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EUROPEAN CHEMICALS AGENCY

GUIDANCE

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

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**Guidance on 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 registration dossiers that cover "nanoforms".

The advice provided in this document outlines the minimum elements potential registrants need to consider when registering substances that fulfil the Commission Recommendation for the definition of nanomaterial[1].

The aim of this document is to define the term "nanoform," the minimum criteria for distinguishing between different nanoforms and the minimum set of elements which should be reported on the characterization of nanoforms.

This appendix intends to provide advice specific to nanomaterials and does not preclude the applicability of the general principles given in the *Guidance on registration*[2] [1]. The parent guidance applies when no specific information for nanomaterials has been given in this appendix.

This guidance does not aim to give potential registrants advice on how to fulfil their information requirements for the substances they are registering. This is addressed in other guidance material (See [2], [3], [4], [5]).

[1] See Recommendation on the definition of nanomaterial adopted by the European Commission
[2] The *Guidance on registration* will be called "parent guidance" in the content of this appendix.

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# 1. Introduction

This Appendix to the Guidance on registration[3] has been developed to provide advice to registrants preparing registration dossiers that cover "nanoforms".

A substance is described by its chemical identity, including any impurity or additive, and any relevant additional parameters for hazard and risk assessment (e.g. morphological aspects such as shape, chemical structure-related parameters such as crystallinity).

A "nanoform" is a substance that meets the requirements of the Commission Recommendation for the definition of nanomaterial[4,5] (hereafter, the definition of nanomaterials) and has a shape and a surface chemistry. This does not imply that nanoforms and non nanoforms have different substance identities. They may be registered with other nanoforms and non-nanoforms under one registration.

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 consistent reporting in registration dossiers and facilitate registrants to clearly demonstrate fulfilment of their registration obligations for substances that fulfil the EC definition (from here on substances that meet the definition of nanomaterial are referred to as nanomaterials in this document).

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 registrations that cover nanomaterials will follow the same principles as for a registration where there is variability in compositions covered and/or any other relevant parameters. For additional information see ECHA Guidance for identification and naming of substances under REACH and CLP [6].

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 in the bulk form, the registration dossier should include the information of the substance in both the bulk form and nanoform[6].*

[3] To avoid confusion the Guidance on registration will be called "parent" guidance in the context of this document

[4] Commission Recommendation of 18 October 2011 on 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

[5] Henceforth in this document referred to as the definition of nanomaterial

[6] Please note that there may also be situation where the substance registered only covers nanoforms.

In the present document, additional guidance is provided to potential registrants to aid them understand what are nanoforms and how to report those that are covered by the registration in section 1.2 of their dossiers consistently and clearly.

## 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 a given substance to be part of the same joint registration. This means that these registrants agree to submit a joint registration covering the substances manufactured/imported by them individually. Sharing of data derived from vertebrate animal studies is mandatory under REACH, and registrants must collaborate and share the testing costs of new studies performed, subject to a data sharing agreement. Such an agreement on the data submitted must be relevant for the scope of the registered substance as jointly registered by the registrants. In this respect, the joint registration is expected to include specification of the boundaries of the registered substance covered by the registration, in terms of its chemical compositional information (and, where relevant, other parameters necessary for the substance identification). The specification of the boundary of the registered substance covered by the registration is commonly known as the **substance identity profile (SIP)**. For further information, please see Appendix III to the *Guidance for identification and naming of substances under REACH and CLP* [6].

For some substances, other parameters in addition to chemical composition need to be considered in order to determine their impact on properties relevant for the hazard profile. These additional parameters should be reflected in the SIP. Note that, each registrant also has to specify these parameters in his own dossier, in order to ensure that any variation in these specific parameters has been considered in Annex VII-XI data submitted for the registration. Thus, for nanomaterials, the variation of morphological parameters (e.g. size, shape) and surface chemistry should be considered in order to ensure that the Annex VII-XI data are applicable to the registered nanoforms. Nanomaterials may have different properties and thus (a) different classification(s) for the relevant physicochemical, human health or environmental endpoint compared with non-nanoform substances.[7]
The tonnage triggers for registration apply to the total tonnage of a substance manufactured or imported by a registrant [7]. Thus, for registrants of non-nanoforms and nanoforms, the total volume determines the need and the timing for registration and the information requirements for the registered substance. The properties of each nanoform need to properly be taken into account, in fulfilling the information requirements of Annex VII to X.

Legal entity specific information requirements are triggered by his aggregated tonnage.

[7] When nanoforms are covered by a registration, they are reported in the SIP. There are fields available in IUCLID 6 to facilitate reporting of size ranges, shape, surface chemistries and specific surface area ranges for the nanoforms covered by a "boundary composition of the substance" record in section 1.2 of the lead registrant dossier. Technically how nanoforms are reported will depend on how the registrants report how they have fulfilled their Annex VII-XI information requirements.

# 3. Nanoform considerations

The European Commission has published a Recommendation on the definition of nanomaterial. The term "nanoform" however has not been defined, nor can it be found within the REACH Regulation. Nevertheless, the term "nanoform" has been used for several years in the context of REACH ( [7], [8]). Before defining the term "nanoform", it is useful to examine whether such a term is necessary, given the available definition for the term nanomaterial, and what additional value such a term may bring.

In order to illustrate the utility of the term "nanoform" it is useful to consider a hypothetical example case. Substances may be manufactured as nanomaterials and non-nanomaterials[8]. Furthermore, for a given substance that is manufactured as a nanomaterial, there may be multiple nanomaterials that have a composition giving them the same substance identity, yet differ among themselves in a variety of other parameters. To illustrate, substances identified for registration as X may involve a combination of multiple parameters having a potential impact on its properties:

- Substance manufactured in a non-nanomaterial size range
- Substance manufactured as a nanomaterial, with spherical shape and surface treated with chemical Y (nanomaterial 1)
- Substance manufactured as a nanomaterial, with rod shape and surface treated with chemical Z (nanomaterial 2)
- Substance manufactured as a nanomaterial, with a spherical shape and no surface treatment (nanomaterial 3)

In order to be able to distinguish between these four substances, all of which fall under the umbrella of substance identity X, yet differ among themselves, it is necessary to have a term that captures the possibility of such distinctions. This term is "nanoform". The term "nanoform" aims at describing nanomaterials that have the same substance identity (substance X in this case), are nanomaterials, and yet differ among themselves in the key characteristics of shape and surface chemistry.

This guidance does not aim to give potential registrants advice on how to fulfil their information requirements for the substances they are registering. This is addressed in other guidance material (See [2], [3], [4], [5]). It rather aims to provide advice on how to report nanoforms so that registrants can demonstrate that they have fulfilled their obligations.

Consequently, the aim of this guidance is to give clear **minimum criteria** for reporting nanoforms that can be applied consistently by different actors, while at the same time being sufficiently flexible to be implementable for the diversity of registered 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 nanomaterial can be distinguished, i.e. **size**, **shape** and **surface chemistry** of the particles. Potential registrants would therefore need to consider, as a minimum[9], the influence of

[8] A substance that does not meet the conditions of the Commission Recommendation for the definition of a nanomaterial
[9] As further explained in following sections of this document, where relevant and appropriate for the substance in question, registrants may determine that additional elements and/or further sub-division by each element is necessary for reporting based on test data and/or to report uses etc.

- the particle size (whether it meets the definition of a nanomaterial);
- its particle shape; and
- the surface chemistry (i.e. the chemical nature of the surface)

on their data-sharing and joint submission obligations.

Consequently, they will need to consider at a minimum these elements for nanoforms. This should be documented in the corresponding registration dossier. 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 clarity 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 that is registered by them. These elements will be further developed in the next section.

Based on these considerations, there are three minimum elements to characterise nanoforms.

1) Size[10],[11]

2) Shape

3) Surface chemistry

As will be outlined below, these are minimum elements necessary to characterize registered nanoforms in a registration dossier. Depending on the registered 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 clearly reported in the registration dossier, it is understood as an explicit statement made by the registrants that nanoforms are not within the scope of their registration. Note that this guidance does not mean that registrants should report nanoforms on a "precautionary" basis, rather it means that registrants should report nanoforms that they intend to cover with their registration.

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. Furthermore, it may be both necessary and useful to use grouping and read-across of different nanoforms, and there may be some aspects specific to nanomaterials when using grouping and read-across between different nanoforms. Additional information can be found in Appendices to Chapters *R7a, 7b, 7c and R6 to the guidance on information requirements and chemical safety assessment* (IR&CSA) [3], [4], [5] and [2]

[10] This criterion specifically refers to whether the substance meets the requirements in the EC recommendation on the definition of a nanomaterial. The determination methods for determining whether a substance meets this definition is up to the registrant.

[11] While the text refers to size, Registrants may determine that a substance meets the EC recommendation on the definition of a nanomaterial using other methods. For example, the current definition considers that the volume specific surface area (VSSA) may be used to identify that a substance meets the definition. In case registrants use the VSSA, or other scientifically valid derogations to determine a substance is a nanomaterial, measurement of size or size distribution is not needed for the purposes of this guidance. Information on particle size/size distribution may nevertheless be necessary for other parts of the registration dossier.

(currently being updated).

## 3.1. Minimum parameters to be reported when nanoforms are registered

In a registration dossier, the compositional profiles for a substance identity are reported in section 1.2 of the dossier as composition records. A given composition profile may be specific to each legal entity, may apply to only a few legal entities, or may be the same for all legal entities. This section describes the minimum reporting elements for nanoforms in composition records in IUCLID (from here on referred to as "nanoform composition records"[12]).

### (1) Size

Size, is a common element to all nanomaterials and plays a central role in defining the term nanomaterial as seen in the commission recommendation on the definition of a nanomaterial. Therefore, size (or more specifically, whether a substance is a nanomaterial) is a minimum reporting element for nanoforms in dossiers. When a registration covers nanoforms, this is recorded in a nanoform composition record; this is the default minimum reporting. When reporting a nanoform, registrants should indicate the range of the D50 values of the constituent particles of the nanoform in question (e.g. D50 of 5-90 nm-see also section 4 for further details on reporting and for potential derogations).

Registrants may need to further refine into size ranges based on data collected/generated on their registered substance and the substance properties. For example, some substances will demonstrate altered properties 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 more or less profound in each specific case (e.g. catalytic activity, conductivity, optical and electronic properties, etc.). In other cases, the change in properties may be gradual and there may be no specific cut-off size. As for any substance, potential registrants will need to consider all the information available and determine the impact of size on properties relevant for hazard profile(s).

It is recognised that there are some scientific and technical challenges in determining whether a given substance is a nanomaterial. These challenges have been highlighted by some publications [9]. Furthermore, it is recognised that the definition of nanomaterial is undergoing review, and this review has highlighted some issues with the definition [10]. 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 substances are nanomaterials 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 is particle shape of the constituent particles. 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 [11]. 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 and thereby the toxicity) [12] and may affect the kinetics of deposition and absorption in the body [13]. Particle shape can also influence the deposition of nanomaterials

[12] See glossary for more detail on the terms "composition record" and "nanoform composition record"

in the lungs upon inhalation [13].

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

- **Spheroidal-like** particles with three similar external dimensions in all projections (i.e. approximately equiaxial forms). This includes a number of different shapes such that can be approximated as spheres, cubes, prisms, etc. This excludes shapes with high aspect ratios (aspect ratio of 5:1 or greater, see below)

- **High aspect ratio**: particles with two similar external dimensions and a significantly larger third dimension (aspect ratio of 5:1 or greater) [14], [15], [16], [17][13] and substantially parallel sides [15]. This includes high aspect ratio particles with hollow structures (nanotubes),as well as solid, non-hollow high aspect ratio particles (nanorods).[14]

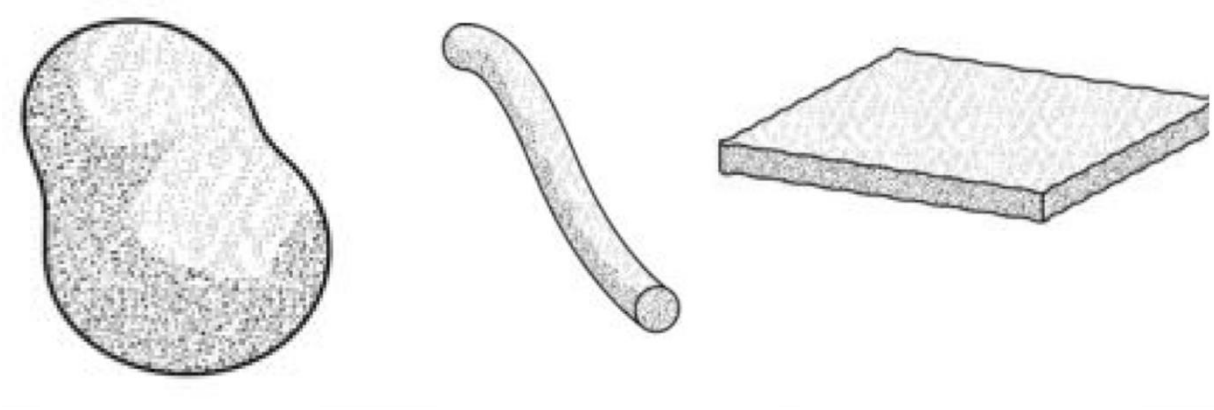
- **Two-dimensional**: particles with one external dimension significantly smaller than the other two external dimensions. The smaller external dimension is the thickness of the particle (e.g. flakes or platelets).

- **Other**: particles with any other irregular shape. This fourth category should 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.

  It should be noted that the definitions of the shape categories closely resemble the terms used nanoparticle, nanofiber and nanoplate as defined in ISO TS 80004-2, and indeed the terms used by ISO served as an inspiration for the shape categories used in this document. However, there are subtle differences between the terms as defined in ISO TS 80004-2 and the terms used in this document, and therefore the terms used are deliberately different in order to avoid confusion. More specifically, the definition of nanomaterial requires that a particle has only one dimension in the 1-100 nm range, whereas the ISO terminology for nanoparticle requires **all three dimensions** to be in the nano range and the ISO terminology for nanofibers requires the presence of **two dimensions** in the nano range. Therefore, it is at least theoretically possible for a nanomaterial to meet the definition of spheroidal-like according to the terminology used in this guidance, but to not meet the definition of a nanoparticle according to ISO terminology. Registrants should be aware of this potential difference.

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

These categories are further illustrated in Figure 1.



a) spheroidal-like b) high-aspect ratio c) two dimensional

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

Thus, after determining that what they manufacture or import are nanomaterials, potential registrants must consider into which of the shape categories mentioned above these fall. This would in practice mean 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.

It should be noted that some nanomaterials may contain a mixture of different shaped particles due to the manufacturing process. In such a case, the shape of the majority of the particles should be used to determine which shape category the particles belongs to. That is, if 50% or more of the particles belong to one shape category, then the particles should be allocated to that particular shape category. If no one particle shape is in a majority (e.g. 30% of the particles are spheroidal-like, 30% are high-aspect ratio particles, and 40% are plate like particles), then such particles should be reported under the "other" shape category. In cases where a mixture of shapes exist, the registrants should also report further details of the shape (e.g. 60% of the particles are spheroidal like, and 40% of the particles are two-dimensional).

Where a registrant controls the shape of the particles (e.g. by controlling the manufacturing process), then the different resulting shape categories should not be reported as a single shape category. That is, if a registrant makes spheroidal-like particles by one manufacturing process, and also makes high aspect ratio particles by changing the manufacturing process or controlling its shape, then these should not be reported as a single shape category containing a mixture of different shapes.

Potential registrants may need to further refine the description of the shapes depending on their substance and the impact shape has on properties relevant for Annex VII-XI information requirements. 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. For example, if the registrant determines that both spherical and tetrahedral particles are present, separate reporting may be necessary if tests indicate that the difference in shape leads to a difference in toxicological profile.

Within the high aspect ratio particles, registrants may find it important to further subdivide particles e.g. based on length, rigidity, friability, solubility in biological media etc. These parameters, together with aspect ratio, are known to influence the toxicity of high aspect ratio

nanoparticles (HARN) [16] (e.g. needle-like vs. tangled HARN).

## (3) Surface chemistry

The third minimum element for reporting nanoforms in a dossier is surface chemistry (i.e. the chemical nature of the surface of a particle). Due to the high specific surface area of nanomaterials, the surface chemistry of the particle can have a profound influence on its properties ( [18], [19], [20].) Surface chemistry depends on the process conditions used to generate the structures and the chemical functionalities introduced to the surface by treatment with surface treating agents. Particles with nominally identical core compositions may have very different surface chemistries due to the differing synthesis methods used (e.g. high temperature pyrolysis vs. wet chemical synthesis), the addition of other agents to their surfaces (e.g. inorganic treatment, organic treatment) or modification of their surface functionalities (e.g. oxidative treatment, reductive treatment). Particles with the same core compositional profile (e.g. amorphous silica) may have very different surface chemistries (e.g. alumina, trichloromethysilane, low silanol group density, high silanol group density, etc.).

Surface chemistry is intentionally varied to control particle properties like dispersibility in specific solvents (water, organic, polymers, etc.), reactivity (e.g. enhance catalytic activity or switch it off completely), solubility (e.g. treatment of calcium carbonate, silver, ZnO, etc.), etc.

The modification of particle surface chemistry essentially introduces a "wild card" in possible variability due to the diversity in the modifications that may be undertaken. The variability in surface chemistry may be as broad as the definition of substance itself as in principle any substance may be added to the surface of a particle. For example, modification of surface chemistry can refer to organic surface treatment (e.g. silica particle surfaces modified with alkylsilane), inorganic surface treatment (e.g. $TiO_2$ particle surfaces modified with alumina, zirconia, silica, etc.) or sequential inorganic and organic treatments to a given particle core (e.g. $TiO_2$ particle surfaces modified sequentially with zirconia, alumina, silica and alkylsilane giving layers of different chemistries with the alkylsilane as the last/outer layer). An idealised schematic representation of the modification of the surface chemistry of the particle core by surface treatment is given in Figure 2. Note that particle cores can also have different compositions and/or different sizes and/or different shapes.

Note that generally, the cumulative w/w (%) contribution of the layers added to the surface is < 20 % (w/w) of the particle compositional profile. In these cases, their substance identity is based on the identity of the particle core substance following the general principles in the *Guidance for identification and naming of substances under REACH and CLP* [6]. Note that when the contribution is > 20 % (w/w), this would trigger separate registration obligations for those substances.

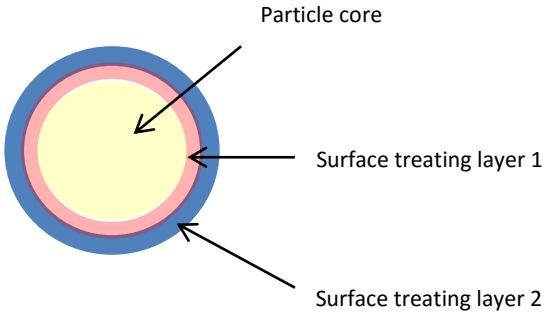



**Figure 2: Idealised schematic representation of particle whose surface chemistry has been modified by sequential surface treatments. In this example, it is assumed that the w/w (%) contribution of the particle core is > 80 % relative to the layers added, in line with the naming principles in the SID guidance. Note that the schematic is not intended in any way to be to scale. The relative change in particle diameter following treatment of the particle core depends both on what is added and how much is added. At one extreme, it can change by the thickness of the monolayer of molecules added (for e.g. a monolayer of alkylsilanes), while at the other extreme thick layers of inorganics are added (e.g. alumina treatment).**

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

Given the impact that surface chemistry has on particle properties, variability in surface chemistry will always need to be addressed by potential registrants in determining how to fulfil their registration obligations [21]. Consequently, the starting point is based on chemical identity. For example, when registrants need to demonstrate how they took surface chemistry variability into account when their registration covers surface treated nanoforms, they would need to report minimum elements based on the **chemical identity/ies** of the surface treating agent(s) in their corresponding registration dossiers.

Consequently, chemical identity is the minimum element that needs to be reported for the surface chemistry of nanoforms; e.g. the chemical identities of the surface treating agents, the identifiers of the functionalities introduced by chemical treatment such as acid washing, oxygen 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 shape is the same).

For surface treated nanoforms, the starting point will be considerations of the chemical identities of the agents used (or alternatively the chemistry that is imparted on the surface). Figure 3 in page 17illustrates that the chemistries may be different. Potential 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. Potential registrants may consider the *Appendix R.6-1: Recommendations for nanomaterials applicable to the Guidance on QSARs and Grouping* of Chemicals [2] when determining how to fulfil their information requirements for the nanoforms to be registered.

For example, where all alkylsilanes 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 also been reported as minimum reporting elements). Different chemical groups (e.g. alkylamines and alkylsilanes) would generally trigger reporting in different nanoform composition records for clarity. 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 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 persistent, bioaccumulative and toxic (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) for a substance identity (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 registration when for example as outlined above, different morphologies, such as fibre and non-fibre morphologies are registered. In this case, fibres and non-fibres are reported as separate composition records in section 1.2 of IUCLID. Each composition record has a "description of composition" field where details of e.g. the manufacturing process(es) covered by the record may be reported.

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 report clearly information in the technical dossier. Registrants may also attach additional documents to Section 1.2 as a way to provide additional characterisation information they consider not covered by available IUCLID fields. Depending on the substance identity, 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.

This is relevant for the implementation of the classification and labelling according to CLP as 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 should therefore be clear in the dossiers of each member of a joint submission. Several compositions can be linked to the same C&L record if they have the same classification. Similarly, potential registrants will need to link composition records to the corresponding use information.

Further details on how to report the compositional information in section 1.2 of IUCLID and linking the composition records to C&L and use records can be found in the *ECHA manual: How to prepare registration and PPORD dossiers* [22]. Technical instructions on how to report the boundary composition record in order to specify the substance identity profile (SIP) are available in the Appendix 3 to the *Guidance for identification and naming of substances under REACH and CLP* [6].

Additionally, the Assessment Entity tool in IUCLID 6 facilitates directly linking the different composition records created in section 1.2 with their physico-chemical/fate/hazard profile [22]. While more composition records can be linked to the 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

The technical instructions below describe how to technically complete the fields available in section 1 of IUCLID. Worked examples of how to structure the information reported for nanoforms in all sections of the registration dossier will be available on the ECHA website in practical guides developed with stakeholder input.

Technical instructions on the fields available in section 1 of IUCLID 6 and how to complete them are given in section 9.4.2 of the IUCLID manual. Potential registrants will also need to report the boundary composition records as relevant when there is more than one registrant for the registered substance (see *Guidance for identification and naming of substances under REACH and CLP* [6]. 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**

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 that refer to this nanoform composition record. More specifically, the registrant will need to at a minimum report the range of the D50 values of the constituent particle of this particular nanoform. Where relevant for the identification, additional information on size may be necessary (see shape below).

Note that the current EC recommendation for the definition of a nanomaterial allows for the use of information on volume specific surface area (VSSA), under certain conditions, as an alternative to particle size distribution in order to determine whether the substance falls under the scope of the definition. In case Registrants have determined used VSSA, or other scientifically valid methods, to determine that the substance is a nanomaterial, they should report the VSSA (or other information), and provide an explanation for why information on particle size is either not necessary.

**(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).

Where the nanoform in question is a high aspect ratio nanoform, the registrant will need to report the range of the aspect ratios covered, as well as the range of the lengths (longest dimension of the particle), in addition to the minimum size range as described under (1). This requirement is specifically for high aspect ratio nanoforms. The aspect ratio and length of such

nanoforms may have a significant impact on their hazard profile and may warrant separate assessment.

**(3)Surface chemistry**

For a given nanoform composition record in section 1.2, the registrant will need to select "none" or "coating"[15] as appropriate from the IUCLID picklist options under Surface treatment in the composition record to report 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 or the chemistry they imparted to the surface in the appropriate fields. Generally, it may be easier to describe the chemistry of the agent in the fields available and to use free text fields to describe the chemistry they impart to the surface. For example, organosilianes are important coupling agents used to modify surface chemistry [23]. The organosilane itself is not attached to the surface but rather it reacts with groups on the surface to covalently attach functional siloxanes. An illustrative example of the organosilane coupling chemistry is given in Figure 3.

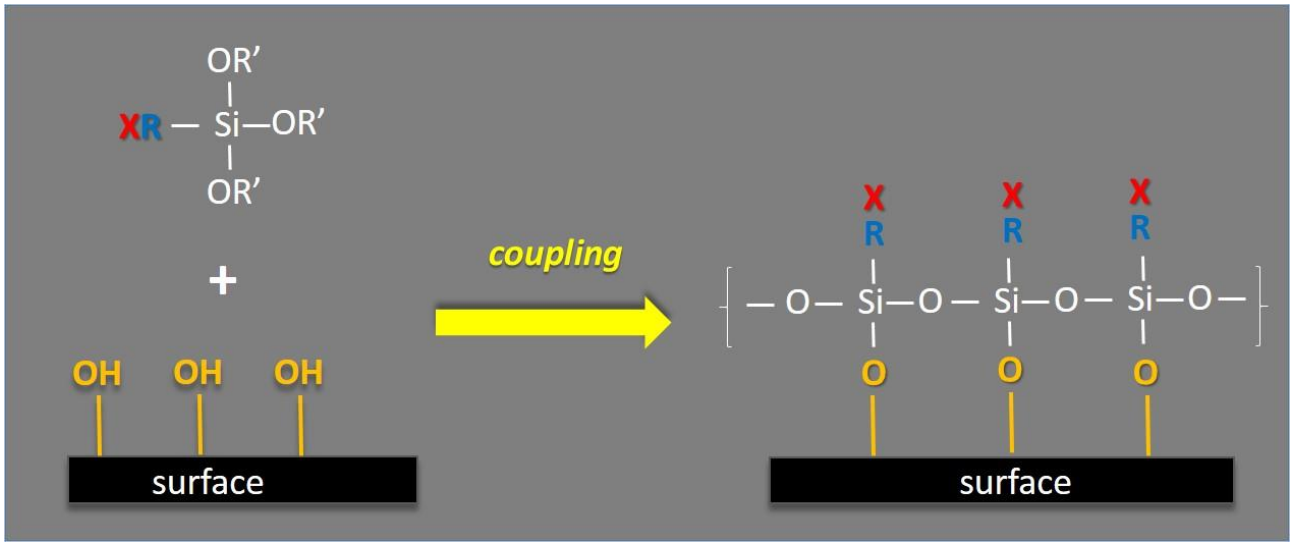



**Figure 3: a schematic of an organosilane surface treating agent XR-Si-(OR')$_3$ and the chemistry it imparts the surface post-surface treatment. The alkoxysilane groups -Si-(OR')$_3$ react via hydrolysis and condensation reactions with the surface hydroxyl groups to covalently bond functional polysiloxanes to the surface. Note the chemistries of the agent and the treated surface are different. X-R-Si(OR')$_3$ organosilane molecule where X = organic (a non-hydrolyzable organic moiety e.g. amino, vinyl, alkyl..), OR' = a hydrolysable group like an alkoxy group, e.g. methoxy, ethoxy, etc. that can react with various forms of hydroxyl groups. These groups can provide the linkage with inorganic and organic substances and R is a spacer which can be an aryl or alkyl chain.**

Schematics of the particle surface chemistry may be attached to visually describe the surface chemistry. The identity of each agent used to treat the surface should 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 record per surface treatment chemical group can be created in a given nanoform composition record.

[15] "coating" refers a picklist option to be selected in the composition record to report surface chemistry. It has no other meaning and serves solely for reporting.

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.

Note that whenever separate nanoform composition records are reported in section 1.2 of IUCLID, the records should differ in terms of one of the reporting of the three main elements described above, or in the compositional profile. Note that the elements are additive to the compositional profile and different profiles may report the same elements (size, shape and surface chemistry) but differ in the composition of the particle core.

**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 nanoform 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 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 and/or to report uses etc.
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 what is manufactured or imported have particle size distributions that fulfil the commission recommendation on the definition of a 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 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 they 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 (e.g. in the same chemical category), 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

**Nanoform**: a substance that meets the requirements of the definition of nanomaterial[16] and always has a specific shape and a specific surface chemistry

**Surface chemistry**: the chemical nature of the surface of a particle

**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.

**Particle core compositional profile**: list of the constituents and their respective concentration ranges that contribute to the particle core composition.

**Particle compositional profile**: list of constituents and their respective concentration ranges that contribute to the core composition and the list of constituents and their respective concentration ranges that contribute to the surface layer composition due to the modification of surface chemistry.

**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.

[16] 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
Please note that the EC Recommendation of definition of a nanomaterial is currently under revision, once it is updated, ECHA will consider it and update the references to it in the ECHA Guidance, if relevant.

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