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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Classification and related hazard communication: Nanomaterials

Review of the applicability of GHS to nanomaterials

Transmitted by the expert from France on behalf of the correspondence group

1. This informal document presents to the Sub-Committee information on issues discussed in the informal correspondence group (ICG) on the review of the applicability of GHS to nanomaterials.

2. The issues to be considered during the meeting of the informal group on 10 December are listed in Annex III.

Action requested from the Sub-Committee

3. The Sub-Committee is invited to take note and comment on the status of the work.

4. The correspondence group invites the Sub-Committee to keep the item on reviewing the applicability of the GHS classification criteria to nanomaterials in its programme of work for 2015-2016.

Issues from the previous meeting of the informal group (3 July 2014)

5. The group has not yet reached a clear consensus on the way to address the need for a working definition of "nanomaterial".

6. The following statements are kept in mind for future work:

(a) GHS criteria should cover all substances (and all their states) which can be classified as hazardous.

(b) Whether or not a definition of "nanomaterial" will be needed in the GHS will be considered in the future when results of the correspondence group's work are available. This issue will be tackled taking into account that there are already several internationally recognized definitions for "nanomaterial" which have not been designed only for hazard assessment. Some specific properties of particles should be assessed even if the particles' size is above 100nm (e.g. surface chemistry, biopersistence, dispersibility in water, etc.).

Present outcome of the classification exercise

7. As agreed during the 27th session, the group has started to work on the question “Can we make classification of nanomaterials by applying the existing criteria in the GHS?” by collecting data from some examples of nanomaterial substances and performing a classification exercise.

8. Currently, the volunteering delegations expressed their interest to the following nanomaterials and hazard properties:

Delegations	TiO_2	Carbone Nanotubes (CNT)
Australia		Health
France	Health	
Finland	Environment	Environment

9. Currently, data were collected by Finland for aquatic environmental hazards of CNT and TiO_2. The aim of this exercise is to provide examples of data on nanomaterials and respective bulk materials that could be used for the determination of the GHS classification for the hazard class "hazardous to the aquatic environment" and to compare the derived GHS classifications of different nano (and bulk) forms to obtain understanding on the suitability of the GHS for nanomaterials. The collected data set presents a preliminary and non-comprehensive review of available data from scientific literature and from the public database of European Chemicals Agency (http://echa.europa.eu/). The data used and the classification results have been submitted to the informal correspondence group on nanomaterials. The description of the work and preliminary conclusions reported to the ICG are presented in Annex I.

10. Based on the preliminary conclusions of the exercise carried out by Finland, for some issues there might be a need to wait for the results of the current testing-related work of the OECD and for other issues clarifications in the GHS might be enough.

11. In compliance with its terms of reference, the GHS informal group considers that more formal links to the work of the OECD should be established, to ensure that work is not duplicated. In particular, possible difficulties for data access should be solved, because it is crucial for the next steps that the data collected in the OECD activities from the "Working Party on Manufactured Nanomaterials" (WPMN) shall be also used for the GHS informal group activities.

Other issues to be tackled within the classification exercise.

12. As previously reported, some issues have been highlighted, but need to be concretely assessed within the classification exercise. For instance :

(a) Review existing references to “dust” "particle", and "powders", in the GHS to determine whether they adequately cover nanomaterials (See ST/SG/AC.10/C.4/2013/3) ; and check available data from the OECD work to consider the need to develop or to add some definitions in the GHS.

(b) Clarify that exercise covers both pure and coated nanomaterials.

(c) Review the existing guidance for application of classification cut-off values.

(d) Review the existing units used for classification in the GHS, and assess their limitations to adequately addressing the hazard properties of nanomaterials.

In addition to the conventionally used mass concentration metric (mg/m^3), there are two main metrics, both of which could also have some utility in measuring exposure to nanoparticles. These are: number concentration (units n/m^3) and; surface area concentration units (m^2/m^3). A case may be made for the use of either of these metrics in addition to the mass concentration metric under certain circumstances. It is noted that:

(i) Mass concentration units may not be sufficient alone, for instance for fibres or (nano)particles. However, mass concentration is consistent with current toxicological studies and exposure monitoring methods. There is currently no reliable method for measuring particles via surface area or number concentration and no studies to bridge exposure based surface area concentrations (or number concentrations) with mass based concentrations.

(ii) Surface area is a new parameter (currently being adopted in the GHS), allowing the use of surface area per mass of the average particle size (not used in the GHS). It often correlates better with a given consistent toxicity parameter.

(iii) Number concentration may be a relevant unit (and convenient for some instrumentations) to express toxicity of fibres (ex.: asbestos) or sometimes particles with size distributions which are complex and/or with non-discriminating states for the toxicity of the substance.

13. Other issues shall be identified during the exercise:

(a) Possibly, work could be also performed on the applicability to nanomaterials of non-testing approaches for the physical hazards, based on the chemical structure or on the physico-chemical data.

(b) Non-testing approaches (such as read-across) and how they could be applied for classification for health hazards should be discussed by the informal group.

(c) The question of the applicability of the additivity approach should also be discussed by the informal group

Other relevant inputs

Nordic Classification Group

14. The Nordic Classification Group, which is a network of government officials/civil servants representing the Competent Authorities for the CLP Regulation in Finland, Sweden, Norway, Iceland and Denmark launched a project under the auspices of the Nordic Chemical Group/Nordic Council of Ministers on the collection of Nordic stakeholders´ views on issues related to nanomaterials in relation to Globally Harmonized System of Classification and Labelling of Chemicals and the CLP Regulation which implements GHS in the European Union. The purpose of the survey was to provide input for the informal correspondence group on nanomaterials of the GHS Sub-Committee to identify possible challenges concerning classification of nanomaterials. The survey was conducted as a web-based questionnaire which was distributed to over 3500 recipients in Denmark, Finland, Norway and Sweden in May 2014. In the report the results and the main outcomes are presented which could be relevant for the work of the GHS informal group on nanomaterials.

15. The conclusions are based on the outcome of the survey and do not necessarily represent views of the Nordic authorities in chemical legislation or the Nordic Council of Ministers.

16. The summary of the conclusions is available in Annex II.

France

17. France would like to present some information from its activities on nanomaterials at different levels:

(a) On the OECD Test Guidelines, the experts in charge of these activities have highlighted that:

(i) Current main technical difficulties concern the test guideline protocols themselves which are not sufficiently precise on the appropriate sample preparation or test bottles for interpreting tests results ("simple" variations in materials or handling during the tests, and allowable by the current test guidelines, directly affect the results).

(ii) Some concepts or criteria used for classification purpose may not be workable or may not make sense for fibres or particles (including nanomaterials), and analogous criteria (not currently used for GHS) could be useful to resolve some interpretation issues. Some of these issues shall be presented in details in 2015 and in connection with the classification exercise (see also paragraph 7 and following). For instance :

- Bioaccumulation versus biopersistence.
- Solubility versus dispersibility.
- Biodegradability (not relevant for inorganic compounds/particles); and degradability versus solubility/dispersibility.

(b) The national works made by its experts on :

(i) Guidance documents. See in particular the INRS document (in English): http://www.inrs.fr/accueil/dms/inrs/CataloguePapier/ED/TI-ED-6050BIS/ed6050bis.pdf

(ii) Scientific expertise reports. See for instance the Anses opinion (in English): https://www.anses.fr/sites/default/files/documents/AP2012sa0273EN.pdf

European Union

18. The following recent developments can be reported:

(a) The European Commission is carrying out an impact assessment on relevant regulatory options, in particular possible amendments to the REACH Annexes, to ensure clarity on how nanomaterials are addressed and safety demonstrated in registration dossiers. In parallel, the Commission has launched an impact assessment to identify the most adequate means to

increase transparency. The substance evaluation process under REACH is also covering some nanomaterials.

(b) New guidance documents on the protection of safety and health of workers are available:

- Guidance for employers:

  Health and safety practitioners and workers: Guidance on controlling the protection of the health and safety of workers from the potential risks related to nanomaterials at work (http://ec.europa.eu/social/BlobServlet?docId=13087&langId=en)

- Guidance for workers:

  Working safely with manufactured nanomaterials (http://ec.europa.eu/social/BlobServlet?docId=13088&langId=en)

OECD

19. As a reminder, the "Working Party on Manufactured Nanomaterials" (WPMN) of the OECD was established in September 2006 to promote international safety cooperation to human health and the environment of manufactured nanomaterials.

20. Among the projects undertaken in the WPMN, the Sponsorship Programme concerns testing and gathering of data on the hazards of selected nanomaterials, and testing of the applicability of the existing OECD test methods. .

21. OECD Council Recommendation on the Safety Testing and Assessment of Manufactured Nanomaterials from 19 September 2013 considered that the approaches for the testing and assessment of traditional chemicals are in general appropriate for assessing the safety of nanomaterials, but may have to be adapted to the specificities of nanomaterials. Currently many important projects are related to test methods, and are part of a wider Test Guidelines Programme (WNT) validation process by sending a Standard Project Submission Form (SPSF) which is a harmonised template to present the proposals. In this context, the SPSFs concerning adaptations of methods for nanomaterials have been accepted on:

(a) Amendments to the Inhalation Test Guidelines and Guidance to Accommodate Nanomaterials (Netherlands, United States of America).

(b) Guidance Document on Assessing the Apparent Accumulation Potential of Nanomaterials (United Kingdom, Finland).

(c) Development of a Draft Test Guideline for Nanomaterial Removal from Wastewater (United States of America).

(d) Guidance Document on Aquatic (and Sediment) Toxicology Testing of Nanomaterials (United States of America, Canada).

(e) Test guideline for dissolution rate of nanomaterials in the aquatic environment (United States of America).

(f) Test Guideline for dispersibility and dispersion behaviour of nanomaterials in aquatic media (Germany).

(g) Guidance Document for dispersion and dissolution of nanomaterials in aquatic media – decision tree (Germany).

Annex I

Classification exercise on aquatic environmental hazards of carbon nanotubes and nano and bulk forms of titanium dioxide

The aim of this exercise is to provide examples of data on nanomaterials and respective bulk materials that could be used for the determination of the GHS classification for the hazard class "hazardous to the aquatic environment" and to compare the derived GHS classifications of different nano (and bulk) forms to obtain understanding on the suitability of the GHS for nanomaterials. The collected data set presents a preliminary and non-comprehensive review of available data from scientific literature and from the public database of European Chemicals Agency. The data used and the classification results have been submitted to the informal correspondence group on nanomaterials. It should be noted that for the present exercise the data have not been reviewed in detail for their compliance with the data quality requirements of the GHS or any regulations.

The GHS classifications in this exercise have been assessed using the harmonized classification scheme presented in Part 4 of the GHS. It is noted that when no information on degradation have been available the substances have been classified on the assumption that the substance is "not rapidly degradable". The data set includes pure nanomaterials (e.g. uncoated titanium dioxide) and nanomaterials with a surface coating (e.g. titanium dioxide, aluminum hydroxide, and dimethicone/methicone copolymer). In this exercise classification has been assessed in each case using the classification criteria for substances (GHS Chapter 4.1.2).

The classification schemes for metals and metal compounds (Annex A9.7) have not been used in this exercise. According to the GHS the hazard classification schemes for metals and metal compounds are limited to the hazards posed by metals and metal compounds when they are available (i.e. exist as dissolved metal ions, for example, as M^+ when present as $M\text{-}NO_3$), and do not take into account exposures to metals and metal compounds that are not dissolved in the water column but may still be bioavailable, such as metals in foods. Even though release of metal ions has been suggested to be important for toxicity of some metal compounds in nanoform, also other effects (not caused by released metal ions) are possible and should therefore be considered in classification. Thus the present classification exercise was performed using the general classification scheme (Part 4 in GHS). However, the applicability of the Annex A9.7 classification scheme for nanomaterials which are (or which include) metals or metal compounds should be assessed.

Preliminary conclusions from this exercise are presented in the following table:

Hazard class	Concerned classification criteria	Why it is not or hardly applicable?	Ongoing work to address the issue	What possible options for GHS?	Comments
Hazardous to the aquatic environment	Aquatic toxicity	Toxicity mechanism can be through shading effect and agglomeration processes in algae tests. For fish and Daphnia toxicity can be through agglomeration, physical interaction and oxidative stress mechanisms.	Test development is done at OECD level. Classification guidance should specify which effects are considered when classifying i.e. are e.g. shading an effect to be taken into account when classifying.	Main GHS? Guidance update.	Considering the carbon nanotubes examples the cut-off values used in aquatic toxicity criteria seem to be working. There is a classification strategy for metals and metal compounds. Different strategy needed for 'nanometal compounds'?
Hazardous to the aquatic environment	Rapid degradation		Test development is done at OECD level. Classification criteria and guidance should give advice also for inorganic substances.	Main GHS and Guidance update.	Metal compounds - according to current metal and metal compounds classification strategy? Carbon nanotubes? Ready biodegradability test not suitable. Need something else?
Hazardous to the aquatic environment	Bioaccumulation			Main GHS and Guidance update.	Oral route should also be considered in relation to possible need for updating/introducing new bioaccumulation criteria for nanomaterials for which oral route is important. The revised OECD 305 test guideline includes a dietary bioaccumulation test suitable for determining the bioaccumulation potential of substances with very low water solubility.
Hazardous to the aquatic environment		The low solubility of hydrophobic carbon nanotubes in water media is one of the major limitations to studying their interaction with aquatic organisms.	Test guideline development. Effect on GHS considered later.	Possible guidance update.	
Hazardous to the aquatic environment		The characterization of the substance needs special attention.		Possible guidance update.	Substance ID and maybe also a testing issue. For classification of nanomaterials it is important to include information on different physico-chemical characteristics which may influence the hazard profile (e.g. particle size). For example, the same CAS number (e.g. titanium dioxide, 13463–67-7) can refer to both bulk and nano forms of the substance and therefore CAS number is not very informative for substance identification in this case.

Annex II

The Nordic survey on nanomaterial hazard classification and labelling

The Nordic Classification Group[1], under the auspices of the Nordic Chemical Group/Nordic Council of Ministers, launched a project on the collection of Nordic stakeholders´ views on issues related to nanomaterials in relation to GHS/CLP Regulation[2]. The purpose of the survey was to provide input for the informal correspondence group on nanomaterials of the UN Sub-Committee of Experts on GHS so as to indicate possible challenges concerning classification of nanomaterials. The survey was conducted as a web-based questionnaire which was distributed to over 3500 recipients in Denmark, Finland, Norway and Sweden in May 2014.

The total response rate was relatively low (199 respondents, 5.7%), which can for the most part be explained by the fact that the majority of recipients were selected from national product registries, representing any chemical sector, and thus in the majority of cases not specifically selecting nanomaterials. The respondents were mainly from industry (79%), whereas authorities were represented by 7% and others by 15%. Twenty eight percent of the industry respondents represented companies placing some kind of nanoproducts on the market. Most of their products were mixtures containing one or more nanomaterials. Seven respondents informed that their company has classified pure nanomaterials and five respondents had experience from classification of coated nanomaterials.

The respondents' knowledge on CLP and GHS was fairly good according to their own evaluation but they were less familiar with issues related to nanomaterials and nanosafety. The fact that the majority of the respondents were not familiar with nanomaterials and related questions was reflected by a relatively high proportion of "no opinion" answers. Some of the questions required in-depth knowledge of classification and others were perhaps too ambiguous and possibly misunderstood which was probably reflected in some of the answers. However, a selection of prevailing views was extracted from responses and from a substantial amount of written comments. These comments were relevant with respect to ongoing discussions of the scientific and regulatory communities regarding nanomaterial identification, characterization, potential hazards, metrics, grouping and read-across. Taken together, the outcome and the conclusions can in the opinion of the Nordic Classification Group be considered as a preliminary mapping of the possible challenges in nanomaterial classification.

[1] The Nordic Classification Group is a network of government officials/civil servants representing the Competent Authorities for the CLP Regulation in Finland, Sweden, Norway, Iceland and Denmark

[2] The CLP Regulation (1272/2008/EC) lays down the rules for classification, labelling and packaging of chemical substances and mixtures in the European Union (EU). CLP implements the UN Globally Harmonised System of Classification and Labelling into the EU chemicals legislation.

Key elements with relevance to the work of GHS Sub-committee informal group on nanomaterials

A summary of the main outcomes with relevance to the work of GHS Sub-Committee informal group on nanomaterials is presented below. The conclusions are based on the outcome of the survey and do not necessarily represent views of the Nordic authorities in chemical legislation or the Nordic Council of Ministers. It is interesting to notice that in their final conclusions, 68% of the respondents considered it in some way necessary to specifically focus on nanomaterials within the GHS/CLP, while 16% had the impression that the current system covers nanomaterials and there is no need for specific consideration.

The full project report is available at http://norden.diva-portal.org/smash/record.jsf?pid=diva2%3A769053&dswid=4287.[3]

Inclusion of a definition for "nanomaterials" in GHS/CLP

Inclusion of a definition was supported by the majority of the respondents, and it was mainly suggested that it be based on the EU commission recommendation for a definition. It should be noted that the respondents are situated in the European Economic Area (EEA).

Amendment of GHS/CLP and update of relevant guidance documents

The best way to handle nanomaterials in relation to classification and labelling was thought to be by amending GHS/CLP and updating relevant guidance documents.

Inclusion of detailed information on the characterization and identification of the nanomaterial

There was clear support for inclusion of detailed information on the characterization and identification of nanomaterial in relation to classification. Data on those properties which are responsible for hazardous behaviour should be included in sufficient detail. Some examples given of such properties were active surface area, fiber properties, form, surface chemistry, and surface charge.

Classification of different forms of nanomaterials

Many of the respondents saw the need to give different classifications to different forms of the same nanomaterial. They could not explicitly name the main driving physico-chemical parameter for hazardous effects, but agreed that primary particle size, shape, surface properties, solubility, aggregation/agglomeration state, and dispersion stability could be such parameters. Also other properties relevant to specific material were suggested. It was also pointed out that the smallest available (and not theoretical primary) particle should drive the classification.

Classification of coated nanomaterials

The best way to handle coated nanomaterials under GHS/CLP would be to consider these, depending on solubility, either as equal to the coating material or as a mixture. Support was also given for a classification of coated nanomaterial as a substance. This was justified on the basis that it might present properties not reflecting either coating or core material.

[3] *Note by the secretariat: At the request of the expert from France and following the publication of the report, the exact reference to the webpage where it can be found has been included here for ease of reference.*

Re-evaluation of classification criteria for substances and mixtures

The question about the need to re-evaluate classification criteria of both substances/mixtures for nanomaterials in each hazard class proved to be difficult. In physical hazards, the major need for re-evaluation was for the hazard class "aerosols". In health hazards, there was equal support for the re-evaluation of each endpoint; however no details were suggested. In environmental hazards a classification criteria re-evaluation was requested especially for aquatic environment hazards.

Read-across possibilities in nanomaterial classification

When considering the usability of read-across data for classification purposes the respondents thought that the most useful read-across data would be from the same nanomaterial in a different size or in a different shape. Read-across from bulk to the nanoform was also supported on the basis of the same chemical structure/composition; however, limitations such as different physico-chemical properties were acknowledged. Limitations were also seen in read-across between same nanomaterials with different coatings.

Suitable metrics for nanomaterials

The most suitable metrics to be used for nanomaterial classification were thought to be surface area, followed by mass and particle number. However, the expression of mass was always considered important in addition to other metrics.

Concentration limits in mixture classification

The current concentration limits were considered to be unsuitable for mixtures of bulk and nanosized materials, as the hazards of a nanomaterial might differ from what can be estimated based on its concentration in the mixture. However, there were opposite opinions supporting the current concentration limits as there were concerns about a more stringent classification of nanos than bulk material.

Applicability of the additivity approach

The applicability of the additivity approach for nanomaterial classification purposes received more support than opposition; however, it was also acknowledged that it could only be used in case the hazard profile is the same for bulk and nanoform. Applying the approach to coated nanomaterials was considered especially problematical as well as the use of mass-based concentrations. Also, the nanoform introduces the possibility of new modes of action for chemical substances, and therefore additive effects may not be relevant.

Communication on nanomaterials

An obvious need for communicating nanospecific information was identified. The majority of respondents would like to have nanospecific information included in Safety data sheets (SDS), with somewhat higher support for including the information regardless of the concentration of nanomaterial.

The most important properties that should be mentioned in the SDS were size, surface area and shape, size being the most important property. For coated nanomaterials, the coating composition should be required.

The majority of the respondents would also communicate nanospecific information to the downstream users by labelling nanomaterial-containing products, with greater support for labelling of these products based on their hazards than for labelling just for being nanomaterial.

Annex III

Issues to be considered during the meeting of the informal group on 10 December 2014

(a) On the classification exercise:

  (i) Information from Finland aquatic environmental hazards of carbon nanotubes and nano and bulk forms of titanium dioxide

  (ii) Other issues to be tackled within the classification exercise

(b) Other relevant inputs

  (i) On the Nordic survey

  (ii) Other information to be tackled by the informal correspondence group

(c) New delegations/contributions and perspectives of the informal correspondence group for the biennium 2015-2016

  (i) Terms of reference

  (ii) Work plan