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GUIDANCE

Appendix 4: Recommendations for nanomaterials applicable to the Guidance on Registration

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PREFACE

This appendix to the Guidance on registration has been developed in order to provide advice to registrants preparing their registration dossiers for nanomaterials (NM).

The aim of this document is to define the term "nanoform," the minimum criteria for distinguishing between different nanoforms and the minimum set of parameters which must be reported to characterize a reported nanoform.

This appendix intends to provide advice specific to nanomaterials and does not preclude the applicability of the general principles given in the parent guidance. The parent guidance applies when no specific information for nanomaterials has been given in this appendix.

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1. Introduction

This Appendix to the Guidance on registration[1] has been developed to provide advice to registrants preparing registration dossiers for substances that cover "nanoforms".

A substance is always manufactured or imported in at least one "form". A substance can also occur in more than one form. A "form" of a substance is described by its chemical identity, including any impurity or additive, and additional parameters (e.g. morphological aspects such as shape but also chemical structure-related parameters such as crystallinity).

A "nanoform" is a form of a substance that meets the requirements of the EC definition of a nanomaterial[2] and always has a specific shape and a specific surface chemistry as additional parameters.

The purpose of this Appendix is to outline minimum elements that potential registrants will need to consider when reporting "nanoforms" in composition records in section 1.2 of their registration dossier.

This will ensure transparency in the reporting of information on registered substances that include forms that fulfil the EU definition of a nanomaterial when potential registrants ultimately submit their registration dossiers.

This Appendix does not preclude the applicability of the general principles given in the parent guidance [1]. The "parent" guidance on registration applies whenever no specific information has been included in this Appendix.

A glossary of terms is included in Section 5.

2. General considerations

The parent guidance outlines the steps that potential registrants need to follow, from determining their registration obligations, to establishing the identity of the substance, considering joint submission where relevant with other parties, and collecting/generating relevant Annex VII-XI data and ultimately submitting this information in technical dossiers to ECHA. This Appendix will not repeat this information, as substances that cover forms that fulfil the EU recommendation for nanomaterial will follow the same principles as for the registration of complex substances in general.

The update to the parent guidance released in 2012 included a reference to "nanoforms" in section 2.2.1 "Overview of the registration scope" and stated the following:

> *When the registrant manufactures or imports the substance in the nanoform as well as the bulk form, the registration dossier should include the information of the substance in both the bulk and nanoform.*

Here, additional guidance is provided to potential registrants to aid them in distinguishing between different nanoforms within a dossier and in reporting information on "nanoforms" transparently in section 1.2 of their dossier.

[1] To avoid confusion the Guidance on registration will be called "parent" guidance in the context of this document
[2] COMMISSION RECOMMENDATION of 18 October 2011on the definition of nanomaterial (2011/696/EU) available at : http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:275:0038:0040:en:PDF

2.1 Registration obligations

The premise of REACH is that "all available and relevant information on substances on their own, in mixtures and in articles should be collected to assist in identifying hazardous properties, and recommendations about risk management measures should systematically be conveyed through supply chains, as reasonably necessary, to prevent adverse effects on human health and the environment" (Recital 17 of REACH, first sentence).

The 'one substance, one registration' principle requires multiple registrants of the same substance to be part of the same, joint registration for that substance. This means that registrants of the same substance agree to submit a joint registration covering the substance manufactured/imported by them individually. Such an agreement on the data submitted must be relevant for the scope of the substance as jointly registered by the registrants. In this respect, the joint registration is expected to include specification of the boundaries of the substance covered by the registration, in terms of its chemical composition. The specification of the boundary of the substance covered by the registration is commonly known as the **substance identity profile (SIP)**. For further information, please see Appendix IV to the *Guidance for identification and naming of substances under REACH and CLP* [2][3] .

For certain types of substance (including nanomaterials) other parameters in addition to chemical composition need to be considered in order to identify the potential hazardous properties. These additional parameters should be reflected in the SIP. Besides, each registrant also has to specify these parameters in their own dossier, in order to ensure that any variation in these specific parameters does not undermine the correct determination of the hazards of the substance. Thus, for nanomaterials, the variation of morphological parameters (e.g. size, shape) should be considered in order to ensure that the hazard data are applicable to the identified nanoforms of the substance.

3. Nanoform considerations

This guidance does not aim to give potential registrants advice on how to fulfil their information requirements for the forms they are registering. This is addressed in other guidance material (See [3], [4], [5], [6]). It rather aims to provide advice on how to transparently report nanoforms such that the registrants can demonstrate that they have fulfilled their obligations.

Consequently, the aim of this guidance is to give clear **minimum criteria** for nanoforms that can be applied consistently by different actors, while at the same time being sufficiently flexible to be implementable for the diversity of substances that may cover nanoforms. Note that this does not preclude the general principles outlined in the Guidance on substance identification for reporting compositional information in registration dossiers.

Three common elements to any manufacturing output that fulfils the EC recommendation EU definition of a nanomaterial can be distinguished, i.e. **size**, **shape** and **surface chemistry** of the particles. Potential registrants would therefore need to consider, as a minimum, the influence of

- the particle size (in one or more dimensions);
- the particle shape; and
- the surface chemistry (surface treatment with additional agents and/or modification of the surface of the particle)

[3] Please note that the Appendix to the guidance on substance identification referred to is under development/ consultation.

on their data-sharing and joint submission obligations.

Consequently, they will need to transparently document in their corresponding registration dossier for the registered substance that they have considered as a minimum these elements for nanoforms. This is irrespective of the ultimate impact the registrants conclude these elements have on the hazard profile, i.e. even when it has been determined that the hazard profile for nanoforms and non-nanoforms registered are equivalent, nanoforms and non-nanoforms will need to be reported as separate composition records. Without this transparency in their reporting, registrants will not be able to demonstrate that they have adequately addressed their obligation to collect/generate a base set of relevant Annex VII-XI data and that the hazard profile is meaningful for all forms registered by them. These elements will be further developed in the next section.

Based on these considerations, there are three minimum elements for defining a nanoform:

1) Whether it meets the EC recommendation on the definition of a nanomaterial
2) Its shape
3) Its surface chemistry

As will be outlined below, these are simply minimum elements necessary to characterize registered nanoforms in a registration dossier. Depending on the substance, additional elements and/or additional refinement of these elements (i.e. specific size ranges, specific shapes, etc.) may need to be reported depending on their impact on properties as determined in the data collected/generated to fulfil information requirements.

Where nanoforms are not reported transparently in the registration dossier for the substance, it is understood as an explicit statement made by the registrants of that substance that nanoforms are not within the scope of their registered substance.

Note that in terms of fulfilling information requirements, specific adaptations may be necessary for some studies performed with test materials that are nanomaterials, and it is likely that future revisions of OECD test guidelines will introduce some adaptations to the test methods to better tailor the studies to nanomaterials. In addition, some studies may not be scientifically appropriate for nanomaterials. Additional information can be found in Appendices R7a, 7b, 7c to the IR&CSA [4], [5] and [6](currently being updated).

3.1. Minimum parameters to be reported when nanoforms are registered

In a registration dossier, the compositional profile(s) of a substance is/(are) reported in section 1.2 of the dossier as composition records. These composition profiles can be specific to each legal entity or the same for all legal entities. This section describes the minimum reporting parameters for nanoforms in composition records in IUCLID (henceforth referred to as "nanoform composition records").

(1) Size

As size, as defined in the EC recommendation, is a common element to all nanomaterials, it is a minimum reporting element for nanoforms in dossiers. The default minimum reporting is all manufacturing outputs considered covered by that nanoform composition record in the dossier that are in the size range between 1-100 (where size refers to that defined in the EC recommendation). This means that as a minimum where nanoforms are within the scope of a registered substance, one nanoform composition record must be reported.

Registrants may need to further refine into size ranges depending on their substance and its properties. For example, some substances will demonstrate so-called "quantum-confinement effects" when the size of the particle is reduced below a cut-off size. The cut-off size is substance dependent and the impact on some properties can be profound (e.g. catalytic activity, conductivity, optical and electronic properties, etc.). As for any substance, potential registrants will need to consider all the information available and determine the impact of size on the hazard profile(s).

It is recognised that there are some scientific and technical challenges in determining whether a given manufacturing output meets the EC definition. These challenges have been highlighted by some publications [7]. Furthermore, it is recognised that the EC definition is undergoing review, and this review has highlighted some issues with the definition [8]. However, this guidance is not aimed at addressing these scientific and technical challenges, nor does it aim to address the issues that are highlighted elsewhere regarding the definition. It rather assumes that registrants themselves determine which manufacturing outputs fulfil the nanomaterial criteria and that they then determine how to fulfil their obligations for all sizes and ultimately report the relevant size ranges in their dossiers depending on the information collected/generated.

(2) Shape

The second minimum element for distinguishing between different nanoforms within a dossier and to report information on "nanoforms" transparently in section 1.2 is particle shape. The rationale for considering shape as one of the minimum reporting criteria is that particle shape may affect the behaviour of a particle and therefore may affect its toxicity [9]. Particle shape can influence the mechanism of interaction of a nanoform with a cell (e.g. shape is an important factor that determines internalisation of nanoparticles) [10] and may affect the kinetics of deposition and absorption in the body [11]. Particle shape can also influence the deposition of nanomaterials in the lungs upon inhalation.[7]

Registrants will need to report nanoforms falling in the following four categories of shapes separately in their dossiers:

- **Spheroidal-like forms**: particles with three similar external dimensions (i.e. approximately equiaxial forms). This includes a number of different shapes such as spheres, cubes, prisms, etc.

- **High aspect ratio forms**: particles with two similar external dimensions and a significantly larger third dimension (aspect ratio of 5:1 or greater) [12], [13], [14], [15][4] and substantially parallel sides [13]. This includes high aspect ratio forms with hollow structures (nanotubes), with electrically conducting or semi-conducting properties (wires), solid – non-hollow high aspect ratio forms (nanorods).[5]

- **Two-dimensional forms**: particles with one external dimension significantly smaller than the other two external dimensions. The smaller external dimension is the thickness of the form (e.g. flakes or platelets).

- **Other**: particles with any other irregular shape. This fourth category must also be used in situations where mixtures of particles with different shapes (e.g. spheres and rods) are produced and therefore none of the options reported above would be suitable.

[4] (See "B" counting rules) in Appendix C
[5] Nanotubes, wires and nanorods are all considered "nanofibres" according to ISO.

These categories are further illustrated in Figure 1.

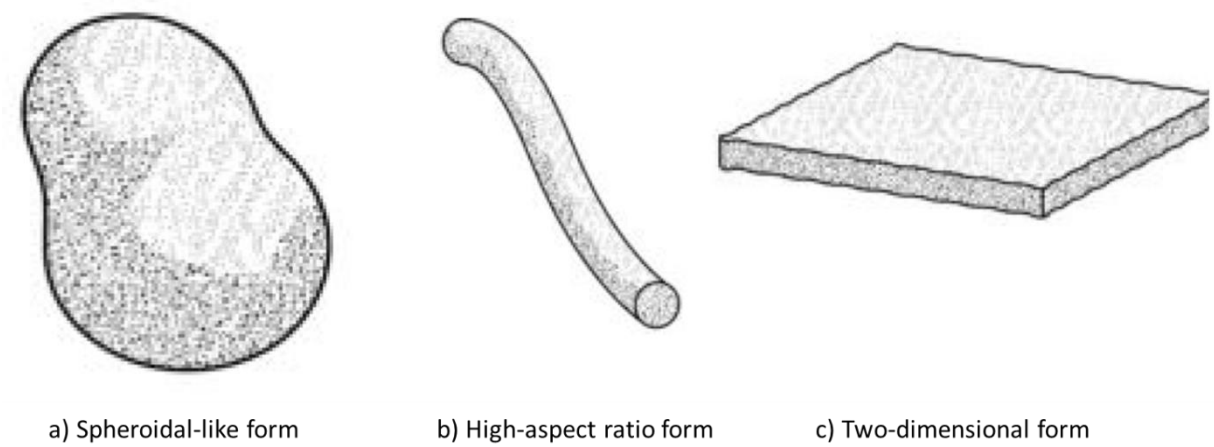

Figure 1: Schematic representation of some shapes for the categories a) spheroidal-like form, b) high-aspect ratio form and c) two dimensional form. Figure adapted from ISO/TS 80004-2 'Nanotechnologies —Vocabulary — Part 2: Nano-objects: nanoparticle, nanofibre and nanoplate'.

Thus, after determining that manufacturing outputs fulfil the EC definition, potential registrants must consider into which of the shape categories mentioned above these manufacturing outputs to be registered fall. This would in practice means that, as a minimum, different composition records would have to be reported in section 1.2 of IUCLID when particles falling in different shape categories are within the scope of the registered substance.

Potential registrants may need to further refine the description of the shapes depending on their substance and its properties. The categories of shape described above are default categories for reporting nanoforms. However, potential registrants may find it relevant for specific substances to report a further subdivision of shape categories based on data collected/generated. An example could be the situation when the registrant determined that within the spheroidal-like category, both spherical and triangular shaped particles are covered and a different toxicological profile was obtained with tests conducted on samples with these shapes, to the extent that separate reporting is necessary for these two subtypes of shape.

Within the high aspect ratio forms, registrants may find important to further (sub)divide forms based on the length and/or the rigidity, as these parameters, together with aspect ratio, are known to influence the toxicity of high aspect ratio nanoparticles (HARN) [14].

(3) Surface chemistry

The third minimum element for reporting nanoforms in a dossier is surface chemistry. Due to the high specific surface area of manufacturing outputs that fulfil the EC definition, the surface chemistry of the particle can have a profound influence on its properties ([16], [17], [18]). depending on the modification made. Surface chemistry can be modified by changing the reactivity of the surface (e.g. acid treatment to generate carboxylate groups on carbon nanotubes), the process conditions used to generate the structures (e.g. high temperature synthesis vs. chemical precipitation of metal oxides particles) or the addition of new chemical functionalities on the surface by surface treatment with surface treating agents (e.g. alkylsilane modification of a silica surface, sequential zirconia, alumina and silica treatment of a titanium dioxide particle).

Surface chemistry is intentionally varied to control properties like dispersibility in specific

solvents (water, organic, polymers, etc.) reactivity (e.g. enhance catalytic activity or switch it off completely), control solubility (treatment of calcium carbonate, silver, ZnO, etc.), etc.

The intentional and deliberate variability in surface chemistries introduces essentially a "wild card" in variability as any combination of treatments may be applied to the "base" particle. Note that the "base" particles themselves can have different compositions and/or different sizes and/or different shapes. The variability in surface chemistry may be as broad as the definition of substance itself as in principle any substance can be added to the surface of the base particle. It can refer to organic surface treatment (e.g. silica modified with alkylsilane), inorganic surface treatment (e.g. TiO2 surface treated with alumina, zirconia, silica, etc.) or sequential inorganic and organic treatments to a given base particle (e.g. TiO2 base particle treated sequentially with zirconia, alumina, silica and alkylsilane giving layers of surface treatment with the alkysilane as the last/outer layer). An idealised schematic representation of surface treatment is given in Figure 2.

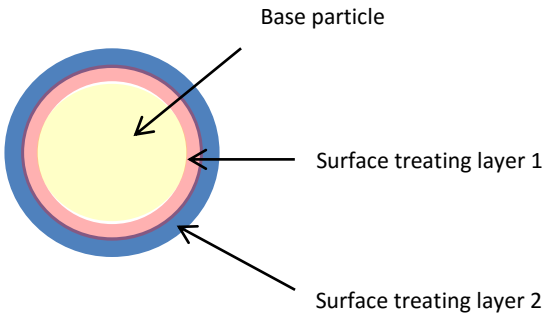

Figure 2: schematic a base particle whose surface chemistry has been modified by sequential surface treatments. The composition of the base particle

In practice, for some manufacturing outputs, the variability is limited to groups of chemical treating agents that are commonly applied to the same base particle; e.g. alkylsilane, alkylsiloxanes for silica base particles. For others the variability will be dependent on the sector of use (e.g. catalysis, cosmetics, paints).

Given the impact that surface chemistry has on properties, the variability in surface chemistry will always need to be addressed by potential registrants in determining how to fulfil their registration obligations [19]. As for all substances, the starting point is based on chemical identity. To demonstrate that they did take surface chemistry variability into account, they would need to report minimum elements based on the **chemical identity/ies** of the surface treating agent(s) in the corresponding registration dossiers.

Consequently chemical identity is the minimum element that needs to be reported for the surface chemistry of nanoforms; i.e. the chemical identities of the surface treating agents and/or the identifiers of the functional groups introduced by chemical treatment such as acid washing, O2 treatment, etc..

In terms of reporting in a registration dossier, where both treated and non-surface treated nanoforms are covered by a registration, then as a minimum two nanoform composition records will need to be reported in section 1.2 of the dossier; one for the non-surface treated nanoforms and one for the surface treated nanoforms (assuming that size and shape are the same).

For surface treated nanoforms, the starting point will be considerations of the chemical identities of the agents used (or the chemistry they impart on the surface) and registrants may

decide to group agents with similar chemistries (e.g. chemical categories) when generating/collecting data to fulfil information requirements. The groups ultimately reported in nanoform composition records in the dossier will depend on the outcome of the data gathering but will need to include, as a minimum, the chemical group and the identities of the agents considered covered by that record.

For example, where all alkysilanes are grouped, the identities of each alkylsilane covered by this group will need to be reported. In this scenario, at least one record for alkylsilane modified nanoforms will be reported (where size and shape have been reported as minimum reporting elements). Different chemical groups (e.g. alkylamines and alkysilanes) would generally trigger reporting in different nanoform composition records for transparency. Where different groups are reported under one nanoform composition record in the dossier, the rationale should be provided and the identities of each agent will need to be reported.

The above are minimum elements for transparently reporting the registered surface chemistries of the nanoforms in a dossier. Registrants may determine that separate reporting of a specific surface treatment or sub-groups within a chemical group is necessary (e.g. the surface treating agent triggers classification and labelling and/or PBT assessment) and additional nanoform composition records will be created to report these.

4. Technical reporting in the registration dossier

4.1.1 Composition Records in IUCLID Section 1.2

In terms of technical reporting in the registration dossier, the compositional profile(s) of a substance (i.e. identification and concentration ranges of the (main) constituents/impurities/additives) are reported in Section 1.2 of the dossier as composition records. Several composition records can be created as necessary for a given substance when for example as outlined above, different forms are registered with differing morphologies, such as fibre and non-fibre morphologies. In this case, fibres and non-fibres are reported as separate composition records in section 1.2 of IUCLID.

Another example of reporting more than one composition record would be simply where the registered substance covers different purity profiles where some have constituents that trigger classification and/or PBT assessment: the Registrant will report separate composition records in section 1.2 for the compositional profiles with these constituents. The reporting of separate composition records in section 1.2 is necessary for registrants to transparently report information in technical dossier.

This is relevant for the implementation of the classification and labelling according to CLP where each composition record is linked to at least one C&L record created in sections 2.1 and 2.2 of the technical dossier. The classification to which a reported composition record belongs must therefore be transparent in the dossiers of each member of a joint submission. Further details on how to report the composition of a substance in section 1.2 of IUCLID can be found in the *ECHA manual: How to prepare registration and PPORD dossiers* [20].

Additionally, the Assessment Entity tool in IUCLID 6 facilitates directly linking the different composition records created in section 1.2 with their phys-chem/fate/hazard profile. While more composition records can be linked to a same hazard profile, a given composition record may not be linked to more than one hazard profile for a specific endpoint. As composition records in section 1.2 are linked to the reporting of classification and labelling information for the substance and to its hazard profile, it is self-evident that composition records in section 1.2 of IUCLID must be created taking into account the outcomes of the hazard assessment

performed on the substance.

4.1.2 Nanoforms technical reporting

Where nanoforms are within the scope of the registered substance, at least one nanoform composition record would need to be reported in section 1.2 of the corresponding registration dossier. This nanoform composition record will include the following additional elements together with its compositional profile:

(1) Size

When manufacturing outputs that meet the EC definition of nanomaterial, potential registrant(s) will need to report the following as minimum elements:

A minimum of one nanoform composition record is created in section 1.2 and the relevant compositional information is included in the available fields.

For each nanoform composition record (as further specified by shape and surface treatment), the potential registrant selects *'solid: nanomaterial'* from the list of options in the picklist for the "physical state/form of the substance". This will open a sub-section on characterisation of nanomaterials, where additional information can be reported.

The potential registrant should provide, for each nanoform composition record created, information on the size ranges from the manufacturing outputs that refer to this nanoform composition record.

(2) Shape

When "solid: nanomaterial" is selected in the State/form picklist in a given composition record, the Registrant will need to select the *shape* of the nanoform from the available options in the picklist (one of the four categories: spheroidal-like, high-aspect ratio, two-dimensional, other).

Size ranges for the three *dimensions x, y, z* and the unit of measurement, together with the *percentile* (e.g. D50) of the size distributions to which the size ranges refer to will need to be provided. Additional information on shape of the nanoform can be provided in the *Remarks* field.

(3) Surface chemistry

For a given nanoform composition record in section 1.2, the registrant will need to select "none" or "coating" as appropriate when reporting the surface chemistries of the registered nanoforms. Where "coating" is selected, the registrant will need to report the group name of the surface treating agents in the appropriate field. The identity of each agent used to treat the surface must be reported in the available fields in the sequence in which the surface has been modified with the outer layer reported last. The lipophilicity of the last/outer layer added can also be reported in the available fields. Where the surface treatments refer to more than one chemical group, a block per surface treatment chemical group can be created in a given nanoform composition record.

Surface chemistry brings variability and therefore complexity in reporting how information requirements were fulfilled in IUCLID. Registrants are encouraged to make use of IUCLID tools such as the Assessment Entity to facilitate reporting.

Other sections of the dossier

In IUCLID section 2.1 "Classification and Labelling according to GHS", the potential registrant will select "nanomaterial" also under "State/form of the substance" when reporting the classification and labelling for a nanoforms record. Finally, in IUCLID section 4.1 "Appearance/physical state/ colour", the potential registrant will select "nanomaterial" as the "form", where the endpoint study record refers to a nanoform of the substance.

4.1.3 Practical illustration of reporting of nanoforms in a IUCLID dossier

A hypothetical example of the minimum elements that would be needed for transparency in

reporting of a nanoform is given below. It is reiterated that these are minimum elements. Where relevant and appropriate for the substance in question, registrants may have determined that additional elements and/or further sub-division by each element is necessary for reporting based on their test data. The illustrative example does not take a position on how registrants have fulfilled their obligation to generate/collect data and solely focuses on technical reporting of this collected/generated information in an IUCLID dossier.

Hypothetical case

The substance registered is an amorphous metal oxide. The compositional profile is 80-100 % of the main constituent metal oxide and none of the impurities were determined to trigger classification and labelling and/or PBT assessment.
Some of manufacturing outputs have particle sizes that fulfil the EU recommendation for nanomaterial. The typical shape of the smallest constituent particle is spherical and the constituent particles are aggregated in string-like chains giving a high specific surface area. The size of the aggregates is controlled by milling. The surface chemistry is controlled either via the manufacturing process conditions or by chemical modification of the surface of the particle (e.g. chemical oxidation/reduction of surface groups or with surface treating agents that introduce new chemistries to the surface of the particle).

The potential registrants have determined that all particles with smallest constituent particles meeting the EU recommendation can be considered as a group and that there is one common shape. Where all particles have the same surface chemistry (no deliberate modification of the surface and the manufacturing processes used yield particles with similar surface chemistry), potential registrants will report as a minimum one nanoform composition record in IUCLID section 1.2.

Where particles have different surface chemistry either from the manufacturing processes used or deliberate modification of the surface of the particles, additional nanoform composition records will be reported. This means that where surface treated and non-surface treated nanoforms are registered, then as a minimum two nanoform composition records will be reported in IUCLID section 1.2: a minimum of one for the non-surface treated and a minimum of one for the surface treated. Where the agents are considered as a group, at least one nanoform composition record for surface treated nanoforms will be reported whereby the chemical identities of the agents considered as a group used will be provided. Depending on the data collected to fulfil information requirements, additional nanoform composition records per relevant chemical group may need to be created. Where different groups are reported in one nanoform composition record, each group is reported separately and the identities/boundaries reported.

5. Glossary

"**Form of a substance**" in this context refers to elements relevant for the identification of a substance but where differences in these elements do not a priori trigger different substances.

Nanoform: a form of a substance that meets the requirements of the EC definition of a nanomaterial[6] and always has a specific shape and a specific surface chemistry as additional parameters.

[6] COMMISSION RECOMMENDATION of 18 October 2011on the definition of nanomaterial (2011/696/EU) available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:275:0038:0040:en:PDF

Composition record: a record created in IUCLID section 1.2 to report the compositional profile (list of constituents and their respective concentration ranges) and additional elements as relevant.

Nanoform composition record: a composition record in IUCLID section 1.2 where *'solid: nanomaterial'* has been selected from the list of options in the picklist for the "physical state/form of the substance" and where information on the size ranges, shape categories and surface chemistries of the particles is reported.

REFERENCES

[1] ECHA, "Guidance on registration," [Online]. Available: http://echa.europa.eu/guidance-documents/guidance-on-reach.

[2] ECHA, "Guidance for identification and naming of substances under REACH and CLP," [Online]. Available: http://echa.europa.eu/guidance-documents/guidance-on-reach.

[3] ECHA, "[DRAFT] Appendix R.6-1: Recommendations for nanomaterials applicable to the Guidance on QSARs and Grouping," [Online]. Available: http://echa.europa.eu/support/guidance/consultation-procedure/ongoing-reach.

[4] ECHA, "Appendix R7-1 Recommendations for nanomaterials applicable to Chapter R7a Endpoint specific guidance," [Online]. Available: http://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment.

[5] ECHA, "Appendix R7-1 Recommendations for nanomaterials applicable to Chapter R7b Endpoint specific guidance," [Online]. Available: http://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment.

[6] ECHA, "Appendix R7-2 Recommendations for nanomaterials applicable to Chapter R7c Endpoint specific guidance," [Online]. Available: http://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment.

[7] T. LINSINGER, G. ROEBBEN, D. GILLILAND, L. CALZOLAI, F. ROSSI, P. GIBSON and K. C, "Requirements on measurements for the implementation of the European Commission definition of the term "nanomaterial. JRC73260," 2012. [Online]. Available: http://publications.jrc.ec.europa.eu/repository/handle/JRC73260.

[8] H. RAUSCHER, G. ROEBBEN, A. BOIX SANFELIU, H. EMONS, P. GIBSON, R. KOEBER, T. LINSINGER, K. RASMUSSEN, J. RIEGO SINTES, B. SOKULL-KLUETTGEN and H. STAMM, "Towards a review of the EC Recommendation for a definition of the term "nanomaterial": Part 3: Scientific-technical evaluation of options to clarify the definition and to facilitate its implementation," 2015. [Online]. Available: https://ec.europa.eu/jrc/en/publication/eur-scientific-and-technical-research-reports/towards-review-ec-recommendation-definition-term-nanomaterial-part-3-scientific-technical.

[9] K. Sellers, N. Deleebeeck, M. Messiean, M. Jackson, E. Bleeker, D. Sijm and F. van Broekhuizen, "Grouping nanomaterials : A strategy towards grouping and read-across. RIVM Report 2015-0061," 2015. [Online]. Available: http://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2015/juni/Grouping_nanomaterials_A_strategy_towards_grouping_and_read_across.

[10] K. Kettler, K. Veltman, D. v. d. Meent, A. v. Wezel and A. Hendriks, "Cellular uptake of nanoparticles as determined by particle properties, experimental conditions, and cell type," *Environmental Toxicology and Chemistry,* vol. 33, no. 3, pp. 481-492, 2014.

[11] G. Oberdörster, A. Maynard, K. Donaldson, V. Castranova, J. Fitzpatrick, K. Ausman, J. Carter, B. Karn, W. Kreyling, D. Lai, S. Olin, N. Monteiro-Riviere, D. Warheit and H. Yang, "Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy," *Particle and Fibre Toxicology,* vol. 2, no. 8, 2005.

[12] A. G. Wylie, "Fiber length and aspect ratio of some selected asbestos samples," [Online]. Available: http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1979.tb18766.x/pdf.

[13] US-EPA, [Online]. Available: https://www.gpo.gov/fdsys/pkg/CFR-2012-title40-vol32/pdf/CFR-2012-title40-vol32-part763-subpartE-appA.pdf.

[14] C. Tran, S. Hankin, B. Ross, R. Aitken and A. Jones, "An outline scoping study to determine whether high aspect ratio nanoparticles (HARN) should raise the same concerns as do asbestos fibres. IOM," 2008. [Online]. Available:

http://nanotech.law.asu.edu/Documents/2009/07/Michael%20Vincent%20IOM%20(2008),%20An%20outline%20scoping%20study_182_2184.pdf.

[15] "NIOSH method 7400 . NIOSH Manual of Analytical Methods (NMAM)," [Online]. Available: http://www.cdc.gov/niosh/docs/2003-154/pdfs/7400.pdf.

[16] ECETOC, "Synthetic Amorphous Silica. ECETOC JACC REPORT No. 51," [Online]. Available: http://members.ecetoc.org/Documents/Document/JACC%20051.pdf.

[17] US-EPA, "Fact Sheet: Nanoscale Materials," [Online]. Available: https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/fact-sheet-nanoscale-materials.

[18] ECHA, "Assessing human health and environmental hazards of nanomaterials-Best practice for REACH Registrants-Second GAARN meeting," 2013. [Online]. Available: http://echa.europa.eu/documents/10162/5399565/best_practices_human_health_environment_nano_en.pdf.

[19] A. Oomen, E. Bleeker, P. Bos, F. van Broekhuizen, S. Gottardo, M. Groenewold, D. Hristozov, K. Hund-Rinke, M. Irfan, A. Marcomini, W. Peijnenburg, K. Rasmussen, A. Sánchez Jiménez, J. Scott-Fordsmand, M. van Tongeren, K. Wiench, W. Wohlleben and R. Landsiedel, "Grouping and Read-Across Approaches for Risk Assessment of Nanomaterials," *International Journal of Environmental Research and Public Health,* vol. 12, no. 10, p. 13415–13434, 2015.

[20] ECHA, "How to prepare registration and PPORD dossiers," 2016. [Online]. Available: http://echa.europa.eu/documents/10162/22308542/manual_regis_and_ppord_en.pdf.

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