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Rules for classification and labelling of chemicals - Part 21: Respiratory or skin sensitization

化学品分类和标签规范 第 21 部分：呼吸道或皮肤致敏

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Rules for classification and labelling of chemicals - Part 21: Respiratory or skin sensitization

1 Scope

This Part of GB 30000 specifies the terms and definitions, general descriptions, classification standards, judgment logic, labels for chemicals with respiratory or skin sensitization.

This Part applies to the classification and labeling of chemicals, which have respiratory or skin sensitization, in accordance with the United Nations' Globally Harmonized System of Classification and Labeling of Chemicals (hereinafter referred to as GHS).

2 Normative references

The following documents are essential to the application of this document. For the dated documents, only the versions with the dates indicated are applicable to this document; for the undated documents, only the latest version (including all the amendments) is applicable to this standard.

GB 13690 General rule for classification and hazard communication of chemicals

GB 16483 General rules to drafting safety data sheet for dangerous chemicals

United Nations "Recommendations on the Transport of Dangerous Goods - Model Regulations" (17th Revised Edition)

United Nations "Globally Harmonized System of Classification and Labeling of Chemicals" (Fourth Revised Edition)

3 Terms and definitions

The terms and definitions as defined in GB 13690, as well as the following terms and definitions, apply to this document.

3.1

Respiratory sensitizer

Substances that can cause respiratory allergies if inhaled.

3.2

Skin sensitizer

Substances that can cause allergies after skin exposure.

4 General instructions

4.1 Sensitization includes two stages: The first stage is when an individual is exposed to a certain allergen and induces a specific immune memory; the second stage is triggering, that is, an allergic individual develops cell-mediated or antibody-mediated allergic reactions due to exposure to a certain allergen.

4.2 As far as respiratory sensitization is concerned, induction is followed by a triggering phase, which is the same characteristic as skin sensitization. For skin sensitization, there needs to be an induction phase, that allows the immune system to respond. If subsequent exposure is sufficient to trigger a visible skin reaction (initiation phase), clinical symptoms may develop. Therefore, predictive tests often follow this pattern, in which there is an induction phase and the response to this phase is measured through a standardized induction phase, typically using a patch test. Regional lymph node trials that directly measure evoked responses are the exception. Evidence of skin sensitization in humans is usually assessed by diagnostic patch test.

4.3 For skin sensitization and respiratory sensitization, the amount required for induction is generally lower than the amount required for triggering.

4.4 The hazard category "Respiratory or skin sensitization" is divided into:

a) Respiratory sensitization;

b) Skin sensitization.

5 Classification criteria

5.1 General principles

General principles for classification and labeling of respiratory or skin sensitization are provided in GB 13690.

5.2 Substance classification criteria

5.2.1 Respiratory sensitizers

5.2.1.1 Hazard category

5.2.1.1.1 In the case where the competent authority does not require subclassification

a) Data derived from clinical cases and appropriate pulmonary function tests related to substance exposure, and they are corroborated by other supporting evidence, including:

- In vivo immunological tests (e.g. skin prick tests);

- In vitro immunological tests (e.g. serum analysis);

- Studies in which the immunological mechanism of action has not yet been confirmed, such as repeated low-level stimulation, pharmacologically mediated effects, indicating other specific allergic reactions;

- Chemical structures related to substances known to cause respiratory allergies;

b) Data obtained from positive bronchial provocation tests, which are performed on substances according to accepted criteria for determining specific hypersensitivity reactions.

5.2.1.2.4 The clinical case shall include both medical and occupational history, to determine the relationship between exposure to specific substances and respiratory allergic reactions. Relevant information includes factors present in the home and workplace that contribute to worsening of the condition, the onset and progression of the disease, the patient's family and medical history. The medical history shall also include documentation of other allergic or respiratory conditions in early childhood and a history of smoking.

5.2.1.2.5 A positive bronchial provocation test result alone provides sufficient evidence for classification. However, it shall be recognized that many of the tests listed above may have been carried out.

5.2.1.3 Animal studies

Data obtained from appropriate animal studies [1)] indicating that a substance has the potential to cause [2)] sensitization in humans by respiration include:

- For example, determination of immunoglobulin E (Ig E) and other specific immunological parameters in mice;

- Specific pulmonary responses in guinea pigs.

5.2.2 Skin sensitizers

[1] There is currently no recognized and effective animal model for testing respiratory allergic reactions. In some cases, data from animal studies can provide important information in the weight of evidence assessment.
[2] The mechanism by which substances cause asthma symptoms is not fully understood so far. For precautionary purposes, these substances may be considered respiratory sensitizers. However, if it can be proven based on the evidence that these substances produce irritating effects and cause asthma symptoms only in people with bronchial hyperreactivity, then they shall not be judged as respiratory sensitizers.

5.2.2.4 Specific matters

5.2.2.4.1 To classify substances, the weight of evidence method shall be used; the evidence shall include any or all of the following:

a) Positive patch test data, usually from more than one hospital;

b) Epidemiological studies show that substances cause allergic contact dermatitis; special attention shall be paid when a high proportion of contacts develop characteristic symptoms, even if the number of cases is small;

c) Positive data from appropriate animal studies;

d) Positive data from experimental studies in humans;

e) Well-documented cases of allergic contact dermatitis, usually from more than one hospital;

f) Severity of reaction.

5.2.2.4.2 Evidence from animal studies is generally more reliable than evidence from human exposure. However, if evidence is obtained from both sources and the results are contradictory, then the quality and reliability of the evidence from both sources shall be evaluated, in order to resolve the classification problem on a case-by-case basis. Typically, human data are not generated from controlled experiments with volunteers for hazard classification purposes, BUT are generated as part of a risk assessment to verify the absence of effects in animal experiments. Therefore, data on positive skin allergy in humans usually come from case-control or other less rigorous studies. Therefore, human data shall be evaluated with caution because, in addition to the intrinsic properties of the substance, case frequency reflects factors such as exposure, bioavailability, individual constitution, precautions taken. Negative human data shall generally not be used to negate positive results from animal studies. For both animal and human data, the effects of the carrier shall be considered.

5.2.2.4.3 If none of the above conditions are met, the substance shall not be classified as a skin sensitizer. However, the combination of two or more indicators of skin sensitization listed below may change the classification decision. Such situations shall be classified on a case-by-case basis.

a) Isolated case of allergic contact dermatitis;

b) Epidemiological studies with limited statistical power, for example when chance, bias or confounding factors are not fully ruled out with reasonable confidence;

c) Data obtained from animal testing conducted in accordance with current guidelines, which do not meet the criteria for a positive result as described in 5.2.2.3, but are close enough to the limit value to be considered valid;

d) Positive data obtained by non-standard methods;

e) Positive results obtained by approximate structural analogy.

5.2.2.4.4 Immune contact urticaria

Substances that meet the classification criteria for respiratory sensitizers may also cause immunological contact urticaria. It shall also be determined whether these substances are classified as skin sensitizers. Substances that can cause immune contact urticaria but do not meet the standards for respiratory sensitizers shall also be judged as to whether they are classified as skin sensitizers.

There are currently no accepted animal models to identify the agents responsible for immunologic contact urticaria. Therefore, classification is often based on human evidence that is similar to the human evidence for skin sensitization.

5.3 Classification criteria for mixtures

5.3.1 Classification of mixtures when data on the entire mixture are available

Where a mixture possesses reliable, high-quality evidence from human experience or appropriate experimental animal studies, as described in the material standard, the mixture may be classified based on an assessment of the weight of evidence of these data. Care shall be taken when evaluating mixture data, so that doses used do not produce ambiguous results.

5.3.2 Classification of mixtures without data on the mixture as a whole: bridging principle

5.3.2.1 If the mixture itself has not been tested to determine its sensitization, but sufficient data are available on the individual components of the mixture and on similar tested mixtures to adequately determine the hazardous properties of the mixture, the following agreed bridging principles use these data. This ensures that the classification process makes maximum use of available data to determine the hazardous properties of mixtures, without the need for additional testing on animals.

5.3.2.2 Dilution

If a tested mixture is diluted with a non-allergenic diluent which does not affect the allergenic properties of the other ingredients, the new diluted mixture may be classified in the same category as the original tested mixture.

5.3.2.3 Product batch

A mixture that has been tested for allergenicity in one production batch may be considered to be virtually identical to the allergenicity of another untested batch of the same commercial product, which is produced by or under the control of the same

7.1.2 See Appendix C for classification and labeling elements related to respiratory tract or skin sensitization.

7.1.3 The information required on the label includes hazard pictograms, signal words, hazard statements, precautionary statements, product identifiers, supplier logos, etc.

Note: Other label elements that have not yet been standardized, such as precautionary statements, also need to be included on the label. Competent authorities may also require additional information, and suppliers may add supplementary information.

7.2 Hazard pictograms

Hazard pictograms specified by GHS shall use black symbols with a white background; the red frame shall be wide enough to be eye-catching.

7.3 Signal words

Signal words are words on labels used to indicate the relative severity of a hazard and to alert readers to potential hazards. The signal words "Danger" and "Warning" are used to classify different hazard categories for respiratory or skin sensitization. Use the signal word "Danger" for Category 1, Category 1A, Category 1B respiratory sensitizers. Use the signal word "Warning" for Category 1, Category 1A, Category 1B skin sensitizers.

7.4 Hazard statements

Hazard statement means a phrase assigned to a hazard type and category that describes the hazardous nature of a chemical and, where appropriate, its degree of hazard. See Appendix C and Appendix D for hazard statements and precautionary statements for respiratory or skin sensitizers.

7.5 Precautionary statements

A precautionary statement is a word (and/or pictogram) used to describe recommended measures to minimize or prevent adverse effects resulting from exposure to a hazardous product or improper storage or handling of a hazardous product. To meet GHS requirements, there are five categories of precautionary statements: General, precautionary, emergency, storage, disposal. See Appendix D for precautionary statements for different hazard categories of respiratory or skin sensitizers.

7.6 Product identifier

7.6.1 The product identifier shall be used on the label and shall be consistent with the product identifier used in the chemical safety data sheet. If a substance or mixture is listed in the Model Regulations, the correct UN shipping name shall also be used on the packaging.

Appendix D

(Informative)

Hazard statements and precautionary statements for respiratory or skin sensitizers

D.1 Overview

D.1.1 This Appendix provides guidance on how to use GHS-compliant hazard statements and precautionary statements for respiratory or skin sensitizers. It lists hazard statements and precautionary statements for each hazard category and hazard category of respiratory or skin sensitizers. See GB 13690.

D.1.2 Coding of hazard statements

D.1.2.1 The coding of hazard statements is as shown in Annex 3 of GHS.

D.1.2.2 Each hazard statement is assigned a special alphanumeric code, consisting of 1 letter and 3 numbers, as follows:

a) The letter “H” (stands for “hazard statement”);

b) The first number represents the type of hazards specified in the hazard statements set by different part numbers, as follows:

- "2" represents physical hazard;

- "3" represents health hazard;

- "4" represents environmental hazard;

c) The last 2 numbers correspond to the serial number of the hazard caused by the inherent properties of the substance or mixture, such as: explosiveness (codes 200 to 210), flammability (codes 220 to 230), etc.

D.1.2.3 Unless otherwise specified, all specified hazard statements shall appear on the label. The competent authority may specify the order in which hazard statements appear on the label. In addition, when a combined hazard statement provides two or more hazard statements, the competent authority may specify whether the combined hazard statement or the corresponding individual statement shall be written on the label, or it shall be left to the discretion of the manufacturer/supplier.

D.1.3 Precautionary statements shall be marked on the label, together with hazard communication elements (pictograms, signal words, hazard statements). Additional supplementary information, such as instructions for use, may also be supplemented at the discretion of the manufacturer/supplier and/or the competent authority.

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