ETUC concept of a regulatory definition of a substance in the nanoform

Summary
The ETUC concept of a substance in the nanoform is based on the primary particle size distribution. This single identifier makes it possible to distinguish a substance in the nanoform, bulk or as a mixture of the two. Agglomeration/aggregation/de-agglomeration/dispersions are processes that modifies the size distribution of the primary particles. These behaviour processes must be captured by indices related to the variation in the primary particle size distribution. The risk characterisation within REACH should be applied to the primary particles with the desired size distribution only.

1. Introduction

When dealing with nanomaterials we usually refer to small solid particles at the nanoscale at room temperature used in many different applications. They are produced and used because of their unique properties. However these unique properties are not only confined to technical aspects or applications. There is sufficient scientific evidence that characteristic properties of substances at the nanoscale may change. Substance parameters like vapour pressure, aqueous solubility, melting point and physical adsorption are examples of properties that change at decreasing particle size. This has long been described in the scientific literature. Some properties change suddenly e.g. the oxidation power of gold nanoparticles or the cleaning mechanisms in the lung due to the aspect ratio of nanoparticles. Especially when crucial parameters for establishing the hazard and risk profile of the nanomaterial are changing substantially compared to its bulk they require a different approach in regulation. This is the case for a number of marketed nanomaterials in the EU. To this end the EU has set up three Reach Implementation Projects, RIP-o1N, -o2N, o3N. RIP-o1N focuses on the substance identification of the nanomaterial while RIP-o2N and –o3N refer to information requirements and exposure assessment + risk characterisation respectively. The proposal put forward in here uses input from the case studies addressed in the RIP-o1N.

Recently a lot of research focussed on the development of methodologies to characterise nanomaterials and the establishment of a risk profile according to current methodologies. Experiences have shown that quite a number of uncertainties and difficulties emerged both in analytical aspects, interpretation of the test result and how to use the outcome in establishing a risk profile. Although the results look sometime contradictive, the ETUC is of the opinion that the scientific literature shows enough evidence for the variation in REACH relevant substance parameters that motivate for a discrimination between the nanoform and the bulk of a substance. It shares this view with many other experts in this field. However current chemicals policy regulation anywhere in the world do not have yet a clear answer on what basis such a distinction between the nano and bulk form should be made.

It is the aim of this leaflet to provide a concept how substance identification of nanomaterial should look like that merit a distinction between the bulk and nanoform of a substance using the REACH concepts. The nanoform of a substance is related to distinct size limits of the shape of the particles. The size limits established by ISO will be followed here. The consequences for the Registration of substances in the nanoform within REACH will shortly be discussed.

2. Parameters used to distinguish nanoform from bulk

The objective of the RIP-o1N is to develop specific advice on how to establish the substance identity of nanomaterials and proposals for general rules on how nanomaterials can be identified, reported and recorded and their "sameness". The approach was to select four substances that are produced in their nanoform, CNT, TiO_2, $CaCO_3$ and Ag, and to identify the parameters that distinguish the nano from the bulk form, to apply the REACH guidance document on identification and to give additional information how to solve discrepancies encountered.

EUROPEAN TRADE UNION CONFEDERATION
CONFEDERATION EUROPEENNE DES SYNDICATS
John Monks, General Secretary
Boulevard du Roi Albert II, 5 • B - 1210 Bruxelles • Tel: +32 2 224 04 11
Fax: +32 2 224 04 54 / 55 • e-mail: etuc@etuc.org • www.etuc.org

Based on the analysis of these case studies the first picture that emerged was that most of these substances produced in its nanoform are surface treated because otherwise their unique properties due to their small size would disappear quickly due to aggregation and agglomeration. Therefore an important difference between a Manufacture NanoMaterial (MNM) and its natural form is the surface treatment. However surface treatment makes it complex to distinguish the "sameness" of a substance in its nano form that is either treated or not.

Although the chemical composition of the core of the nanomaterial, the purity and the crystal form of the core are important parameters to describe nanomaterials, they are also used to describe the bulk form and are therefore not unique for the nano form. However the unique parameters that are required to identify the nanoform of a substance are related to its size, the *particle size distribution* (PSD) and the *shape* of the nanomaterial. These parameters are currently not used in the identification process of a substance within REACH. Therefore to make a distinction between the bulk and the nano the chemical composition alone is not sufficient in this case. If one or more additional physical parameters are defined the substance in the nanoform will end in the box of a substance of defined chemical composition and other main identifiers according to the REACH guidance document on substance identification. If it is not possible to identify additional physical parameters the substance will end in the box of a UVCB substance. For a substance in the nanoform we will identify the required physical parameter in the REACH guidance document.

3. Physical parameter to distinguish a substance in the nanoform from the bulk

The PSD of the nanomaterial is generally determined by the raw materials manufacturer and from the PSD-curve the D50-value is derived. However the established PSD by the manufacturer is usually based on the mass distribution with size and therefore the reported D50 is linked to the mass fraction. Thus when a D50 = 150 nm is reported for a substance it reflects the fraction for which 50% of the *mass* of the material is below 150 nm. This makes it difficult to derive for this material what fraction of the substance is for example below 100 nm, the current ISO standard for nanomaterial. Therefore we may conclude that there are several disadvantages to use the D50 as a parameter to distinguish the nano form from the bulk form. However the concept is well known and can easily be turned into an identifier for a substance in the nanoform if not the D50 is communicated but the fraction below a predefined size e.g. 100 nm. To this end the following modifications are proposed:

1) The PSD varies due to agglomeration/aggregation/dispersion and so on. However, these variations are caused by mutual interactions of the primary particles and their environment e.g. water, air, lung fluids and so on. These variations can be captured in indices that reflects variations in the *primary particle size distribution curve (PPSD)*, the particle size distribution from the production process itself. Therefore *the ETUC proposes that the core parameter to distinguish a substance between the nano and bulk form is the PPSD.*
2) The PPSD is often based on the variation of the mass or weight of the substance and size. However it is not the mass that is relevant for nanomaterial but the number of particles with size. Therefore *the ETUC proposes that the PPSD should be based on the number of particles (PPSD^n)* rather than the mass or volume.
3) There are currently several analytical methods to establish the *PPSD^n* of a substance. However these methods can be distinguished into two categories: I) methods that establish only an „average" or „mean" *PPSD^n* like Dynamic Light Scattering (DLS) and II) cartesian methods that are able to establish a *PPSD^n* in one, two or three Cartesian coordinates, x, y or z-length, diameters and shape respectively like Transmission or Scanning Elecotron Microscopy (TEM or SEM). Therefore shape factors and thus aspect ratio variations cannot be reflected in an average *PPSD^n* -curve established by DLS etc. but only by a *PPSD^n* -curve established by TEM/SEM methods. Therefore the aspect ratio of the nanomaterial determines what method must be used and what must be reported.

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The ETUC proposes that when the aspect ratio of the primary particles is smaller than 2 (two) the average primary particle size distribution can be established and the number fraction below 100 nm must be reported (e.g. $PPSD^n_{av<100}$ = 50%). In case the aspect ratio is higher or equal than 2 (two) a cartesion method must be used and at least the diameter fraction below 100 nm and the 80% length range must be reported (e.g. $PPSD^n_{d<100}$ = 50% and $PPSD^n_{length}$(80%) = 0.2 – 1.5 µm). For the time being the ETUC refers to nanomaterials that are at least in the nanorange by two or more dimensions, omitting therefore materials with only 1 dimension in the nanorange like nanoflakes. However the methodology does not change at all if materials with only 1 dimension in the nanorange are included.

4. Use of $PPSD^n$ parameter to identify a substance in its nanoform.

After establishing a $PPSD^n$ -curve of the primary particles cut-off values must be selected to identify uniquely a substance in the nanoform. This can be done in two ways. Either a unique size definition is used as is generally done nowadays e.g. the size range of around 1 nm to 100 nm in the ISO documents or a size cut-off value is selected from specific parameters that vary because of their size. The general trend is to use a generic cut-off value where it is envisaged that most variations of the substance in its nanoform compared to the bulk is captured. We use the one that is currently stated by ISO for nanomaterials, being from around 1 nm to 100 nm in one or more dimensions. Therefore the value of the $PPSD^n_{<100}$ is used in uniquely defining a substance in its nanoform or not.
The second part is that the size fraction below 100 nm must be set. Without any additional proof the ETUC set this number size fraction at 80%. Therefore if the $PPSD^n$ shows that at least $PPSD^n_{av\ or\ d<100}$ = 80% , that is when 80% of the primary particles is below 100 nm, the substance is *fully defined in the nanoform*. If the $PPSD^n$ indicates that less than $PPSD^n_{av\ or\ d<100}$ = 10%, that is when 10% of the primary particles is below 100 nm than the substance is fully in the bulk form. If the $PPSD^n$ shows that only for example $PPSD^n_{av\ or\ d<100}$ = 50%, that is when 50% of the primary particles is below 100 nm than the nanomaterial is composed of 50% in the nanoform and 50% in the bulk form. If this distribution is formed directly from the manufacturing process the REACH substance guidance document indicates such a substance to be called a multi-constituent substance and the way such a multi-constituent substance should be registered. Therefore *by using the $PPSD^n$ and establishing a cut-off size and fraction number any nanomaterial can be distinguished into one substance in the nanoform or bulk, or can be identified as a multi-constituent substance of the two (nanoform and bulk).*

5. Identifying the „sameness“ of two substances in the nanoform

Two substances with the same chemical composition, impurities and/or doped and each with a number-fraction of 80% of primary particles below 100 nm are in the ETUC concept considered to be similar substances in the nanoform. We do not suggest here what standard method must be selected and how much deviation we allow within the measured value. They refer to the analytical aspects of the proposed concept but it is known that several analytical methods are available to establish these parameters. The unique properties of nanomaterials are nearly always assigned to its surface. Therefore the influence of surface treatment on these unique properties including toxicological ones can be quite large.
Surface treatment can be performed by other substances that are usually attached to the surface by physical or chemical bonding. Within the REACH Regulation only chemical treatment leads to a distinction of substances. However the current approach within REACH is quite pragmatic and usually the substance remains the same when the particle(s) are macroscopic and the surface treatment modifies only a minor part of the mass of the substance.
When dealing with surface treatment for substances in the nanoform one needs to deal with the fraction of surface that is covered after the treatment; a minor part of the surface can then be allowed to be changed chemically. This fraction of coverage can be reflected in the Specific Surface Area (SSA). Since the surface is modified so will its SSA-value be different.

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The ETUC proposes that when more than 20% of the untreated surface is covered chemically by one or more substances the two substances in the nano form are different from each other. Scientific research needs to answer whether this is a reasonable fraction or not by establishing at least the hazard profile of such surface treated substances.

6. Consequences for the REACH registration of substances in the nanoform

By using the $PPSD_n$ as physical parameter in the substance identification process a distinction is made between a substance in the bulk or in the nanoform. Since substances in the nanoform were not recorded before 1981 these substances do not have a EINECS number. Consequently a substance in the nanoform cannot be categorised as a phase-in substance but should be categorised as a non phase-in substance. In addition the distinction between the nanoform and bulk is not mass based. By distinguishing a substance in the nanoform and bulk**,** the production volumes of substances in the nanoform may decrease substantially since they are not included in the overall production volume of the substance anymore**.** As a consequence many substances in the nanoform may escape the REACH registration requirements (i.e production volume below 1 tonne per year). In addition it is already certain that several REACH related physical-chemical parameters are changing by decreasing the size of the material. This will influence the hazard and risk profile of substances in the nanoform compared to the bulk and the amount of data required under REACH should be sufficient to allow a risk assessment and the derivation of adequate risk management measures. Therefore ETUC proposes that the REACH registration requirements for nanomaterials are amended to take into account the specific cases of nanomaterials**.**

Regulating substances in the nanoform

The ETUC wishes to establish as soon as possible risk profiles of substances in the nanoform. However apart from technical issues this is first of all hampered by a lack of a solid definition of substances in their nanoform. Therefore the following points are put forward to identify a substance in its nanoform so that hazard profiles can be established as soon as possible. Therefore

For regulatory purposes a substance in the nanoform :

- **Is defined when it is a solid at room temperature**

  and

  its $PPSD^n_{av\ or\ d<100}$ of the production process shows that more than 80% of the (number-) fraction is below 100 nm. (In case the number fraction below 100 nm is less than 10% the substance is fully in the bulk. In between 80% and 10% the substance is called a multi-constituent substance between its nanoform and bulk.)

- **Is different when the surface area of the primary particles is treated chemically by more than 20%, the untreated substance in the nanoform is different from the treated one.**

- **The REACH registration requirements for nanomaterials are amended to take into account the specific cases of nanomaterials.**

- **Agglomeration/aggregation/dispersion and so on are reflected in indices that only characterise the variation in the primary particle size distribution. These parameters are phys-chem characterisers of nanomaterials.**

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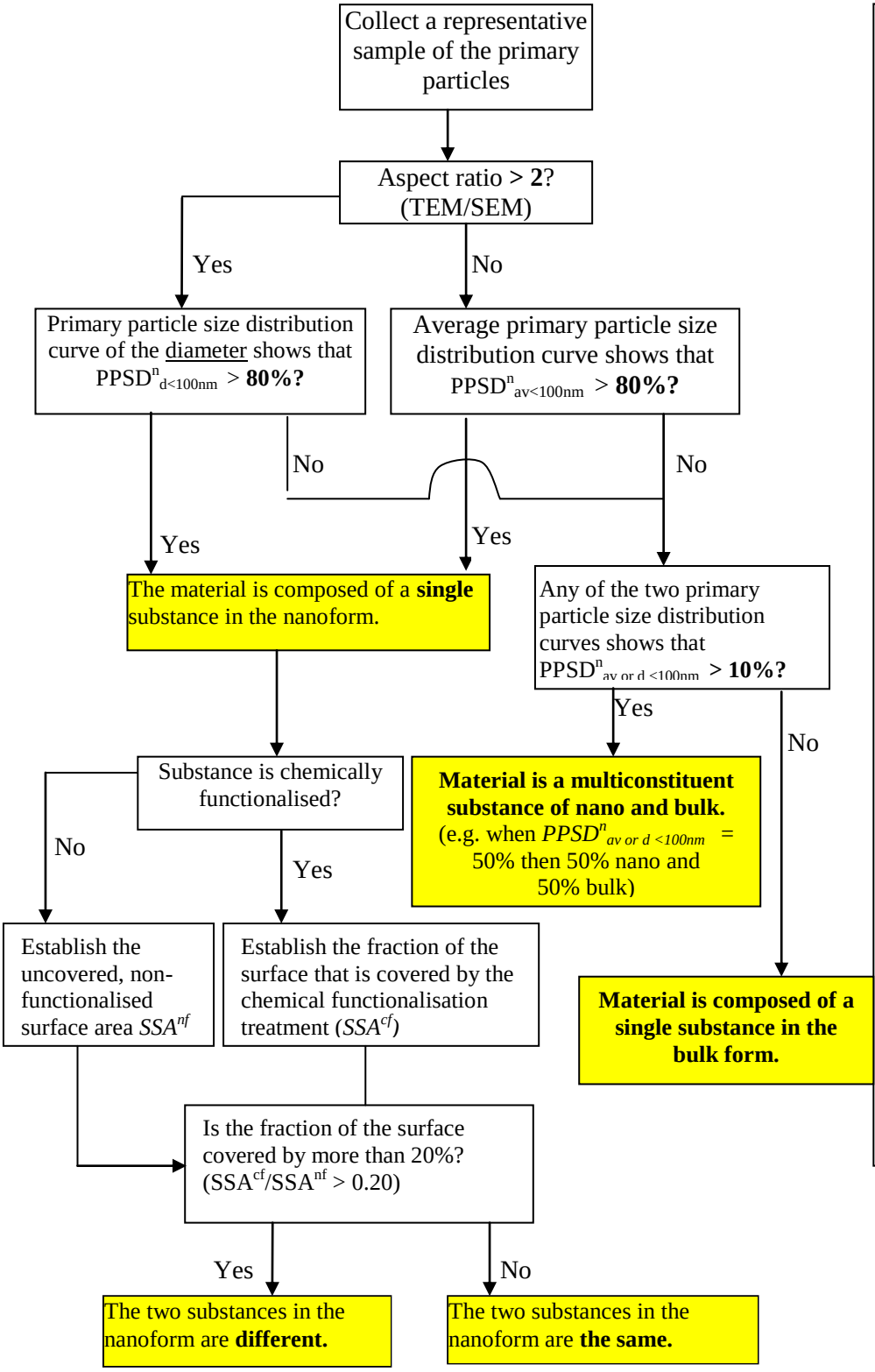
The ETUC concept of a substance in the nano form is based on the primary particle size distribution. Agglomeration/aggregation/de-agglomeration/dispersions are processes that modifies the size distribution curve of the primary particles and must be captured in indices related to the phys-chem behavior of these particles. The risk characterisation within REACH should be focused on the primary particles with the desired size distribution.



The primary particles are the particles directly formed at the production process.
(See paragraph 2)

Aspect ratio
This determines when an average size distribution (easier) or diameter size distribution curve (more difficult) must be established. **(See paragraph 3)**

Fraction limit and size
The definition of a nano-substance must be based on the fraction of primary particles below or above the nanoscale limit. This is selected to be 100 nm in line with the ISO concept.
(See paragraph 4)

The primary number particle size distribution can be used to distinguish between a single substance in the nanoform, a multiconstituent substance of a nano and bulk or a single substance in the bulk form.
(See paragraph 4)

Fraction of surface covered
Distinguish nano-substances from each other by the fraction of the surface that is chemically covered by surface treatment.
(See paragraph 5)

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