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HARMONISED INTEGRATED CLASSIFICATION SYSTEM FOR HUMAN HEALTH AND  
ENVIRONMENTAL HAZARDS OF CHEMICAL SUBSTANCES AND MIXTURES

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**HARMONISED INTEGRATED  
CLASSIFICATION SYSTEM FOR HUMAN HEALTH  
AND ENVIRONMENTAL HAZARDS OF CHEMICAL  
SUBSTANCES AND MIXTURES**

**As endorsed by:**

- **the 28th Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, November 1998 (Part I; Part II: Chapters 1-7, 10);**
- **the 31<sup>st</sup> Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, November 2000 (Part II: Chapters 8-9; Part III: Chapters 1, 2, 4-8);**
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No. 1, *Guidance Document for the Development of OECD Guidelines for Testing of Chemicals (1993; reformatted 1995)*

No. 2, *Detailed Review Paper on Biodegradability Testing (1995)*

No. 3, *Guidance Document for Aquatic Effects Assessment (1995)*

No. 4, *Report of the OECD Workshop on Environmental Hazard/Risk Assessment (1995)*

No. 5, *Report of the SETAC/OECD Workshop on Avian Toxicity Testing (1996)*

No. 6, *Report of the Final Ring-test of the Daphnia magna Reproduction Test (1997)*

No. 7, *Guidance Document on Direct Phototransformation of Chemicals in Water (1997)*

No. 8, *Report of the OECD Workshop on Sharing Information about New Industrial Chemicals Assessment (1997)*

No. 9, *Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides During Agricultural Application (1997)*

No. 10, *Report of the OECD Workshop on Statistical Analysis of Aquatic Toxicity Data (1998)*

No. 11, *Detailed Review Paper on Aquatic Testing Methods for Pesticides and industrial Chemicals (1998)*

No. 12, *Detailed Review Document on Classification Systems for Germ Cell Mutagenicity in OECD Member Countries (1998)*

No. 13, *Detailed Review Document on Classification Systems for Sensitising Substances in OECD Member Countries 1998)*

No. 14, *Detailed Review Document on Classification Systems for Eye Irritation/Corrosion in OECD Member Countries (1998)*

No. 15, *Detailed Review Document on Classification Systems for Reproductive Toxicity in OECD Member Countries (1998)*

No. 16, *Detailed Review Document on Classification Systems for Skin Irritation/Corrosion in OECD Member Countries(1998)*

No. 17, *Environmental Exposure Assessment Strategies for Existing Industrial Chemicals in OECD Member Countries (1999)*

No. 18, *Report of the OECD Workshop on Improving the Use of Monitoring Data in the Exposure Assessment of Industrial Chemicals (2000)*

No. 19, *Draft Guidance Document on the Recognition, Assessment and Use of Clinical Signs as Humane Endpoints for Experimental Animals used in Safety Evaluation (1999)*

No. 20, *Revised Draft Guidance Document for Neurotoxicity Testing (in preparation)*

No. 21, *Detailed Review Paper: Appraisal of Test Methods For Sex Hormone Disrupting Chemicals (2000)*

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No. 26, *Revised Analysis of Responses Received from Member Countries to the Questionnaire on Regulatory Acute Toxicity Data Needs (2001)*

No. 27, *Guidance Document On The Use Of The Harmonised System For The Classification Of Chemicals Which Are Hazardous For The Aquatic Environment (2001)*

No. 28, *Guidance Document for the Conduct of Skin Absorption Studies (in preparation)*

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No 30, *Detailed Review Document on Hazard Classification Systems for Mixtures (2001)*

No 31, *Detailed Review Paper on Non-Genotoxic Carcinogens Detection: The Performance of In-Vitro Cell Transformation Assays(draft)*

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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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**PART 2:**

**HARMONISED HAZARD CLASSIFICATION SYSTEM FOR  
CHEMICAL SUBSTANCES**

**Chapter 2.1:**  
**HARMONISED SYSTEM FOR THE CLASSIFICATION OF CHEMICALS  
WHICH CAUSE ACUTE TOXICITY**

**PURPOSE, BASIS AND APPLICABILITY**

32. The purpose of this document is to present a harmonised system of classification for acute toxicity by the oral, dermal, and inhalation routes to be used internationally.

33. The basis for the harmonised criteria are those which are currently in use in OECD countries as well as those recommended by the United National Committee of Experts on the Transport of Dangerous Goods (UNCETDG). Elements from these sources have been integrated so as to maintain a high level of protection under a globally harmonised system of classification.

34. The classification scheme included elements that will be used by all authorities as well as other categories that will be applied only by some ( e.g. transport).

**CLASSIFICATION CLASSES**

35. Chemicals can be allocated to one of five toxicity categories based on acute toxicity by the oral, dermal or inhalation route according to the numeric criteria expressed as (approximate) LD50 (oral, dermal) or LC50 (inhalation) values are shown in the table below. Explanatory notes are shown in italics following the table.

**Table 1: Acute toxicity hazard categories and (approximate) LD50/LC50 values defining the respective categories.**

	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg)	5	50	300	2000	5000 See detailed criteria
Dermal (mg/kg)	50	200	1000	2000	
Gases (ppm) see: Note a	100	500	2500	5000	
Vapours (mg/l) see: Note a Note b Note c	0.5	2.0	10	20	
Dusts and Mists (mg/l) see: Note a Note d	0.05	0.5	1.0	5	

Notes:

- a: *Inhalation cut-off values in the table are based on 4 hour testing exposures. Conversion of existing inhalation toxicity data which has been generated according to 1 hour exposures should be by dividing by a factor of 2 for gases and vapours and 4 for dusts and mists.*
- b: *It is recognised that saturated vapour concentration may be used as an additional element by some regulatory systems to provide for specific health and safety protection. (e.g. UN Recommendations for the Transport of Dangerous Goods).*
- c: *For some chemicals the test atmosphere will not just be a vapour but will consist of a mixture of liquid and vapour phases. For other chemicals the test atmosphere may consist of a vapour which is near the gaseous phase. In these latter cases, classification should be based on ppm as follows: Category 1 (100 ppm), Category 2 (500 ppm), Category 3 (2500 ppm), Category 4 (5000 ppm). Work in the OECD Test Guidelines Programme should be undertaken to better define the terms "dusts", "mists" and "vapours" in relation to inhalation toxicity testing.*
- d: *The values for dusts and mists should be reviewed to adapt to any future changes to OECD Test Guidelines with respect to technical limitation in generating, maintaining and measuring dust and mist concentrations in respirable form.*

**CRITERIA FOR CATEGORY 5**

36. Criteria for Category 5 are intended to enable the identification of substances which are of relatively low acute toxicity hazard but which, under certain circumstances may present a danger to vulnerable populations. These substances are anticipated to have an oral or dermal LD50 in the range of 2000-5000 mg/kg or equivalent doses for other routes.

37. The specific criteria for Category 5 are:

- a) The substance is classified in this category if reliable evidence is already available that indicates the LD50 or (LC50) to be in the range of Category 5 values or other animal studies or toxic effects in humans indicate a concern for human health or an acute nature.
- b) The substance is classified in this category, through extrapolation, estimation or measurement of data, if assignment to a more hazardous category is not warranted, and :
  - reliable information is available indicating significant toxic effects in humans; or
  - any mortality is observed when tested up to Category 4 values by the oral, inhalation, or dermal routes; or
  - where expert judgement confirms significant clinical signs of toxicity, when tested up to Category 4 values, except for diarrhoea, piloerection or an ungroomed appearance, or
  - where expert judgement confirms reliable information indicating the potential for significant acute effects from other animal studies.

38. Recognising the need to protect animal welfare, testing in animals in Category 5 ranges is discouraged and should only be considered when there is a strong likelihood that results of such a test would have a direct relevance for protecting human health.

## **RATIONALE FOR THE PROPOSED SYSTEM**

### **General considerations**

39. The harmonised classification system for acute toxicity has been developed in such a way as to accommodate the needs of existing systems. A basic principle set by the IOMC CG/HCCS is that "harmonisation means establishing a common and coherent basis for chemical hazard classification and communication from which the appropriate elements relevant to means of transport, consumer, worker and environment protection can be selected." To that end, five categories have been included in the acute toxicity scheme.

40. The preferred test species for evaluation of acute toxicity by the oral and inhalation routes is the rat, while the rat or rabbit are preferred for evaluation of acute dermal toxicity. As noted by the CG/HCCS, "Test data already generated for the classification of chemicals under existing systems should be accepted when reclassifying these chemicals under the harmonised system." When experimental data for acute toxicity are available in several animal species, scientific judgement should be used in selecting the most appropriate LD50 value from among valid, well-performed tests.

41. Category 1, the highest toxicity category, has cut off values of 5 mg/kg by the oral route, 50 mg/kg by the dermal route, 100 ppm for gases or gaseous vapours, 0.5 mg/l for vapours, and 0.05 mg/l for dusts and mists. These toxicity values are currently used primarily by the transport sector for classification for packing groups.

42. Category 5 is for chemicals which are of relatively low acute toxicity but which, under certain circumstances, may pose a hazard to especially vulnerable populations. Criteria for identifying substances in Category 5 are provided in addition to the table. These substances are anticipated to have an oral or dermal LD50 value in the range 2000 - 5000 mg/kg or equivalent doses for other routes of exposure. In light of animal welfare considerations, testing in animals in Category 5 ranges is discouraged and should only be considered when there is a strong likelihood that results of such testing would have a direct relevance for protecting human health.

### **Special considerations for inhalation toxicity**

43. Values for inhalation toxicity are based on 4 hour tests in laboratory animals. When experimental values are taken from tests using a 1 hour exposure, they can be converted to a 4 hour equivalent by dividing the 1 hour value by a factor of 2 for gases and vapours and 4 for dusts and mists.

44. Units for inhalation toxicity are a function of the form of the inhaled material. Values for dusts and mists are expressed in mg/l. Values for gases are expressed in ppm. Acknowledging the difficulties in testing vapours, some of which consist of mixtures of liquid and vapours phases, the table provides values in units of mg/l. However, for those vapours which are near the gaseous phase, classification should be based on ppm. As inhalation test methods are updated, the OECD and other test guideline programs will need to define vapours in relation to mists for greater clarity.

45. Vapour inhalation values are intended for use in classification of acute hazard for all sectors. It is also recognised that the saturated vapour concentration of a chemical is used by the transport sector as an additional element in classifying chemicals for packing groups.

46. Of particular importance is the use of well articulated values in the high toxicity categories for dusts and mists. Inhaled particles between 1 and 4 microns mean mass aerodynamic diameter

(MMAD) will deposit in all regions of the rat respiratory tract. This particle size range corresponds to a maximum dose of about 2 mg/l. In order to achieve applicability of animal experiments to human exposure, dusts and mists would ideally be tested in this range in rats. The cut off values in the table for dusts and mists allow clear distinctions to be made for materials with a wide range of toxicities measured under varying test conditions. The values for dusts and mists should be reviewed in the future to adapt to any future changes in OECD or other test guidelines with respect to technical limitations in generating, maintaining, and measuring dust and mist concentrations in respirable form.

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