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COMMITTEE OF EXPERTS ON THE TRANSPORT OF DANGEROUS GOODS AND ON THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS
Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals
(Second session, 12 -14 December 2001, agenda item 3)

GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS)

Annexes 9 to 12

Transmitted by the Inter-Organization Programme for the Sound Management of Chemicals (IOMC)

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Annex 9

Guidance document on the use of the Harmonized System for the Classification of Chemicals which are hazardous for the aquatic environment

**(see document ST/SG/AC.10/C.4/2001/11, Annex 2,
OECD Guidance document No 27)**

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Annex 10

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media

**(see document ST/SG/AC.10/C.4/2001/11, Annex 3,
OECD Guidance document No 29)**

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Annex 11

Testing of aerosols

**(see document ST/SG/AC.10/C.3/38/Add.2,
Appendix 2, Ignition distance test;
Appendix 3, Enclosed space ignition test; and
Appendix 4, Aerosol foam flammability test)**

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Annex 12
Areas to be considered for future work

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Areas to be considered for future work

1. **Harmonization of Standard Precautionary Statements**: The GHS label elements include precautionary statements. Whilst precautionary information was considered for standardization, there was insufficient time to develop detailed proposals. Examples of precautionary statements and pictograms are found in Annex 4. The goal is to develop them fully into fully standardized label elements.

2. **Guidance on the Preparation of a Safety Data Sheet**: The Sub-Committee on the GHS may wish to consider the development of guidance on how to prepare a SDS

3. **Sensitization**

    1. There has been considerable discussion about what to convey about sensitisation effects to those exposed, and at what point it should be conveyed. While the current cut-off for mixtures is 1%, it appears that the major systems all believe information should be conveyed below that level. This may be appropriate both to warn those already sensitised, as well as to warn those who may become sensitised. This issue was not clear during the initial deliberations on the criteria for mixtures containing sensitizers, and thus has not been adequately discussed nor options explored.

    2. Before the system becomes implemented, this issue should be revisited by the ECOSOC Subcommittee on the GHS as one of its first priorities. It should be noted that the sensitisation criteria for substances will also have to be re-opened to consider this issue and the inclusion of new information and evolving testing approaches that addresses the question of strong sensitizers versus those that are weaker. Appropriate hazard communication should be considered along with the discussions on the criteria and the availability of an appropriate test method.

    3. The following text was provided as "Background Information" in the OECD *Harmonized Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures.*

        1. Categorisation of sensitizers accounting for differences in sensitising capacity among substances would be a useful concept to develop. It may be appropriate to allocate both respiratory and dermal sensitizers to, for example, one of the following categories:

            Category 1, Strong Sensitizer:

            A strong sensitizer would be indicated by

            - a high frequency of occurrence and/or severity of occurrence within an exposed population; or
            - a probability of occurrence of a high sensitisation rate in humans based on animal or other tests.

            Category 2, Sensitizer:

            A low to moderate sensitizer would be indicated by

            - a low or moderate frequency or severity of occurrence within an exposed population; or

- a probability of occurrence of a low to moderate sensitisation rate in humans based on animal or other tests.

2. Some authorities currently categorise strong sensitizers. However, at present, animal or other test systems to subcategorise sensitizers as indicated above, have not been validated and accepted. Work is going on to develop such models for the potency evaluation of contact allergens.

4. **Carcinogenicity**

1. The following text was provided as "Background Information" in the OECD *Harmonized Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures.*

Considerations of Potency for Labelling Limits

(1) The considerations as laid out below were excerpted from the Report of the Meeting of the Working Group on Harmonisation of Classification and Labelling of Carcinogens, Washington, DC, 17-18 October 1995.

Purpose

(2) The purpose of establishing a potency scheme to be used for labelling of substances, preparations (mixtures) and contaminants is to provide for practical minimum levels of carcinogens in substances for which labelling would be required. It will result in labelling highly potent materials more strictly and less potent materials less strictly. A further purpose is to eliminate unnecessary labelling. In addition, use of a potency scheme may encourage risk reduction through purification of chemical substances or reformulating preparations.

Background

(3) A large number of chemicals have been classified as carcinogenic and placed into various categories for labelling or other regulatory purpose. Chemicals that have been identified as carcinogenic may also occur as components of preparations (mixtures), impurities or additives. Gold and co-authors (Environ Health Perspect 79: 259, 1989) calculated doses from animal testing which result in tumours in half the dosed animals (TD50 values span a range of more than eight orders of magnitude). Most classification systems do not take into account the wide range of potencies of these chemicals.

(4) Carcinogens are in some countries divided into three potency groups: high, medium and low. Potency is in these instances determined using dose-response data in the observed dosing range for laboratory animals. Additional indicators of potency such as tumour site and species specificity, or species differences in toxicokinetics may also be used. Such potency groups are used to set upper limits for the classification of substances as carcinogens and for the purpose of initiating labelling. They have also been used for the classification and determination of labelling provisions for preparations (mixtures) of carcinogenic chemicals.

(5) Some countries have implemented a scheme where 0.1% is used as a default limit value for labelling of substances and preparations (mixtures) as carcinogens with sufficient

data for carcinogenicity. In these countries chemicals with medium carcinogenic potency are labelled if they occur in chemical substances at or above this level. Many carcinogenic compounds fall into the medium range. Carcinogens with high potency might be classified and labelled at lower levels and carcinogens with low potency could be classified and labelled only when they occur at higher levels. Some countries use 1% as a default limit value for low potency carcinogens and for carcinogens with more limited data.

(6) Some regulatory authorities do not have the obligation to perform potency determinations. If a chemical carcinogen is a candidate for a potency rating outside of the default range, such chemicals should be referred to an international group for its determination.

Observations

(7) The Working Group agreed that it would be useful to explore further the concept of using potency to make labelling decisions. Initial thoughts of the Working Group are presented here.

(8) Potency ranking of carcinogens should not be determined or refined more precisely than by ten-fold factors in light of differences in species response, tumour types and the limits of standardisation of test protocols. In light of these points, a scheme for classification and labelling purposes which separates carcinogens into potency groupings serves the practical purposes listed above.

(9) The use of potency for establishing limits does not preclude the ability of authorities to perform quantitative risk assessments of exposures to carcinogenic substances for regulatory purposes.

(10) Potency determinations should be based on well performed studies which are peer reviewed, performed according to good laboratory practices, or are deemed acceptable by regulatory authorities.

5. **Reproductive toxicity**

1. **Classification of mixtures containing substances having effects on or via lactation**

(1) Harmonised criteria for the classification of mixtures containing substances which have effects on lactation have to date not been developed. The data base for this hazard category is extremely limited, and experience will have to be gained in using the category in the harmonised system before the issue of classification of mixtures containing components which can contaminate breast milk can be addressed.

2. **Potency and cut-off doses:** The following text was provided as "Background Information" in the OECD *Harmonized Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures*.

(1) In the present scheme, the relative potency of a chemical to produce a toxic effect on reproduction is not included in the criteria for reaching a conclusion regarding classification. Nevertheless, during the development of this scheme it was suggested that cut-off dose levels should be included, in order to provide some means of assessing and categorising the potency of chemicals for the ability to produce an adverse effect on

reproduction. This concept has not been readily accepted by all member countries because of concerns that any specified cut-off level may be exceeded by human exposure levels in certain situations, e.g. inhalation of volatile solvents, the level may be inadequate in cases where humans are more sensitive than the animal model, and because of disagreements about whether or not potency is a component of hazard. There has been interest in this concept to further consider it as a future development of the classification scheme.

3. **Limit dose**: The following text was provided as "Background Information" in the OECD Harmonized Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures.

(1) There is general agreement about the concept of a limit dose, above which the production of an adverse effect may be considered to be outside the criteria which lead to classification. However, there was no agreement within the OECD Task Force regarding the inclusion within the criteria of a specified dose as a limit dose. Some Test Guidelines specify a limit dose, other Test Guidelines qualify the limit dose with a statement that higher doses may be necessary if anticipated human exposure is sufficiently high that an adequate margin of exposure would not be achieved. Also, due to species differences in toxicokinetics, establishing a specific limit dose may not be adequate for situations where humans are more sensitive than the animal model.

(2) In principle, adverse effects on reproduction seen only at very high dose levels in animal studies (for example doses that induce prostration, severe inappetence, excessive mortality) would not normally lead to classification, unless other information is available, e.g. toxicokinetics information indicating that humans may be more susceptible than animals, to suggest that classification is appropriate. Please also refer to the section on Maternal Toxicity for further guidance in this area.

(3) However, specification of the actual 'limit dose' will depend upon the test method that has been employed to provide the test results, e.g. in the OECD Test Guideline for repeated dose toxicity studies by the oral route, an upper dose of 1000 mg/kg unless expected human response indicates the need for a higher dose level, has been recommended as a limit dose.

(4) Further discussions are needed on the inclusion within the criteria of a specified dose as a limit dose.
