UNITED NATIONS **ST**

Secretariat

Distr.
GENERAL

ST/SG/AC.10/C.4/2008/28
23 October 2008

ENGLISH ONLY

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

Sixteenth session
Geneva, 10-12 (a.m) December 2008
Item 5 (c) of the provisional agenda

OTHER IMPLEMENTATION ISSUES

Terminology issues: Use of "endpoint"

Proposal by the expert from Australia and the Secretariat[1]

Introduction

1. The informal correspondence working group on implementation issues has identified the use of the term "endpoint" as one of the implementation issues relating to terminology (see ST/SG/AC.10/C.4/2008/22, paragraph 4.1, issue 1.3). This term is used in Chapters 3.4, 3.7, 3.8 and 4.1 and in Annexes 4, 5, 8, 9 and 10 of the GHS.

2. During the discussions, some members of the correspondence group explained that the intended meaning of "endpoint" in the GHS was "hazard class" or "hazard category", as appropriate. However, it was noted that the term was often used in the GHS text to designate an adverse effect in general and not necessarily a GHS hazard class or category. In fact, in

[1] In accordance with the programme of work of the Sub-Committee for 2007-2008 approved by the Committee at its third session (refer to ST/SG/AC.10/C.4/24, Annex 2 and ST/SG/AC.10/34, para. 14).

physico-chemical, health and environmental hazard assessment, this latter use of the term "endpoint" seems to be widely understood and accepted. Moreover, it was also noted that while the terms "hazard class" and "hazard category" were clearly defined in chapter 1.2, no definition was given for "endpoint".

3. While recognizing that this issue was not considered to be a priority for the Sub-Committee, the informal group was of the opinion that the inconsistent use of this term could be easily solved and therefore concluded that proposals to address this issue could be submitted for consideration of the Sub-Committee at any time.

4. To avoid using terms which have not been defined in the GHS as synonyms of other terms for which a definition exits in chapter 1.2, and also to ensure the consistency of the translations into languages other than English, the expert from Australia and the secretariat suggests that the word "endpoint" be defined and used in accordance with that definition. Where the term "endpoint" is meant to be synonymous with "hazard class or hazard category" or with some other meaning, those terms have been proposed to be used to replace "endpoint" in the GHS.

Proposal

5. All paragraphs where the word "endpoint" is currently used in the GHS have been considered. In some cases, the intended meaning appears to be hazard class or hazard category, while in many the intended purpose is consistent with "effect" or "parameter", or other words.

6. A definition will be required for "endpoint", on the understanding that an "endpoint" is commonly understood to mean the measured or estimated test result from a physicochemical, environmental fate, health hazard or ecotoxicity study. The definition should be placed in Chapter 1.2, and the term should be used where appropriate.

7. The Sub-Committee is asked to agree to revise the text and replace "endpoint" with the appropriate terms throughout the document, and to agree to a suitable definition for the term "endpoint" when it is retained.

8. All paragraphs where the word "endpoint" is currently used in the GHS are reproduced hereafter, together with the suggested options for replacement. The term "endpoint" is underlined in for clarity. For reference purposes, the equivalent translation into English of the terms currently used in the French version of the GHS is also given.

Proposed amendments

Chapter 1.2

Insert the following new definition:

> "***Endpoint*** means response measure in a toxicity test, i.e. the measurement(s) or value(s) derived from a toxicity test which constitute the results of the test.".
>
> *(Source: van Leeuwen CJ and Hermens JLM (1995). Risk Assessment of Chemicals: An Introduction. Kluwer Academic Publishers, Dordrecht).*

Chapter 3.4

3.4.3.3 Current English text:

"The mixture should be classified as a respiratory or skin sensitizer when at least one ingredient has been classified as a respiratory or skin sensitizer and is present at or above the appropriate cut-off value/concentration limit for the specific endpoint as shown in Table 3.4.1 for solid/liquid and gas respectively."

Currently translated into French as "specific effect" ("*effet particulier*").

Proposal: Delete "for the specific endpoint"

(Note: This proposal mirrors the approach taken by the European Commission).

Chapter 3.7

3.7.2.3.1 Current English version:

"[….] The weight given to the available evidence will be influenced by factors such as the quality of the studies, consistency of results, nature and severity of effects, level of statistical significance for intergroup differences, number of endpoints affected, relevance of route of administration to humans and freedom from bias. Both positive and negative results are assembled together into a weight of evidence determination. […]".

Currently translated into French as "number of effects observed" ("*nombre d'effets observés*")

Proposal: Retain "endpoints affected".

3.7.2.4.4 Current English text:

"Some of the end-points used to assess maternal toxicity are provided below. Data on these end points, if available, need to be evaluated in light of their statistical or biological significance and dose response relationship."

Currently translated into French as "observations" (first sentence) and "effects" (second sentence) ("*observations*" et "*effets*").

Proposal: Replace "end-points" and "end points" with "endpoints".

Chapter 3.8

3.8.2.2.1 (c) (second sentence) Current English text:

"Ambiguous reports simply of "irritation" should be excluded as this term is commonly used to describe a wide range of sensations including those such as smell, unpleasant taste, a tickling sensation, and dryness, which are outside the scope of this classification endpoint;"

Currently translated into French as "which are outside the definition of this criterion" ("*qui n'entrent pas dans la définition de ce critère*").

Proposal: Replace "which are outside the scope of this classification endpoint" with "which are outside the scope of classification for respiratory irritation;"

Chapter 4.1

4.1.1.7.3 Current English text:

"Two guidance documents (see Annexes 9 and 10) have been prepared to cover issues such as data interpretation and the application of the criteria defined below to such groups of substances. Considering the complexity of this endpoint and the breadth of the application of the system, the Guidance Documents are considered an important element in the operation of the harmonized scheme. […]"

Currently translated into French as "toxic effect" ("*effet toxique*")

Proposal 1: Replace "endpoint" with "hazard class";
Proposal 2: Replace "this endpoint" with "the complexity of aquatic toxicity"

4.1.2.8.1 Current English text:

"The organisms fish, crustacea and algae are tested as surrogate species covering a range of trophic levels and taxa, and the test methods are highly standardized. Data on other organisms may also be considered, however, provided they represent equivalent species and test endpoints. […]."

Currently translated into French as "experimental effects" (*effets expérimentaux")*

Proposal: Retain "test endpoints"

Annex 4

A4.2.1 (second sentence) Current English text:

"The CA may also require SDS for substances or mixtures that meet the criteria for classification as hazardous for non-GHS classes/end-points.".

Currently translated into French as "for non GHS classes" ("*pour des classes non GHS*").

Proposal: Replace "non-GHS classes/end-points" with "non-GHS hazard classes"

Annex 5

A5.2.2.7 Current English text:

"The extent of the exposure assessment would depend on the hazard. For example, for non-cancer chronic endpoints, an "acceptable daily intake" (ADI) would be calculated from the "no observed adverse effect level" (NOAEL) […]".

Currently translated into French as “non-cancer chronic affection” *(affection chronique non cancéreuse).*

Proposal: Retain “non-cancer chronic endpoints”

Annex 8

A8.3 (first sentence) Current English text:

“Classification as a Category 4 flammable liquid is proposed for the physico-chemical endpoints).”

Currently translated into French as “physico-chemical classification criteria” *(“critères de classification physico-chimiques”).*

Proposal: Amend the sentence to read as follows: “Classification as a Category 4 flammable liquid is justified”

(Justification: see first sentence under A8.4.1)”.

A8.4.3 (First paragraph) Current English text:

“The only available study involved exposure of rabbits to considerably lower amounts of the test substance than the standard protocols for this endpoint recommend.”

Currently translated into French as “effect” *(effet).*

Proposal: Replace “endpoint” with “hazard class”

Annex 9

A9.1.5 Current English text:

“A9.1.5 […] Even where standard tests have been used, some substances, such as complex substances, hydrolytically unstable substances, polymers etc, present difficult interpretational problems when the results have to be used within the classification scheme. Thus data are available for a wide variety of both standard and non-standard test organisms, both marine and freshwater, of varying duration and utilizing a variety of endpoints […].”

Currently translated into French as “test objectives” *(“objectifs d’essai”).*

Proposal: Replace “variety of endpoints” with “variety of “test endpoints”

A9.3.2.2 Current English text (first paragraph):

“The GHS criteria for determining health and environmental hazards should be test method neutral, allowing different approaches as long as they are scientifically sound and validated according to international procedures and criteria already referred to in existing systems for the endpoints of concern and produce mutually acceptable data.”

Currently translated into French as “hazard types” (“*types de danger*”)

Proposal: Replace “endpoints of concern” with “hazard classes of concern”

Current English text (second paragraph):

“Chronic testing involves an exposure that is lingering or continues for a longer time; the term can signify periods from days to a year, or more depending on the reproductive cycle of the aquatic organism. Chronic tests can be done to assess certain endpoints relating to growth, survival, reproduction and development.”

Currently translated into French as “hazard types” (“*types de danger*”)

Proposal: Retain “endpoints”

A9.3.2.5.1 Current English text:

“Acute tests are generally performed with young juveniles 0.1 - 5 g in size for a period of 96 hours. The observational endpoint in these tests is mortality. […].”

Currently translated into French as “effect” (“*effet*”)

Proposal: Retain “observational endpoint”

A9.3.2.5.2 (Fourth sentence) Current English text:

“Observational endpoints can include hatching success, growth (length and weight changes), spawning success, and survival.”

Currently translated into French as “effects” (“*effets*”)

Proposal: Retain “observational endpoints”

A9.3.2.6.1 (Third sentence) Current English text:

“The observational endpoint is mortality or immobilization as a surrogate to mortality. Immobilization is defined as unresponsive to gentle prodding.”

Currently translated into French as “effect”.

Proposal: Retain “observational endpoint”

A9.3.2.6.2 (Third sentence) Current English text:

“Observational endpoints include time to first brood, number of offspring produced per female, growth, and survival.”

Currently translated into French as “effects” (“*effets*”)

Proposal: Retain “observational endpoints”

A9.3.2.7.1 (second paragraph) Current English text:

"The algal test is a short-term test and, although it provides both acute and chronic endpoints, only the acute EC50 is used for classification in the harmonized system. The preferred observational endpoint in this study is algal growth rate inhibition because it is not dependent on the test design, whereas biomass depends both on growth rate of the test species as well as test duration and other elements of test design. If the endpoint is reported only as reduction in biomass or is not specified, then this value may be interpreted as an equivalent endpoint."

Currently translated into French as "effect" or "effects" ("*effets*")

Proposal: Retain "endpoints", "endpoint".

A9.3.2.7.2 Current English text:

"[…] The Lemna test is a short-term test and, although it provides both acute and sub-chronic endpoints, only the acute EC50 is used for classification in the harmonized system. The tests last for up to 14 days and are performed in nutrient enriched media similar to that used for algae, but may be increased in strength. The observational endpoint is based on change in the number of fronds produced. […]."

Currently translated into French as "effects".

Proposal: Retain "endpoints", "endpoint".

A9.3.3.2.1 Current English text:

[…] Such chronic effects usually include a range of sub-lethal endpoints and are generally expressed in terms of a No Observable Effect Concentration (NOEC), or an equivalent ECx. Observable endpoints typically include survival, growth and/or reproduction. Chronic toxicity exposure durations can vary widely depending on test endpoints measured and test species used.

Currently translated into French as "effects".

Proposal: Retain "endpoints"

A9.3.3.2.3 (first paragraph) Current English text:

"Testing with algae/Lemna cannot be used for de-classifying chemicals because (1) the algae and Lemna tests are not long-term studies, (2) the acute to chronic ratio is generally narrow and (3) the endpoints are more consistent with the endpoints for other organisms."

Currently translated into French as "final experimental values" *("valeurs expérimentales finales"*)

Proposal: Replace "endpoints" with "effects"

A9.3.5.2 (fourth sentence) Current English text:

"When testing algae, coloured materials may interfere with the test endpoint by attenuating the light needed for cell growth."

Currently translated into French as "test result" *("résultat de l'essai")*

Proposal: Replace "test endpoint" with "test result".

A9.4.2.4.8 (Footnote 2) Current English text:

" (b) The time for adaptation within each test should be limited, the test endpoint should refer to the mineralization only and the pass level and time for reaching these should be […]"

Currently translated into French as "end point of the test" *(point final de l'essai")*

Proposal: Retain "test endpoint".

A9.6.3.2 Current English text:

"For example, if 96-h LC50 test data for fathead minnow are available for ethanol, n-butanol, n-hexanol, and n-nonanol, there is some confidence in making a prediction for this endpoint for n-propanol and n-pentanol. […] Even the toxicity of branched chain alcohols may be an unreasonable extrapolation, depending upon the endpoint in question. Such extrapolation becomes more unreliable to the extent that toxicity is related to production of metabolites for a particular endpoint, as opposed to the properties of the parent compound. […]."

Currently translated into French as "effects" *("effets")*

Proposal: Retain "endpoint"

A9.6.3.3 Current English text:

"What ultimately governs the validity of such predictions is the degree to which the compounds used to derive the QSAR for a specific biological endpoint, are acting by a common molecular mechanism. […]. "

Currently translated into French as "effect" *("effet")*

Proposal: Retain "endpoint"

A9.6.4.2 (second sentence) Current English text:

"Since the available QSARs are of varying reliability and application range, different restrictions apply for the prediction of each of these endpoints.".

Currently translated into French as "effects" *("effets")*

Proposal: Retain "endpoints"

A9.6.4.5 Current English text:

One approach being proposed "...where this is scientifically justifiable ... is to consider closely related chemicals as a group, or category, rather than test them as individual chemicals. In the category approach, not every chemical needs to be tested for every SIDS endpoint". Such limited testing could be justified providing that the "...final data set must allow one to assess the untested endpoint, ideally by *interpolation* between and among the category members." The process for defining such categories and in the development of such data are described in the proposal.

Currently translated into French as "effect" *("effet")*

Proposal: Retain "endpoint"

A9.6.4.8 Current English text:

"[…] QSARs are described for predicting environmental fate and aquatic toxicity. The report notes that "a consistent dataset for [an endpoint] covered ... for a well defined scope of chemical structures ("domain") [is needed] ... from which a training set is developed."

Currently translated into French as "effect" *("effet")*

Proposal: Retain "endpoint"

A9.7.2.1.2.3 (fourth sentence) Current English text:

"The BLM model has at present only been validated for a limited number of metals, organisms, and endpoints […]."

Currently translated into French as "effects" *("effets")*

Proposal: Retain "endpoints"

Annex 10

A10.2.3.1 Current English text:

"[…] The short-term transformation/dissolution endpoints are based on the dissolved metal ion concentrations obtained after a 7 days transformation/dissolution period. The long term transformation/dissolution endpoint is obtained during a 28 days transformation/dissolution test, using a single load of 1 mg/l."

Currently translated into French as "result" *("résultat")*

Proposal: Replace "endpoints" with "results".
