United Nations ST/SG/AC.10/C.4/2013/3

Secretariat

Distr.: General
17 April 2013
English
Original: French

Committee on 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

Twenty-fifth session
Geneva, 1–3 July 2013
Item 2 (f) of the provisional agenda
Classification criteria and hazard communication: nanomaterials

Review of the applicability of the GHS as regards the hazardous properties of nanomaterials: Overview of current knowledge and initial considerations

Transmitted by the expert from France[1]

Introduction

1. In this document, France wishes to follow up on its previous document ST/SG/AC.10/C.4/2012/30 and on the conclusions of the GHS Sub-Committee set out in document ST/SG/AC.10/C.4/48, by introducing an initial document with the aim of:

(a) Establishing an informal correspondence group on the issue and taking stock of the work carried out at the international level so as to avoid duplication;

(b) Studying the applicability of the GHS to nanomaterials and planning for eventual adaptations if necessary.

2. This document compiles several scientific and technical elements concerning the definitions and physico-chemical properties of nanoparticles as well as considerations about which properties are relevant when characterizing the hazards associated with these nanoparticles.

3. Lastly, a preliminary analysis of the GHS points out the technical considerations that can be gleaned from it, such as:

[1] In accordance with the programme of work of the Sub-Committee for 2013–2014 approved by the Committee at its sixth session (refer to ST/SG/AC.10/C.3/84, para. 86 and ST/SG/AC.10/40, para. 14).

(a) The general guidelines allowing for technical adaptations or an expert judgement to meet the classification criteria in the GHS;

(b) The terms “dust”, “powder”, “particle”, “nano” and “fibre”.

Proposal

4. On this non-exhaustive basis, it is proposed that the members of the GHS Sub-Committee should answer the questions found in the annex and contribute to the Sub-Committee’s knowledge through commentary, supplementary documents or amendments to the present document (particularly the references contained in sections C and D), with a view to the submission of the correspondence group’s initial document at the December 2013 session. This information may be sent to the following address: matthieu.lassus@travail.gouv.fr.

A. Definitions of nanomaterials

1. Scientific approaches focusing on measurement and health

5. In terms of measurement alone, a nanoparticle can be considered to be a piece of matter with a size of 1 to 999 nm.

6. SCENIHR[2] has been mandated by the European Commission to provide sufficient scientific information on “nanomaterials”. One of the key points it highlighted in its opinion[3] of 8 December 2010 was that “nanomaterial” is a categorization of a material by the size of its constituent parts. The term does not imply any specific risk or new intrinsic hazard properties compared to its chemical constituent parts in a more conventional state and/or of a larger size.

7. This concept of size is fundamental, because it also partially demonstrates the importance of the surface/volume ratio and thus indicates the potential reactivity and, in the case of a nanoparticle, the level of bioavailability of a compound in living organisms. This parameter is necessary but is nonetheless considered insufficient, as different nanostructures (e.g. crystallography) of a given compound that are the same size can have different toxicological profiles.

8. Thus, on the basis of the scientific knowledge[4] at the time the opinion was issued, SCENIHR considered that:

(a) Size is a basic parameter for evaluating the risks of nanomaterials, whose upper and lower limits should by definition cover the whole metric scale under consideration (1–999 nm);

(b) However, there is no clear scientific distinction at 1 nm, because particles (or some of their dimensions) that are smaller than this can still have nanoparticle properties;

(c) 100 nm is a commonly used upper limit (see also subsection A.2) but does not have any scientific basis. SCENIHR proposed defining size categories in order to appraise at different levels the need for more in-depth risk assessment using nano-specific

[2] The Scientific Committee on Emerging and Newly Identified Health Risk is one of three committees that support the European Commission by providing scientific advice for use in proposing regulations.

[3] http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_032.pdf.

[4] http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr/o/032_biblio.pdf.

methods (for example, categories such as >500, <100–500 and 1 <100 nm) (see also section B);

(d) The complex nature of structures should be described so that all nanomaterials may be incorporated, including multi-component materials and/or those that form microagglomerates or microaggregates or larger clusters (see subsection A.2):

(i) The two concepts of "internal structure" and "external structure" should supplement the definition of nanomaterials so as to cover agglomerate or aggregate forms;

(ii) The specific surface area is a supplementary criterion that describes the total surface of a material per unit volume. This expression of the reactive surface/volume (regardless of the density) is a priori more accurate and discriminating from a toxicological viewpoint than the classic representation used for conventional substances (usually in mg/l) (see also section B);

(iii) Size distributions should be proposed, and hence thresholds beyond which a nanoscale fraction would be considered an integral part of the characterization of a given substance (>0.15% is proposed, on an empirical statistical basis of normal law).

(e) The origin (e.g. natural, manufactured/designed or unintentional by-product of human activity) might also be specified to target more precisely the intended scope of application of the regulations;

(f) Many other intrinsic properties (physico-chemical, structural, coating on the particles, etc.) are key to understanding the hazards and risks and should not be ignored. However, they provide very little added value to a "universal definition" to be used in the regulation of nanomaterials.

9. The SCENIHR document is based on the main internationally-recognized definitions that are still currently valid (ISO TC 229, Organization for Economic Cooperation and Development (OECD) regulations, European regulations, as well as the main regulations in force in the United States of America and Canada). The technical considerations taken into account by SCENIHR go well beyond these definitions and are particularly appropriate in that they fully cover the dangerous properties of and the potential risks posed by nanomaterials (see section B).

2. Political approaches to management and safety regarding the use of nanomaterials

10. The European Commission adopted a recommendation on the definition of nanomaterial. According to this recommendation a nanomaterial is:

> "A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm.
>
> In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50%."

11. This definition, more limited than the one proposed by SCENIHR (see subsection A.1), is a basis for amendments to European Union legislation. It covers all sources of nanomaterials, including manufactured nanomaterials, which are the first to have been subject to regulatory clarification (see section C).

12. It has the following points in common with the definitions established by the International Organization for Standardization (ISO):

(a) The concept of a “manufactured nanomaterial”: material with any external dimension in the nanoscale … [and] intentionally produced for commercial purposes to have specific properties or specific composition” (ISO/TS 80004-1:2010);

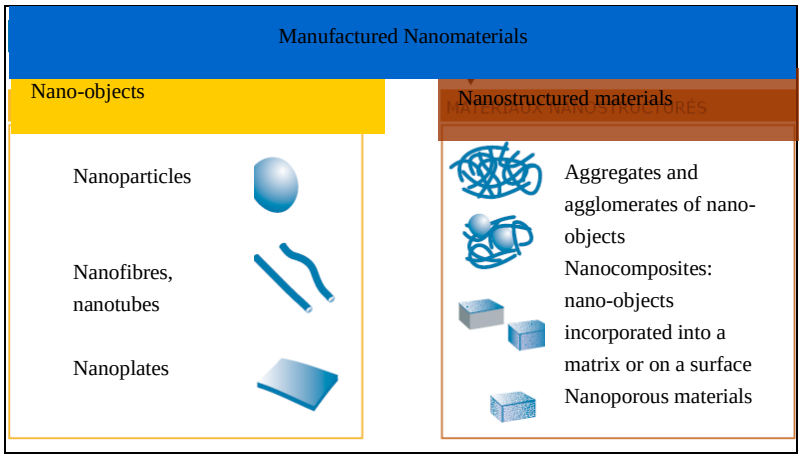
(b) Concept of a “particle: minute piece of matter with defined physical boundaries” (ISO/TS 27687:2008);

(c) Concept of an “agglomerate: collection of weakly bound particles” (ISO/TS 27687:2008);

(d) Concept of an “aggregate: particle comprising strongly bonded or fused particles” (ISO/TS 27687:2008);

(e) Concept of “nanoscale: size range from approximately 1 nm to 100 nm” (ISO/TS 27687:2008).

Figure 1
Manufactured nanomaterials



13. These definitions, along with other technical specifications (see Figure 1), constitute a first step towards clarifying the regulations and norms in order mainly to identify the markets for the production and use of nanomaterials and to determine which methodologies would make it possible to evaluate and control the associated risks.

B. Properties that are difficult to understand and detect

1. Dimensions that enable exposure

14. A nanometre corresponds to one billionth of a metre (0.000000001 metre), which is to say:

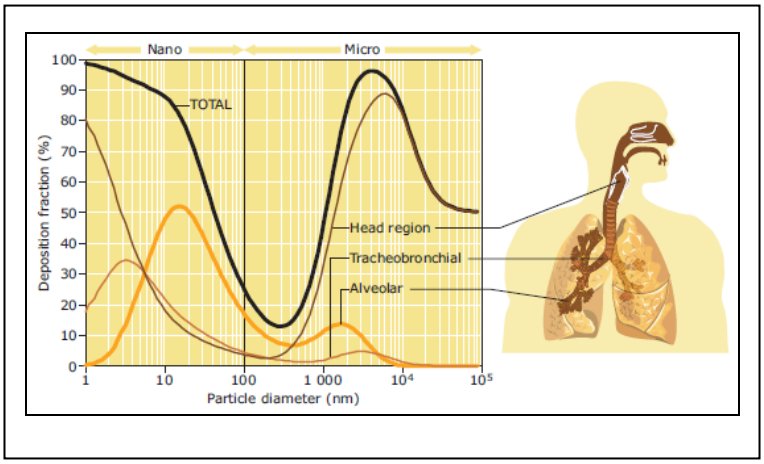
(a) 1/50,000th of the thickness of a hair;

(b) The ratio between a particle a few nanometres in size and a tennis ball is the same as the ratio between a human being and the Earth.

15. At this scale, the behaviour of particles is generally the same as in the dispersion of a gas, but with a stronger tendency towards sedimentation and absorption on surfaces.

Figure 2

Fraction deposited in the parts of the lung according to the size of the particles (excerpt from ED6050 INRS)



16. The lungs are one of the main routes of exposure that can cause toxicity. The amount deposited is not uniform and largely depends on the diameter of the particle and the state of aggregation and agglomeration as well as the particles' dispersive behaviour in the air. This type of behaviour is generally comparable to that of fine particles <10µm (see Figure 2).

17. The fraction of particles with a diameter of 10 to 100 nm is deposited deeper in the lungs and in greater proportion than microparticles (with a maximum diameter of 1 to 2µm).

18. Nanoparticles with diameters of less than 10 to 100 nm are deposited much further up the pulmonary route. This typical filtration behaviour is explained by the Brownian motion of the particles (the thermal agitation of molecules), which increases in inverse proportion to the particles' size. This random movement in space, in addition to the movement of the respiratory flow, also increases the probability of contact and thus of deposit on surfaces.

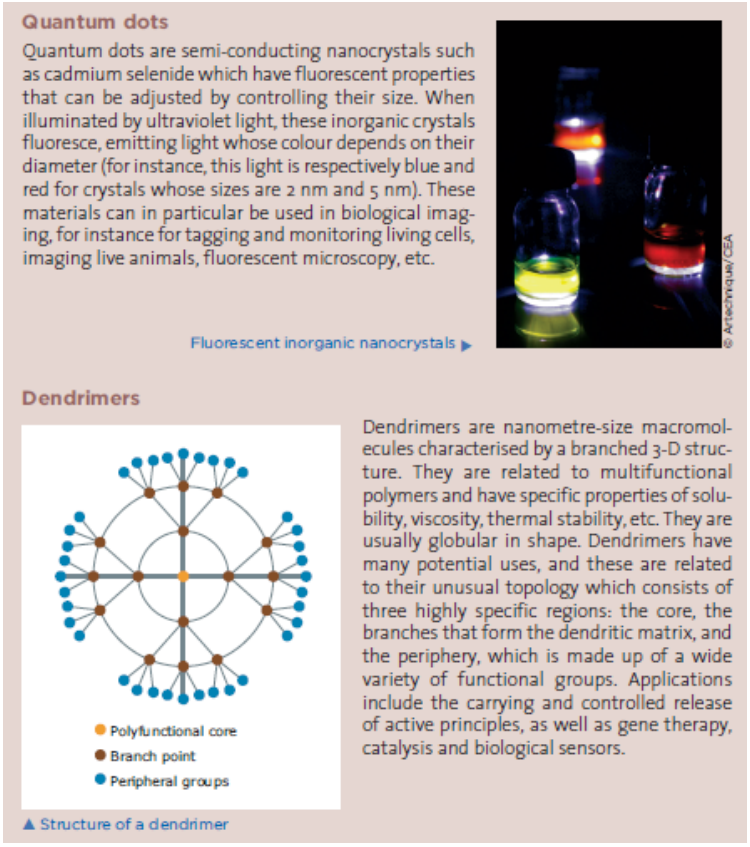
19. On the other hand, studies under way, while not yet entirely conclusive, indicate that small nanoparticles are capable of penetrating more deeply into biological barriers (nasal, alveolar, intestinal, etc.) than microparticles. The surface or elastic properties of nanoparticles (see also subsection B.2) in interaction with tissues and organic media (sweat, sebum, pH, wounds, pores, etc.) can amplify the exposure to and potentially the toxicity of nanoparticles.

20. Therefore, in the absence of more specific information, none of the three routes of human exposure (by inhalation, oral and cutaneous) should be ruled out in the first instance.

2. Dimensions and structures that can lead to new or more intense properties

21. Certain structures can have radically different properties (see Figure 3). More typically, nanoparticles have a combined surface area that is much larger than that of the same amount of material in the form of microparticles or macroparticles (1 kg of particles with a volume of 1 mm^3 has the same surface area as 1 mg of particles with a volume of 1 nm^3). This also implies that, in the same volume of space, the probability of contact and therefore of chemical interaction is greater. For example, gold is an inactive metal on a microscale but becomes an excellent catalyst for chemical reactions on a nanoscale.

Figure 3
Examples of structures with special properties
(excerpt from ED6050 INRS)



22. Such an increase in reactivity can also lead to much more severe expressions of known physico-chemical or toxicological mechanisms. This could involve a greater explosive potential (which is inversely proportional to the size of particles of dust or fine powder), or a greater inflammatory potential, which can also increase the long-term likelihood of contracting respiratory pathologies (allergies, respiratory failure, etc.), and in some cases even cancer.[5]

[5] See Gebel; Arch. Toxicol. (2012) 86; 995–1007: A comparison of studies on rats exposed to granular biodurable particles (GBP) by chronic inhalation, without a significant known specific toxicity but with an assumed common toxicological mode of action characterized by inflammation and carcinogenicity by chronic inhalation, indicates that the difference in the carcinogenic potential of GBP "nanomaterials" and conventional alveolar GBP micromaterials is low and can be described by a factor of 2–2.5 referring to the mass concentration.

C. Information that is necessary and possible to obtain but not yet very formalized

1. In existing regulations and methodologies

23. As pointed out in the previous document,[6] while current methods of assessing the hazards and risks are generally appropriate, subject to some technical adaptations, they are not yet sufficient to the extent that gaps remain in current scientific knowledge on all the potential adverse effects of nanomaterials.

24. However, current data and risk management methods tend to show that progressive solutions exist and provide effective collective or individual protection from dust and ultrafine nanoparticles and microparticles,[7] whether they are produced intentionally or generated by a given process (such as combustion, sanding, cutting or welding).

25. Nevertheless, in order to be able to adapt these risk management measures, particularly in the case of nanoparticles that are intentionally manufactured and used, we must be able to clearly identify them and describe the fundamental properties that can affect the level of hazard they pose (powderiness, surface reactivity, specific surface area, etc.).

26. Australia has already presented these findings to the Sub-Committee in detail, along with its regulatory approach regarding additional information to be provided in the safety data sheet for nanomaterials.[8]

27. The European Commission has previously informed the Sub-Committee[9] about its work under the REACH Regulation, annex II of which regulates measures to be taken regarding the safety data sheet. The previous document submitted by France also provided information about some progress made on the issue at the national and European levels. Since then, the Group for Assessing Already Registered Nanomaterials (GAARN) has made its initial recommendations,[10] and the European Chemicals Agency (ECHA) continues its work to collect and ensure an adequate level of information about nanomaterials in the REACH registration dossiers[11] (including an urgent request to provide several methods of analysis, given the intrinsic technical limitations and the lack of harmonized methods).

28. Generally speaking, there is consensus at the international level on using the following information (including in the context of ISO standardization) to characterize nanomaterials:

(a) Particle size:

(i) The size of the three dimensions of the main particle;

(ii) The specific surface area, and more particularly the specific surface area/volume ratio (SSV), which makes it possible to distinguish between the different states of agglomeration and aggregation of nanoparticles;

(iii) States of aggregation and agglomeration.

(b) Surface chemistry:

(i) Crystalline structure;

[6] ST/SG/AC.10/C.4/2012/30.

[7] See the detailed references in section D.2.

[8] ST/SG/AC.10/C.4/2010/19.

[9] UN/SCEGHS/20/INF.25.

[10] http://echa.europa.eu/documents/10162/5399565/best_practices_physiochem_subst_id_nano_en.pdf.

[11] http://echa.europa.eu/chemicals-in-our-life/nanomaterials.

(ii) Reactivity;

(iii) Treatment (including coating), which is seen in REACH as an important characteriser for identifying and characterizing chemical substances, and which can influence the reactivity and interaction of a nanoparticle with biological systems.

(c) Dispersibility (powderiness) and resuspension ability.

Other toxicological considerations on which there also tends to be consensus:

(d) One of the characteristics of nanoparticles is that the difference in toxicity compared with equal masses of larger particles correlates with the specific surface. This means that differences in the levels of toxicity are possible only if there is a change in the dimensions of the area of exposure (m^2/m^3) or in the number of particles ($1/m^3$) as used when counting fibres;

(e) Biodurability and biopersistence are two key parameters for assessing the long-term risks of toxicity. They are used to describe the accumulation in the routes of exposure and the capacity for chemical elimination (dissolution and excretion in biological fluids) and physical elimination (the transport of non-soluble or poorly soluble particles via mucociliary clearance, sneezing, nose blowing, or macrophages).

29. Difficulties in interpretation arise when the data available on the hazards are derived from substances in a conventional physical form. It is not always possible to make a clear link between these data and possible extrapolation to nanoparticles.

30. At the European level, the guidance on the application of the classification, labelling and packaging criteria,[12] in the spirit of the GHS (see subsection C.2), mentions the need to provide certain data about the state of the substance, including the following:

> "Putative forms comprise properties such as crystal structure, particle size, homogeneity (e.g. emulsions) and texture (e.g. viscosity or tablet form). Examples of physical state factors are: surface treatment (e.g. coating), state of aggregation, moisture content, residual solvent, activation or stabilisation."
>
> "In general, testing should be performed on the smallest available particle size and the default approach is to test for different routes of exposure (oral, dermal, inhalation)."

31. Generally speaking, the European Union considers that:

(a) The hazards and risks posed by nanomaterials must be evaluated on a case-by-case basis, using as a foundation all the technical guidelines made available by the European Chemicals Agency;

(b) If necessary, the matter of clarification should be taken up with the GHS Sub-Committee to enable a harmonized approach to the application of the classification and labelling criteria for nanomaterials.[13]

2. In the GHS for the application of the classification criteria

32. The GHS allows for a certain degree of flexibility in the use of expert judgement and technical adaptations to apply the classification criteria when specific data are available or when conducting tests is complex or difficult and requires adaptations (paragraphs: 1.3.2.4.4 Previously classified chemicals; 1.3.2.4.8 Expert judgement; 1.3.2.4.9 Weight of evidence).

[12] http://echa.europa.eu/documents/10162/13562/clp_en.pdf.

[13] http://ec.europa.eu/environment/chemicals/reach/pdf/classif_nano.pdf.

33. The GHS does not explicitly mention nanomaterials but does provide technical guidelines that are more or less specific to particles and dust (see table below).

34. The following points can be gleaned from this initial analysis of the GHS:

(a) Expert judgement must provide a general appraisal of the usefulness of the data with regard to their quality and relevance;

(b) When the data are convincing and a body of evidence can be produced, its weight may allow the expert to assign the appropriate class and category of risk to the substance being studied. This is possible even in the absence of corresponding laboratory testing (for example on the basis of robust epidemiological studies or work on the toxicological mechanisms);

(c) The GHS does not offer any clarification on nanomaterials, nanoparticles or fibres. Distinctions are made only between metal and non-metal particles/powders;

(d) The standard sizes of particles put forward in the GHS are as follows:

(i) 1 µm for the dissolution of metals. However, it specifies that the smallest available particle size must be tested in order to cover the maximum requirements for the dissolution of metals and expression of their specific toxicity (mentioned in the particular case of using data to evaluate irritation);

(ii) 1 to 4 µm for tests of toxicity by inhalation.

(e) The toxicity criteria for particles are expressed in mg/l. In the case of toxicity by inhalation, the GHS mentions the need to review the criteria;

(f) The GHS sets out several requirements for the dissolution of metals, namely:

The equipment used and the preparation of the test piece. Consideration is also given to the size/surface ratio and crystallography. The nanoscale forms should also be adequately described to ensure that they are appropriate for the tests conducted (and especially if the tests were performed on the conventional form of the substance);

(g) Inappropriateness of the tests or lack of available data must not be used as justification for not classifying the form in question (this is true, for example, in the case of data on metal macroparticles and their use in nanoscale forms that might be more toxic).

Information should be included on the label and the safety data sheet if inhalable dust is present.

Table: Occurrence of certain words in the GHS (English version)

Keywords		
"**Dust**"	**Part 1**	Chapter 1.2: Definition Table 1.5.2: "Dust explosion hazard" is not covered by a classification and is therefore not covered by the GHS
	Part 2	2.11.4.2: Detail on self-heating substance (Determination of safety characteristics of dusts)
	Part 3	Table 3.1.1 with notes (e) and (f): Acute toxicity estimate (ATE) is possible with powders that "generally have less than 1 to about 100µm particle size" but the values "should be reviewed to adapt" to any changes in the Organization for Economic Cooperation and Development (OECD) tests. 3.1.2.6: Similar considerations + units in mg/l + focus on "1 to 4µm particle size … mean mass aerodynamic diameter (MMAD) … maximum dose of about 2 mg/l". 3.1.3.3 + Tables 3.1.2 + 3.1.5.1 Decision logic 3.1.1 + 3.2.3.3.1 + 3.3.3.3.1 + Tables 3.8.1 + 3.9.1 + 3.9.2: The relevant ingredients for the classification of mixtures are taken into account according to a % m/m (including for dust); the values are expressed in mg/l.
	Annexes	Annex 2: A2.17: Acute toxicity: Values are expressed in mg/l Annex 3: A3.2.3.6: Explanation on the use of text in italics, using the example of P241, which applies for flammable solids "if dust clouds can occur" Table A3.2.2: P241; P260 "do not breathe dust" to be used specifically when there are inhalable particles of dust (see "particle") P261 "Avoid breathing dust/" A3.3.5: Matrix of precautionary statements by hazard class/category: P241 with flammable solids cat. 1–2 P260 with acute toxicity cat. 1–2, skin corrosion/irritation 1A to 1C, Reprotox. (lactation), STOT(r) 1–2 P261 with acute toxicity cat. 3–4, respiratory/skin sensitization 1-1A-1B, STOT 3 Annex 4: A4.3.2.3: Other information on hazards which do not result in classification (including dust explosion hazards) A4.3.8.2: Appropriate engineering controls (including explosive dust handling controls)
	Comments	Part 3 specifically begins with a recommendation to review the ATE values by taking into account any changes to the OECD guidelines. The particles studied are by default microparticles.

(*Continued on next page*)

Keywords

"**Particle**"	**Part 1**	Chapter 1.2: Definition of dust ("solid particles")
	Part 2	2.3.1: Aerosols definition: "device allowing the contents to be ejected as solid or liquid particles"
	Part 3	Table 3.1.1 note (e): In the meaning of inhalable fraction of dust or mist (see "dust")
		3.1.2.6.4: Focus on 1 to 4µm particle size – mean mass aerodynamic diameter (MMAD) (2 mg/l max. dose)
	Annexes	Annex 3: Table A3.2.2: P260, phrase "do not breathe dust" to be used particularly "if inhalable particles of dusts or mists may occur during use" P335 "Brush off loose particles from skin" A3.3.5: Matrix of precautionary statements by hazard class/category: P260 idem "Dust" P335 with pyrophoric solid cat.1, emit flammable gases cat.1 and 2 when in contact with water Annex 9: A9.3.5.10.2: In reference to the problem of the dissolution/dispersal of polymers: "true solubility related to particle size". A9.7.1.3: Consideration of the choice between the method of dissolution or transformation in the case of metals: "The transformation will be affected by a number of factors ... In addition to these properties, other factors such as the size and specific surface area of the particles ... will all play a part in determining the level of dissolved metal ions in the water." A9.7.5.4: Particle size and surface area: "the classification data generated would have used the smallest particle size marketed to determine the extent of transformation. There may be cases where data generated for a particular metal powder is not considered as suitable for classification of massive forms [... for instance when] the tested powder is structurally a different material (e.g. different crystallographic structure) ... However, in normal circumstances it is not anticipated that more than two classification proposals would be made for the same metal. Metals with a particle size smaller than the default diameter value of 1 mm can be tested on a case-by-case basis. [... The] powders give rise to a higher dissolution (or reaction) rate than the massive form leading to a more stringent classification." Annex 10: A10: Considerations identical to annex 9 + developments regarding the transformation/dissolution protocol
	Comments	Correlation between size and specific surface area to connect these two parameters with the quantity of metal ions solubilized in water and to define the associated toxicity. By default, the test is conducted on particles with a diameter of 1 mm. In the case of nanomaterials this value must be changed, and the classification of the metals concerned might also need to be modified.

(*Continued on next page*)

Keywords		
"**Powder**"	**Part 1**	Chapter 1.2: Definition of "Readily combustible solid"
	Part 2	2.3.1: Aerosols definition: "device allowing the contents to be ejected as [... a] powder" 2.7.1: Definition of "Readily combustible solid" 2.7.2: Criteria for classification as a flammable solid for "powdered ... substances and mixtures" 2.11.4.2: Detail on self-heating substance (The Bulk Powder Screening Test)
	Part 3	3.2.2: Classification criteria for skin corrosion/irritation: "Solid substances (powders) may become corrosive or irritant when moistened or in contact with moist skin or mucous membranes."
	Annexes	Annex 2: A2.7: Flammable solids Annex 9: A9.7.5.4: Particle size and surface area: "There may be cases where data generated for a particular metal powder is not considered as suitable for classification of massive forms [... for instance when] the tested powder is structurally a different material (e.g. different crystallographic structure) ... The powder may be classified separately based on the data generated on the powder. However, in normal circumstances it is not anticipated that more than two classification proposals would be made for the same metal. Metals with a particle size smaller than the default diameter value of 1 mm can be tested on a case-by-case basis. [... The] powders give rise to a higher dissolution (or reaction) rate than the massive form leading to a more stringent classification." Annex 10: A10: Considerations identical to annex 9 + developments regarding the transformation/dissolution protocol (see "particle").
	Comments	Distinction between metal and non-metal powders
Fibre/ fiber		
Nano		

D. References

1. Formal documents of the GHS Sub-Committee

- ST/SG/AC.10/C.4/2009/3;
- ST/SG/AC.10/C.4/2010/19;
- ST/SG/AC.10/C.4/2012/30;
- ST/SG/AC.10/C.4/48.

2. Information, methods and technical tools

- Anses (France):
  - http://www.anses.fr/en/content/nanomaterials/.
- Control banding tool:
  - http://www.anses.fr/sites/default/files/documents/AP2008sa0407RaEN.pdf.
- BAuA (Germany):
  - http://www.baua.de/en/Topics-from-A-to-Z/Hazardous-Substances/Nanotechnology/Nanotechnology.html;
  - Workshop on "Safe handling of nanomaterials at workplaces – Practical Guidance for the Safe Use of Nanomaterials": http://www.baua.de/en/Topics-from-A-to-Z/Hazardous-Substances/Workshops/Nano-2012/Nano-2012.html.
- ECHA (European Union):
  - http://echa.europa.eu/chemicals-in-our-life/nanomaterials.
- HSE (United Kingdom of Great Britain and Northern Ireland):
  - http://www.hse.gov.uk/nanotechnology/;
  - Guide on "Using nanomaterials at work": http://www.hse.gov.uk/pubns/books/hsg272.pdf.
- INRS (France):
  - http://www.inrs.fr/accueil/risques/chimiques/focus-agents/nanomateriaux.html;
  - ED6050 "Nanomaterials" (available in both French and English): http://www.inrs.fr/accueil/produits/mediatheque/doc/publications.html?refINRS=ED%206050.
- ISO:
  - http://www.iso.org/iso/fr/iso_technical_committee?commid=381983.
- NICNAS (Australia):
  - http://www.nicnas.gov.au/Current_Issues/nanomaterials.asp;
  - Guide "on new chemical requirements for notification of industrial nanomaterials": http://www.nicnas.gov.au/Current_Issues/Nanomaterials/Guidance on New Chemical Requirements for Notification of Industrial Nanomaterials.pdf.

- NIOSH (United States):
    - http://www.cdc.gov/niosh/topics/nanotech/;
    - Guide on “General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories”: http://www.cdc.gov/niosh/docs/2012-147/pdfs/2012-147.pdf.
- SCENIHR (European Union):
    - http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_032.pdf.

Annex

On the basis of this initial synthesis, France asks the following questions to inform the upcoming discussions of the correspondence group

1. Is it necessary/relevant to define “nanomaterials” in the GHS?

1.1 In reality, a nanoparticle should have a size range of 1 to 999 nm. However, the scientific and political choices made with regard to definitions have limited nanomaterials to a smaller size range because the definitions included in regulations are generally the result of a political compromise focused on managing the release of chemical products onto the market and therefore do not entirely reflect environmental or health concerns.

1.2 This concept of “nanomaterials” therefore covers several issues that lie outside the strict framework of classification and labelling. It can include particles as well as macroscopic materials with nanostructures (nanostructured surfaces or nanoporous materials) that do not necessarily require classification (such as massive forms of metals and alloys, or certain polymers and elastomers).

1.3 The health and environmental concerns, however, generally relate to ultrafine particles, including nanoparticles and microparticles.

2. Should the GHS explicitly mention the relevant physico-chemical properties of nanomaterials on the safety data sheet?

2.1 Although the GHS remains flexible on the subject, consensus has been reached in other forums on providing explicit guidance on properties that are useful for describing nanomaterials.

2.2 Some of these properties nevertheless seem more useful for nanoparticles than for microparticles.

2.3 In any case, the information should make it possible to assess the appropriateness of prevention and protection measures in relation to the potential for exposure to particles, regardless of their intrinsic (eco)toxicological properties.

3. How can we specify/adapt the appropriate measurement for expressing the toxicity criteria?

3.1 The current criteria in the GHS are based on considerations used for ultrafine microparticles. These principles remain relevant but seem inadequate in the case of nanoparticles.

3.2 Thus, the mass concentration of particles is not always sufficient, but it is the only measurement proposed in the GHS.

3.3 This issue also arises in the case of fibres, whether they are on a microscale (such as asbestos) or a nanoscale (such as a carbon nanotube).