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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

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Implementation of the GHS: development of a list of chemicals classified in accordance with the GHS

Highlights of the report on the pilot project on assessing the potential development of a global list of classified chemicals

Transmitted by the secretariat of the Organisation for Economic Cooperation and Development (OECD)[1]

Purpose

1. By way of this document, the secretariat of the OECD provides a summary of the results of a pilot project on assessing the potential development of a global list of classified chemicals to the United Nations Sub-Committee on experts on the Globally Harmonized System of classification and labelling of chemicals (GHS Sub-Committee) for consideration in their deliberations on the potential development of this list. The summary is based on the report of the pilot project, which is circulated in full as informal document INF.4.

Background

2. In 2014, the OECD Task Force on Hazard Assessment (TFHA) and the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and

[1] In accordance with the programme of work of the Sub-Committee for 2015–2016 approved by the Committee at its seventh session (see ST/SG/AC.10/C.3/92, paragraph 95 and ST/SG/AC.10/42, para.15).

Biotechnology (JM) agreed to provide a coordination role for a pilot classification project upon invitation from the GHS Sub-Committee.

3. The pilot project objectives were to:

- To define the process for evaluating chemicals which should provide insight into the level of effort needed to create and maintain a global classification list.
- To provide insight into the expertise needed to classify chemicals against the various endpoints, the process(es) to be used for evaluating data and making recommendations on a classification, and the process to be used to finalize and update a classification.
- To determine if non-binding agreement on classification and labelling could be reached on the pilot substances.

4. It was also agreed that the following data would be tracked about resources used:

- Time reviewing data and preparing the assessment
- Time spent in classification
- Time spent in reviewing and responding to comments
- Time spent in discussions with the working group on the classifications

5. The organisation, process and learnings of the pilot project are outlined in informal document INF.4 “Report on the pilot project on assessing the potential development of a global list of classified chemicals”, along with an analysis of the time taken in preparing and reviewing the reports. In order to facilitate the pilot project a classification and assessment report form and associated Annex to the report, for more detailed study information, were developed.

6. Chemicals to be considered in the pilot were nominated to the GHS Sub-Committee. Three chemicals were selected and sponsored by three different jurisdictions:

- Dimethyltin dichloride (DMTC), CAS No. 753-73-1 (European Chemicals Agency)
- Dicyclopentadiene (DCPD), CAS No. 77-73-6 (Russian Federation)
- Di-n-butyl phthalate (DBP), CAS No. 84-74-2 (United States)

7. The proposed classification and labelling dossiers and the associated annex for each of these substances are circulated as informal documents (INF.4/Add.1, INF.4/Add.2 and INF.4/Add.3).

Summary of learnings from the pilot project

Drafting of the initial reports: General comments

8. The drafting of the initial reports took longer than anticipated. Contributing factors included large datasets, consistently reporting studies of various types, describing and tabulating the details of studies in the Annex to the report, consideration of the strength and quality of various studies and confidentiality/property rights issues. In the environment section of the template the denotation between "Key or Supportive study" was challenging to differentiate and the “Key and Supportive” column was therefore suggested to be deleted

in the summarising tables in the classification and labelling report template. Instead the text could include an evaluation of the use and relevance of the study for classification purposes.

9. In order to summarise information and propose classification and labelling for all GHS endpoints, the sponsors needed to draw from a wide range of expertise within their organisations. This adds to the complexity of drafting the report and underlines that necessity to bring together various technical capabilities to draft a report.

10. Particularly with sponsor authors who were newer to proposing classification and labelling, it was also a learning process as to how much information to provide in the report versus the Annex. Another challenge centred on how to communicate the comparison of the available information against the specific GHS criteria, particularly when there were conflicting data and a weight of evidence determination was needed to be used in order to apply the criteria.

Reviewing, discussing and revising of draft reports: General comments

11. Several reviewers noted that it was at times difficult to determine which study, or group of studies, were critical to a classification proposal and commented that more clarity could be sought in this aspect. Related to this, the description of the quality of a study, whether by Klimisch scores, or denoting a study as "Key or Supportive", and the bearing of its quality on its contribution to a classification proposal, was at times lacking in clarity for the reviewer. However, it was noted by one party, that a given Klimisch score does not necessarily reflect all aspects of the quality of a study. Also, it was suggested that if referred to, it should be clarified who has assigned the score (as it is the result of a subjective assessment). In addition, while this assessment was sometimes reported in the Annex of the report, some reviewers thought this information would be better placed in the report for all the studies. Nevertheless, it is clear that an assessment of reliability has to be included in some way in the classification and labelling report and an explanation of the justification for the proposed classification needs to be clearly communicated.

12. In addition, other study details were sometimes absent or difficult to find. These include for example the guideline used, species, exposure route, and test concentrations. Especially for endpoints for which there are large data collections, a clear presentation of the studies is very helpful.

13. Some reviewers noted that they would have liked to have more information on particular studies that were cited in some cases from secondary sources, and others noted that only primary sources should be used, (which however, may restrict the data considered, as published reports are not always available). Note that in discussions of the GHS Sub-Committee, it was agreed that unpublished studies could be used in particular circumstances because if a classification and labelling report "could only rely on published reports of data, the universe of substances that could be addressed in a global list was substantially narrowed" (INF.22, GHS Sub-Committee 28th session).

14. Also, there was a discussion on whether previous classification and labelling decisions by authorities should be cited and incorporated in a report. If so, several additional questions arose. Where, and what information should be included? How does this help in deriving the current classification? Is there clarity on what data was used and under what classification system? Initial considerations from participants include that such classifications may provide a source of data and be of value if an independent expert committee has concluded on a classification proposal on the same data base or provided a hazard assessment on some of the same data.

15. A reviewer noted that the review process for DCPD triggered a discussion amongst global industry for proposed revised classification. Therefore the pilot project itself has led to further harmonisation.

16. It was helpful to have a template for comments, so that all comments could be provided to the sponsors to enable them to develop written responses to the comments. Due to the considerable amount of comments for some of the substances, the step of addressing comments took longer than anticipated. Although the development of written responses was time consuming for the sponsors, when completed in a detailed manner it provided reviewers with a clear sense of how their comments were taken on. This expedited dealing with a significant portion of the comments, focusing the web-meetings on key remaining issues.

17. The web-meetings proved necessary and helpful in discussing outstanding issues following the written process. It was through these discussions and dialogue that agreement on a number of more difficult issues was found. Therefore, either web-meetings or face to face meetings are necessary for a successful process.

Technical learnings

18. There were a number of specific technical issues and learnings that were identified in the pilot process in relation to proposing specific classification and labelling. These are briefly summarized here.

(a) **Expert judgement -** The application of expert judgement in order to apply the criteria is necessary e.g. in borderline cases between two potential classification outcomes and in case there are contradicting results from the same type of data (e.g. within the same animal species) or between different type of data (such as animal and human data). This may lead to differences in opinion on what a classification should be. An example of this manifested itself in the context of the DMTC pilot substance for the Reproductive Toxicity (developmental toxicity) - whether a Category 2 vs 1B was warranted. Although consensus was obtained on this issue for this substance, the discussion highlighted the need to bring specialised expertise to the discussion of such cases, and that such cases can lead to a variation in classification outcome.

(b) **Physical state of the substance -** In the case of DCPD, the physical state of the substance varies in the range of possible handling conditions, depending on its purity and temperature. This led to a discussion on whether a temperature range should be added to a classification. A possibility to use a split “entry” for the solid and liquid (only with regard to flammability) was also mentioned, if considered appropriate. It was agreed that this was impractical, as it would apply for all chemicals, but that the purity could be specified where it impacts the classification. For example, for DCPD a purity-dependent classification for "Flammable Liquids" could be proposed, as commercial grades with purity < 97% are liquids at room temperature (20° C/68° F), and those with higher purity are solids at 20° C/68° F and liquids above 32.2° C/90° F. Also, the temperature of testing, and hence physical state of the substance, can impact endpoints such as aspiration and therefore should be specified when the information is available.

(c) **Acute Toxicity (oral) -** There was some debate with regard to the selection of species for proposing a classification. Test guidelines typically denote that when selecting a species for acute toxicity testing, the rat is preferred in case of no available data justifying another species; however, when test results from more than one species are available, the general consensus was that the most conservative

study should be selected, regardless of species, if there is no further information on species specificity and relevance to humans. This discussion took place in the context of classification proposal for DCPD for Acute Oral Toxicity, where using the mouse study is more conservative.

(d) **Irritation -** There are differences in reporting and interpretation of the scores for skin and eye irritation. For example, in the case of dibutyl phthalate, the scores for skin and eye irritation in one study were given as primary dermal irritation index (PDII) scores: 0.54/8 for skin irritation and 0.11/110 for eye irritation. The PDII score is the overall score of a Draize test, calculated as the average of the scores of all animals and time points for erythema and oedema combined. However, classification under GHS is based on the scores of individual animals in combination with information on reversibility and exposure duration. This information cannot be derived from a single PDII score. To ensure consistency and transparency between classifications in the future, there should be consensus on the reporting and interpretation of irritation scores. For example, the result of a skin irritation study of DBP on the ECHA site is given as follows: "After 4 and 24 hours very slight (grade 1) erythema were observed for 2/3 animals. They were completely reversible within after 48 hours". Even where studies are reported through single PDII scores, they can support a weight of evidence approach; however, their limitations need to be accounted for during the classification process.

(e) **Specific Target Organ Toxicity - Repeated Exposure -** An issue was highlighted regarding what hazard statement to include with a classification for STOT-RE, particularly in terms of level of specificity. Should it be an organ system or the level of a specific organ(s)? This discussion was also supplemented with the sense that since the classification and labelling is used as a communication tool, the hazard statement should also be the most meaningful to the user, including workers and/or general public. This issue arose during the discussion for DMTC. The hazard statement of H372 (nervous system, immune system) for STOT RE 1 was proposed. It was agreed that effects on the thymus were observed; (and according to the dossier submitter, also effects on the spleen were observed, but to a lesser extent) some participants brought forth the case that the effects on the thymus do not represent a general effect on the competence of the immune system and therefore the hazard statement should be limited to the thymus. A counter to this included that 'immune system' is easier to communicate to the public, in similarity with damage to “fertility” or to "the unborn child”. This issue was noted to be captured as a lesson from the pilot project that could result in different hazard statements being proposed.

(f) **Environmental hazards -** For the pilot substances there was discussion on how best to present and justify a proposal for environmental hazards classifications. It was suggested that the most practical approach is to conclude for all species at once using the most conservative approach by selecting the most sensitive species, instead of working through each individual species and comparing them to the GHS criteria. The proposed classification will anyhow derive from the most stringent classification across the species.

Other learnings

19. The strength of the process is very much dependent on the active participation of both sponsors and reviewers, drawing from a breadth of expertise. The initial draft classification and labelling reports improved with the input of reviewers and active

discussion amongst participants. Therefore a successful on-going process would need to entail commitment from a larger number of countries and other interested parties to put forward time and resources to both sponsor and actively review substances.

20. The GHS Sub-Committee's guiding principles require opportunities for stakeholders to provide input into the classification process, and industry participants provided comments on and participated in the teleconferences for each of the three pilot chemical classification and labelling reports. However, some stakeholders expressed concerns that they had learned of the exercise by chance, and that a more deliberate means to include to non-member participants be made in future classification exercises.

General conclusions

21. This pilot project has demonstrated that it is possible to move towards agreement on proposed classification and labelling for substances as for 3 of 3 pilot substances consensus was reached on draft conclusions in a non-binding environment. However, as on average 38 days was spent drafting and updating reports per sponsor, and an average 5 days spent reviewing the reports per reviewer, this is feasible only with the sustained commitment of time and resources by countries and other interested parties.

22. The GHS Sub-Committee is invited to consider the results of this pilot project in their deliberations of the potential to develop a global list of classified chemicals. The OECD secretariat would welcome an invitation from the GHS Sub-Committee to further support this process pending outcomes of the discussions.