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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

Tenth session, 7-9 December 2005
Item 2 (b) of the provisional agenda

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

Health hazards

Proposal for revision of GHS Chapter 3.4 (Respiratory and skin sensitization)

Transmitted by the Organization for Economic Co-operation and Development (OECD)

Introduction

1. In December 2002, the UN Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals requested that OECD, during the biennium 2003-2004, examine the issue of elicitation and induction and propose amendments to the criteria as appropriate. In December 2004, this mandate was renewed for the next biennium.

2. Elicitation occurs when sensitized individuals are exposed to an allergen. Usually, lower levels are necessary for elicitation than required for induction. The objective is therefore to alert previously sensitized individuals to the presence of a particular sensitizer in a mixture.

3. There has been considerable discussion about (i) whether the mixtures should be classified and labelled or only labelled for elicitation and (ii) whether a particular default cut-off value should be included for elicitation classification and/or labelling.

4. Although available information shows that elicitation generally occurs at levels lower than required for induction, the data on elicitation thresholds are not yet regarded to be sufficient by all experts for reaching a general agreement on a particular default cut-off level for protection of humans from elicitation. This issue may be revisited in light of progress in knowledge in the coming years.

5. As a result of the discussions, it is proposed that certain authorities may choose to require the name of the ingredient as supplementary information on the label even though the mixture as a whole is not classified as a sensitizer, while others may choose to classify and label the mixture as a sensitizer in accordance with notes 1, 3 and 5 to Table 3.4.1.

6. The proposal includes the following changes:

(a) insertion in paragraph 3.4.1 of some general considerations for explaining the two phases of sensitization (induction and elicitation);

(b) replacement of "induce" with "lead to" in the definitions in paragraph 3.4.1 and in paragraphs 3.4.2.1.1 and 3.4.2.2.1, for clarifying that the two phases (induction and elicitation) are taken into account;

(c) insertion of "guinea pig" in 3.4.2.2.4.1 to specify that non adjuvant methods, for which a response of at least 15% of the animals is considered positive, only apply to tests on Guinea Pigs and not to the LLNA. Animal studies either give information on induction (LLNA) or observe elicitation following induction (GPMT and Buehler test);

(d) insertion of a new paragraph under Table 3.4.2 to include the proposal included in Paragraph 5 above;

(e) slight revision of the decision logics and insertion of a new footnote to the decision logics to reflect the changes of Chapter 3.4.

Proposal

3.4.1 Add "and general considerations" in the title after "Definitions";

Replace "induce" with "lead to" in the definition of "respiratory sensitizer" and in the definition of "skin sensitizer";

Add the following paragraphs after the definition of "skin sensitizer":

"For the purpose of this chapter, sensitization includes two phases: the first phase is induction of specialized immunological memory in an individual by exposure to an allergen. The second phase is elicitation, i.e. production of a cell-mediated or antibody-mediated allergic response by exposure of a sensitized individual to an allergen.

For respiratory sensitization, the pattern of induction followed by elicitation phases is shared in common with skin sensitization. For skin sensitization, an induction phase is required in which the immune system learns to react; clinical symptoms can then arise when subsequent exposure is sufficient to elicit a visible skin reaction (elicitation phase). As a consequence, predictive tests usually follow this pattern in which there is an induction phase, the response to which is measured by a standardized elicitation phase, typically involving a patch test. The local lymph node assay is the exception, directly measuring the induction response. Evidence of skin sensitization in humans normally is assessed by a diagnostic patch test.

Usually, for both skin and respiratory sensitization, lower levels are necessary for elicitation than are required for induction. Provisions for alerting sensitized individuals to the presence of a particular sensitizer in a mixture can be found at section 3.4.4".

3.4.2.1.1 and 3.4.2.2.1 In the box, replace "induce" by "lead to";

3.4.2.2.4.1 At the beginning of the second sentence, insert "Guinea pig" between "non-adjuvant" and "test method".

3.4.4 Insert "**3.4.4.1**" before the first paragraph.

Insert a new paragraph 3.4.4.2 after table 3.4.2 as follows:

"**3.4.4.2** Some chemicals that are classified as sensitizers may elicit a response, when present in a mixture in quantities below the cut-offs established in Table 3.4.1, in individuals who are already sensitized to the chemicals. To protect these individuals, certain authorities may choose to require the name of the ingredient as supplementary information on the label even though the mixture as a whole is not classified as sensitizer. Others may choose to classify and label the mixture as a sensitizer in accordance with notes 1, 3 and 5 to Table 3.4.1."

3.4.5. Decision logic 3.4.1 and 3.4.2

- In the central box, in the sentence starting with "is there evidence in humans…" replace " "induce" with "lead to";

- In the last but one box on the left, after "sensitizer at [4]", insert "[5]:" and a new footnote after current footnote 4 as follows:

  "[5] *See 3.4.4.2.*".
