardness of mixtures do not exist, the decision is made based on the hazardness of the component substances of the mixture.	none			

Is there any other information regarding the approach to mixture classification that needs to be addressed?	It is very important to understand the definition, designation criteria and scope of toxic chemicals	no	no			
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	not yet however, if classification scheme of the mixture will be globally harmonized, it will be introduced in a positive manner.	no	no			

NEW ZEALAND					
System Element	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law	Hazardous Substances & New Organisms (HSNO) Act (Regulations under development) This statute encompasses all substances (including mixtures) above a certain degree of hazard regardless of end use – e.g. pesticides, explosives etc all included.	Hazardous Substances & New Organisms Act (Regulations under development) **and** Agricultural compounds and Veterinary Medicines (ACVM) Act	Hazardous Substances & New Organisms Act (Regulations under development)	Limited control under the Medicines Act	Fair Trading Act requires all goods to be fit for purpose
Which health or environmental endpoints are covered by the system?	any of the following hazardous properties, provided a threshold is exceeded explosive capacity flammability oxidising capacity corrosiveness toxicity ecotoxicity	As at left plus (ACVM Act) animal welfare export produce certification compliance with food standards	As for general use/ workplace	Extensive power to take action if a person injured by product	Extensive power to take action of product fails in intended purpose
Definition of substance/chemical	(s.2 HSNO Act) (a) Any element, defined mixture of elements, compounds, or defined mixture of compounds, either naturally occurring or produced synthetically, or any mixtures thereof: (b) Any isotope, allotrope, isomer, congener, radical, or ion of an element or compound which has been declared by the Authority, by notice in	As at left	As at left	any natural or artificial substance, whether in solid or liquid form or in the form of a gas or vapour:	

	the Gazette, to be a different substance from that element or compound: (c) Any mixtures or combinations of any of the above: (d) Any manufactured article containing, incorporating, or including any hazardous substance with explosive properties:				
Definition of mixture/preparation	Identical to that for substance	As at left	As at left	As above	
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	Definition is in the statute. Definition is limited by a regulation making power to set thresholds for hazardous substances below which the statute does not apply	As at left	As at left	Substances generally considered product by product	
Who is responsible for the classification of the mixture?	Classification scheme is in regulations – administering authority may alter the controls attached to the classification.	Classification will be primarily as at left. However the ACVM Act provides for "purpose specific" controls for the reasons given above on a case by case basis (in practice much will be done with certain classes)	As for first column	Classification generally not undertaken	
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Generally, yes. In the absence of test data, judgements based on estimation or extrapolation are used. This area will be better defined over the next 3-4 months as part of methodology development under the	Test data for the (pesticide) mixture may be required for pesticides. NB test results from other countries are accepted any only NZ specific matters require further testing.	As for first column		

	HSNO Act.				
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	Generally no. However, in some cases (e.g. pesticide formulations) test data may be required.	See above	As for first column		
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	Generally, yes. (see response above)	Yes – subject to above qualifications	As for first column		
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	NZ presently does not have "standardised approaches" in regulation or statute. However judgements have historically been based on practices recommended by international organisations (e.g. WHO recommendations for human toxics, UNCETDG approach for explosive, flammable etc).	As at left noting above qualifications	As for first column		
Please briefly describe the rationale for the standardized approach to untested mixtures.	See above – approach used is because historically NZ has been a largely an importer rather than manufacturer of these substances.		As for first column		
How are mixtures classified when some	This has been based on expert judgement (& is	See above	As for first column		

endpoints have test data and others don't?	likely to continue) with a weighting in favour of test information about the actual mixture.				
Is there any other information regarding the approach to mixture classification that needs to be addressed?					
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	New Zealand will complete regulations and a methodology under s.9 of the HSNO Act by September of this year – both will have effects on the attitudes taken	ACVM Act will be in force at the same time as HSNO Act.	As for first column		

NORWAY					
System Element	**General Use/Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	Regulations relating to the classification, labelling, etc. of dangerous chemicals With supplementary regulations: Regulations relating to criteria for the classification of dangerous chemicals Regulations relating to symbols, symbol letters, indications of danger and warning phrases to be used in labelling dangerous chemicals Regulations relating to the choice of safety advice phrases and requirements for the labelling of dangerous chemicals Regulations relating to packaging fitted with child-resistant fastenings and tactile warning of danger Regulations relating to the labelling of chemicals, substances and preparations, containing organic solvents (OAR-labelling)		General use		
Which health or environmental endpoints are covered by the system?	= Directive 67/548/EEC + 88/379/EEC and in addition organic solvents which may be used in such a way that they are dangerous to health		= General use		
Definition of substance/chemical	= Directive 67/548/EEC + 88/379/EEC and *chemicals* is the generic term both for substances and preparations		= General use		
Definition of mixture/preparation	= Directive 67/548/EEC + 88/379/EEC and *chemicals* is the generic term both for substances and preparations		= General use		
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	In the regulation		= General use		
Who is responsible for the classification of the mixture?	Any person that manufactures, imports and/or places on the market dangerous chemicals		= General use		
Are available test	= Directive 67/548/EEC + 88/379/EEC except for		= General use		

data on the mixture used as the basis for classification of the mixture? Any exceptions?	sensitising properties Norwegian regulation do not accept testing (classification on the basis of their constituents)				
Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	No – testing is not accepted for sensitising, cancerogenic, mutagenic or reproductive property		= General use		
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	= Directive 67/548/EEC + 88/379/EEC		= General use		
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	= Directive 67/548/EEC + 88/379/EEC except for cancerogenic chemicals. Norwegian legislation includes a two step system: firstly the substance is evaluated to determine whether or not it is cancerogenic on the basis of any results available from studies and secondly the dose-response relationship is assessed to decide the potency of the substances as a carcinogen. On the basis of these results, carcinogenic substances are classified in three groups (high (K1), medium (K2) and low (K3) potency). Preparations are classified solely on the basis of the concentrations of their constituents and the classification of these. A preparation shall be classified as cancerogenic if it contains more than 0.01 % of a high potent substance (K1), 0.1 % of a medium potent substance (K2) or 1 % of a low potent substance (K3).		= General use		
Please briefly describe the rationale for the standardized approach to untested mixtures.	= Directive 67/548/EEC + 88/379/EEC The exception for sensitising properties (from the EU system) is based on the lack of validated test methods for testing of preparations. The test methods are designed for substances and not for preparations. In		= General use		

	these, the substance is diluted and the concentration is too low to give optimal test conditions. False negatives might be expected.				
How are mixtures classified when some endpoints have test data and others don't?	= Directive 67/548/EEC + 88/379/EEC		= General use		

Is there any other information regarding the approach to mixture classification that needs to be addressed?	= Directive 67/548/EEC + 88/379/EEC		= General use		
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	Any changes in the EU system (i.e. Directive 67/548/EEC + 88/379/EEC)		= General use		

SLOVENIA					
System Element	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	Articles 19-23 of the proposal of the Act on Chemicals which is in the Parliamental procedure just now, as well as two new regulations on CPL of substances and of preparations	the same as for general use	the same as for general use	final cosmetic products are exempted from the Regulation on CPL of preparations; however the products like dispensers with flammable aerosols are to be labelled according to their flammability with additional warning text	The provisions of the new Slovene Regulation on CPL of preparations do not apply to the following substances and preparations which are, in their final state, intended for the final user and governed by other regulations: medicinal products in human and veterinary use, drugs, cosmetic products, mixtures of waste substances, unless otherwise prescribed in the regulations related to waste, foodstuffs, animal feedingstuffs, radioactive preparations, ammunitions and explosives placed on the market for pyrotechnical purposes or for blasting. In addition, the provisions of the new Slovene Regulation on CPL of preparations also do not apply to: - the transportation of dangerous goods by road, rail, on inland waterways, sea or air, preparations in transit which are under customs control and are not processed, re-packaged or treated on the territory of the Republic of Slovenia.
Which health or environmental endpoints are covered by the system?	beside physico-chemical properties as extremely, very toxic, toxic, harmful, corrosive, irritant, sensitizing, carcinogenic, mutagenic, preparations toxic for reproduction, preparations dangerous	the same as for general use	the same as for general use		

	for the environment (aquatic environment - fish, Daphnia, algae, non-aquatic environment - flora, fauna, soil organisms, bees, ozone layer, degradability - COD, BOD)				
Definition of substance/chemical.	a) substances are chemical elements or their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the products and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. b) chemicals are substances and preparations	the same as for general use	the same as for general use		
Definition of mixture/preparation.	Preparations are mixtures or solutions composed of two or more substances	the same as for general use	the same as for general use		
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.	definitions are from the proposal of the Act on chemicals which is in the Parliamental procedure just now, and also from two new Regulations on CPL of substances and preparations	the same as for general use	the same as for general use		
Who is responsible for the classification of the	the person putting it on the market, for control	the same as for general use	the same as for general use		

mixture?	of proper CPL Ministry of Health with Health Inspectorate is responsible (according to the new Act on chemicals specialized inspectors for chemicals will be trained).				
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?	Yes. Available test data or data deriving from practical experience in humans are superior to the calculation method (for detailed wording see Annex - Article 5 of our new Regulation on CPL of preparations)	the same as for general use	the same as for general use		

Is testing obligatory? Are there any exceptions to the obligatory testing requirements?	If any of the toxicological properties of the preparation was not ascertained during the experimental procedure referred to in paragraph 2 (b) of the Article 5, it must be assessed in accordance with the agreed calculation method from paragraph 2 (a) of the Article 5. Responsible persons carrying out manufacturing, importing and distributing of dangerous preparations are obliged to perform all necessary investigations in order to obtain existing data on the properties of the preparation and its effects on human health and the environment. In the case of preparations for which there is no data available, or where the data was not obtained in accordance with the methods referred to in Annex V to the Regulation on Dangerous Substances, the requirements for further testing shall be considered on a case-by-	the same as for general use	the same as for general use		

	case basis in order to reduce the tests on animals. In order to avoid the need to perform tests on vertebrates, responsible persons manufacturing, importing or distributing the same preparation should agree in writing on mutual use of obtained toxicological and ecotoxicological data if it is possible to prove that the preparations are identical to such a degree that their toxicological and ecotoxicological properties are the same. (for detailed wording see Annex - Article 5 of our new regulation on CPL of preparations)				
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.	Yes. For instance it could be possible for isomeres if we suppose that they dont have very different toxicological properties. We still lack practical experience	the same as for general use	the same as for general use		
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or	It is the agreed calcualtion method of EU which we adopted. We dont describe the detailes here because the	the same as for general use	the same as for general use		

percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.	system is completely the same as of EU.				
Please briefly describe the rationale for the standardized approach to untested mixtures.	They shall be classified according to all the test data collected and for other properties calculation method is to be used. When the preparation contains at least one component labelled (in accordance with the Regulation on Dangerous Substances) with the special notice "Warning Substance not thoroughly tested", the preparation should be clearly labelled with the notice: "Warning preparation contains substance which has not been thoroughly tested"	the same as for general use	the same as for general use		
How are mixtures classified when some endpoints have test data and others don't?	on a case-by-case basis (for detailed wording see Annex - Article 5 of our new regulation on CPL of preparations)	the same as for general use	the same as for general use		
Is there any other information regarding the approach to mixture classification that needs	all the details of the EU system are to be addressed	the same as for general use	the same as for general use		

to be addressed?					
Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?	approximation to EU	the same as for general use	the same as for general use		

SWEDEN					
System Element	**Workplace**	**Pesticides**	**Consumer Products**	**Cosmetics**	**Other**
Regulation/law.	See EU legislation.		See EU legislation. Besides that, Sweden has a national derogation as described below.	See EU legislation	
Which health or environmental endpoints are covered by the system?			See EU legislation. Sweden has a national derogation concerning the endpoint acute oral toxicity: An additional category of danger "Moderately harmful" covers certain preparations which do not fulfill the criteria for classification as "Harmful".		
Definition of substance/chemical.					
Definition of mixture/preparation.					
Are these definitions in the regulation or legislation, or have they been developed as interpretational or working definitions? Give regulatory cites where available.					
Who is responsible for the classification of the mixture?					
Are available test data on the mixture used as the basis for classification of the mixture? Any exceptions?					
Is testing obligatory? Are					

there any exceptions to the obligatory testing requirements?					
Where complete testing data are not available on the mixture itself, is the use of other data (such as structure/activity relationships) allowed to estimate or extrapolate the hazards? Give examples.					
Please describe any standardized approach to classifying mixtures when test data are not available (e.g., formulae or percentage cut-offs). Where a different approach is used for any of the health or environmental endpoints, please identify the endpoints and the approach used.					
Please briefly describe the rationale for the standardized approach to untested mixtures.					
How are mixtures classified when some endpoints have test data and others don't?					
Is there any other information regarding the approach to mixture classification that needs to be addressed?					

Is there any future or pending work or activity that is likely to have an impact on the harmonization of mixture criteria?					

APPENDIX V: EU ENVIRONMENTAL CRITERIA

Article 7
Evaluation of environmental hazards

1. The hazards of a preparation for the environment shall be assessed by one or more of the following procedures :

   (a) by a conventional method described in [...] Annex III to this Directive [...].

   (b) by determining the hazardous properties of preparation for the environment necessary for appropriate classification in accordance with the criteria in Annex VI of Directive 67/548/EEC. These properties will be determined by means of the methods laid down in Part C of Annex V to Directive 67/548/EEC unless, in the case of plant protection products, other internationally recognised methods are acceptable in accordance with the provisions of Annexes II and III of Directive 91/414/EEC. Without prejudice to the testing requirements set out in Directive 91/414/EEC the conditions for application of the test methods shall be described in Annex III Part C to this Directive.

3. When an ecotoxicological property is established by method 1(b) [...] to obtain new data, the test shall be conducted in compliance with the principles of good laboratory practice provided for in Directive 87/18/EEC and with the provisions of Directive 86/609/EEC.

Where the environmental hazards have been assessed by both the procedures mentioned above, the results of the methods referred to in 1(b) [...] shall be used for classifying the preparation.

4. For preparations of a known composition with the exception of those covered by Directive 91/414/EEC classified in accordance with method 1(b) above a new

evaluation of environmental hazard either by method 1(a) or 1(b) shall be performed whenever:

– changes of composition of the initial concentration as a weight/weight or volume/volume percentage, of one or more of the dangerous constituents are introduced by the manufacturer, in accordance with the following table :

Initial concentration range of the constituent	Permitted variation in initial concentration of the constituent
$\leq$ 2.5%	$\pm$ 30%
> 2.5 $\leq$ 10%	$\pm$20%
> 10 $\leq$ 25%	$\pm$10%
> 25 $\leq$ 100%	$\pm$5%

– changes of composition involving the substitution or addition of one or more constituents, which may or may not be dangerous within the meaning of the definitions of this Directive, are introduced by the manufacturer.

This will apply unless there is valid scientific justification for considering that a re-evaluation of the hazard will not result in a change of classification.

ANNEX III

PART A

METHODS FOR THE EVALUATION OF THE ENVIRONMENTAL HAZARDS OF PREPARTIONS IN ACCORDANCE WITH ARTICLE 7

Introduction

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

Part A gives the calculation procedure according to Article 7(1)(a) and 7(2)(a) and gives the R phrases to be assigned to the classification of the preparation.

Part B gives the concentration limits to be used when applying the conventional method and the relevant symbols and R phrases for classification.

In accordance with Article 71(a) the environmental hazards of a preparation shall be assessed by the conventional method described in parts A and B of this Annex, using individual concentration limits.

(a) Where the dangerous substances listed in Annex 1 to Directive 67/548/EEC are assigned concentration limits necessary for the application of the method of assessment described in part A or this Annex (...), these concentration limits must be used.

(b) Where the dangerous substances do not appear in Annex 1 to Directive 67/548/EEC or appear there without the concentration limits necessary for the application of the method of evaluation described in Part A of this Annex (...), the concentration limits shall be assigned in accordance with the specification in part B of this Annex (...).

Part C gives the test methods for the evaluation of the hazards for the aquatic environment.

Procedure for evaluation of environmental hazards

a) Aquatic environment

I. Conventional method for the evaluation of hazards to the aquatic environment

The conventional method for the evaluation of hazards to the aquatic environment takes into account all the hazards that a substance may entail for this medium according to the following specifications.

The following preparations shall be classified as dangerous for the environment

I.1. and assigned the symbol 'N', the indication of danger 'dangerous for the environment' and the risk phrases R50 and R53 (R50-53):

I.1.1. preparations containing one or more substances classified as dangerous to the environment and to which is assigned phrases R50-53 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 1) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.1.2. preparations containing more than one substance classified as dangerous for the environment and to which is assigned phrases R50-53 in lower individual concentrations than the limits specified under I.1.1a) or b) if:

$$\sum \left(\frac{P_{N,R50-53}}{L_{N,R50-53}} \right) \geq 1$$

where: PN,R50-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R50-53 in the preparation,

LN,R50-53 is the limit R50-53 for each substance dangerous for the environment to which is assigned the phrases R50-53, expressed as percentage by weight

I.2. and assigned the symbol 'N', the indication of danger 'dangerous for the environment' and the risk phrases R51 and R53 (R51-53) unless the preparation is already classified according to I.1. above.

I.2.1. preparations containing one or more than one substance classified as dangerous to the environment and to which is assigned phrases R50-53 or R51-53 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 1) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.2.2. preparations containing more than one of the substances classified as dangerous for the environment and to which is assigned phrases R50-53 or R51-53 in lower individual concentrations than the limits specified under I.2.1a) or b) if:

$$\sum\left(\frac{P_{N,R50-53}}{L_{N,R51-53}}+\frac{P_{N,R51-53}}{L_{N,R51-53}}\right)\geq 1$$

where: $P_{N,R50-53}$ is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R50-53 in the preparation,

$P_{N,R51-53}$ is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R51-53 in the preparation,

$L_{N,R51-53}$ is the respective limit R51-53 for each substance dangerous for the environment to which is assigned phrases R50-53 or R51-53, expressed as percentage by weight

I.3. and assigned the risk phrases R52 and R53 (R52-53) unless the preparation is already classified according to I.1. or I.2. above.

I.3.1. preparations containing one or more than one substance classified as dangerous to the environment and to which is assigned phrases R50-53 or R51-53 or R52-53 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 1) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.3.2. preparations containing more than one of the substances classified as dangerous for the environment and to which is assigned phrases R51-53 or R50-53 or R52-53 in lower individual concentrations than the limits specified under I.3.1a) or b) if:

$$\sum\left(\frac{P_{N,R50-53}}{L_{R52-53}}+\frac{P_{N,R51-53}}{L_{R52-53}}+\frac{P_{R52-53}}{L_{R52-53}}\right)\geq 1$$

where: PN,R50-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R50-53 in the preparation,

PN,R51-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R51-53 in the preparation,

PR52-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R52-53 in the preparation,

LR52-53 is the respective limit R52-53 for each substance dangerous for the environment to which is assigned phrases R50-53 or R51-53 or R52-53, expressed as percentage by weight

I.4. and assigned the symbol 'N', the indication of danger 'dangerous for the environment' and the risk phrase R50unless the preparation is already classified according to I.1. above:

I.4.1. preparations containing one or more than one substance classified as dangerous to the environment and to which is assigned phrase R50 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 2) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.4.2. preparations containing more than one substance classified as dangerous for the environment and to which is assigned phrase R50 in lower individual concentrations than the limits specified under I.4.1a) or b) if:

$$\sum\left(\frac{P_{N,R50}}{L_{N,R50}}\right)\geq 1$$

where: PN,R50 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R50 in the preparation,

LN,R50 is the limit R50 for each substance dangerous for the environment to which is assigned phrases R50, expressed as percentage by weight

I.4.3. preparations containing one or more than one of the substances classified as dangerous for the environment and to which is assigned phrase R50 not meeting the criteria under 1.4.1 or I.4.2. and containing one or more than one substance classified as dangerous for the environment and to which is assigned phrases R50-53 if:

$$\sum\left(\frac{P_{N,R50}}{L_{N,R50}}+\frac{P_{N,R50-53}}{L_{N,R50}}\right)\geq 1$$

where: PN,R50 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R50 in the preparation,

PN,R50-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrases R50-53 in the preparation,

LN,R50 is the respective limit R50 for each substance dangerous for the environment to which is assigned phrases R50 or R50-53, expressed as percentage by weight

I.5. and assigned the risk phrase R52 unless the preparation is already classified according to I.1., I.2., I.3. or I.4. above:

I.5.1. preparations containing one or more than one substance classified as dangerous to the environment and to which is assigned phrase R52 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 3) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.5.2. preparations containing more than one substance classified as dangerous for the environment and to which is assigned phrase R52 in lower individual concentrations than the limits specified under I.5.1a) or b) if:

$$\sum \frac{P_{R52}}{L_{R52}} \geq 1$$

where: PR52 is the percentage by weight of each substance dangerous for the environment to which is assigned phrase R52 in the preparation,

LR52 is the limit R52 for each substance dangerous for the environment to which is assigned phrase R52, expressed as percentage by weight

I.6. and assigned the risk phrase R53 unless the preparation is already classified according to I.1., I.2. or 1.3 above:

I.6.1. preparations containing one or more than one substance classified as dangerous to the environment and to which is assigned phrase R53 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or
b) the concentration specified in Part B of this Annex (Table 4) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.6.2. preparations containing more than one substance classified as dangerous for the environment and to which is assigned phrase R53 in lower individual concentrations than the limits specified under I.6.1a) or b) if:

$$\sum\left(\frac{P_{R53}}{L_{R53}}\right)\geq 1$$

where: PR53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrase R53 in the preparation,

LR53 is the limit R53 for each substance dangerous for the environment to which is assigned phrase R53, expressed as percentage by weight

I.6.3. preparations containing one or more than one of the substances classified as dangerous for the environment and to which is assigned phrase R53 not meeting the criteria under I.6.2. and containing one or more than one substance classified as dangerous for the environment and to which is assigned phrases R50-53 or R51-53 or R52-53 if:

$$\sum\left(\frac{P_{R53}}{L_{R53}}+\frac{P_{N,R50-53}}{L_{R53}}+\frac{P_{N,R51-53}}{L_{R53}}+\frac{P_{R52-53}}{L_{R53}}\right)\geq 1$$

where: PR53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrase R53 in the preparation,

PN,R50-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrase R50-53 in the preparation,

PN,R51-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrase R51-53 in the preparation,

PR52-53 is the percentage by weight of each substance dangerous for the environment to which is assigned phrase R52-53 in the preparation,

LR53 is the respective limit R53 for each substance dangerous for the environment to which is assigned phrase R53 or R50-53 or R51-53 or R52-53, expressed as percentage by weight

b) Non-aquatic environment

b1) Ozone layer

I. Conventional method for the evaluation of preparations dangerous for the ozone layer

The following preparations shall be classified as dangerous for the environment

I.1. and assigned the symbol 'N', the indication of danger 'dangerous for the environment' and the risk phrase R59

I.1.1. preparations containing one or more substances classified as dangerous to the environment and to which is assigned the symbol 'N' and the risk phrase R59 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 5) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

I.2. and assigned the risk phrase R59:

I.2.1. preparations containing one or more substances classified as dangerous to the environment and to which is assigned R59 in individual concentrations equal to or greater than:

a) either the concentration specified in Annex I to Directive 67/548/EEC for the substance or substances under consideration, or

b) the concentration specified in Part B of this Annex (Table 5) where the substance or substances do not appear in Annex I to Directive 67/548/EEC or appear in it without concentration limits;

b2) Terrestrial environment

I. Evaluation of preparations dangerous for the terrestrial environment

Classification of preparations using the risk phrases below will follow after the detailed criteria for use of the phrases have been incorporated in Annex VI to Directive 67/548/EEC.

R54 Toxic to flora
R55 Toxic to fauna
R56 Toxic to soil organisms
R57 Toxic to bees
R58 May cause long-term adverse effects in the environment.

ANNEX III

PART B

Concentration limits to be used in evaluation of environmental hazards

I. For the aquatic environment

The concentration limits fixed in the following tables, expressed as a weight/weight percentage, determine the classification of the preparation in relation to the individual concentration of the substance(s) present whose classification is also shown.

Table 1. : Acute aquatic toxicity and long-term adverse effects

Classification of the substance	Classification of the preparation		
	N, R50-53	N, R51-53	R52-53
N, R50-53	$C_n \geq 25\%$	$2.5\% \leq C_n < 25\%$	$0.25\% \leq C_n < 2.5\%$
N, R51-53		$C_n \geq 25\ \%$	$2.5\% \leq C_n \leq 25\%$
R52-53			$C_n \geq 25\%$

Table 2. : Acute aquatic toxicity

Classification of the substance	Classification of the preparation N, R50
N, R50	$C_n \geq 25\%$
N, R50-53	$C_n \geq 25\%$

Table 3. : Aquatic toxicity

Classification of the substance	Classification of the preparation R52
R52	$C_n \geq 25\%$

Table 4. : Long-term adverse effects

Classification of the substance	Classification of the preparation R53
R53	$C_n \geq 25\%$
N, R50-53	$C_n \geq 25\%$
N, R51-53	$C_n \geq 25\%$
R52-53	$C_n \geq 25\%$

II. For the non-aquatic environment

The concentration limits fixed in the following tables, expressed as weight/weight percentage or, for gaseous preparations as a volume/volume percentage, determine the classification of the preparation in relation to the individual concentration of the substance(s) present whose classification is also shown.

Table 5. : Dangerous for the ozone layer

Classification of the substance	Classification of preparation N, R59
N with R59	C ≥0.1 %

Classification of the substance	Classification of preparation R59
N with R59	C ≥ 0.1 %
R59	C ≥ 0.1 %

ANNEX III

PART C

Test methods for the evaluation of the hazards for the aquatic environment

Normally, the classification of a preparation is made on the basis of the conventional method. However, for the determination of the acute aquatic toxicity, there may be cases for which it is appropriate to carry out tests on the preparation.

The result of these tests on the preparation may only modify the classification concerning acute aquatic toxicity which would have been obtained by the application of the conventional method

If such tests are chosen by the person responsible for the placing on the market, it must be ensured that the quality criteria of the test methods in Part C of Annex V to Directive 67/548/EEC have been complied with.

Furthermore, the tests shall be carried out on the three species in conformity with the criteria of Annex VI to Directive 67/548/EEC (algae, daphnia and fish), unless the highest hazard classification relating to acute aquatic toxicity has been assigned to the preparation after testing on one of the species.