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ICCA Core Elements of a Regulatory Definition of Manufactured Nanomaterials

Innovative technologies such as nanotechnology (the ability to engineer materials at the nanoscale) and manufactured nanomaterials have the potential to improve quality of life, providing benefits to the environment, and enabling societal advances. They are crucial to help answer some of the world's toughest environmental, energy and health challenges and provide a growing range of tools to improve product performance beyond what could normally be achieved using conventional non-nano technologies.

Most conventional nanomaterial manufacturing processes are "top down," in which the material is produced in bulk (large primary particles) and grinded or milled down to a smaller particle size (broken into smaller pieces). Depending on the process and the applied forces / energy the final content of particles at nano size can vary. Any top down process even if not intentionally manufactured is likely to result in a certain fraction of nano-objects and their aggregates and agglomerates. However, true manufactured nanomaterials are intentionally processed to achieve an intended functionality and therefore contain a significant weight percentage of nano-objects and their aggregates and agglomerates.

By contrast, "bottom up" nanomaterial manufacturing processes are those in which atoms are intentionally controlled during the manufacturing operation to result in nano-objects and their aggregates and / or agglomerates. These materials are synthesized from atomic or molecular species via chemical reactions, allowing for the precursor particles to grow in size.

A definition is required in order to provide increased clarity and consistency with respect to the term nanomaterial for use in regulations laying down provisions on substances. The definition should not prejudge nor reflect the scope or application within various legislations or of any provisions potentially determining requirements on nanomaterials, including those of a risk management nature. Any assessment of nanomaterials identified by the definition will vary on a material by material basis and will have to account for intrinsic properties of the substance as well as for potential of exposure.

The following key principles should be taken into consideration for the development of a regulatory definition of manufactured nanomaterials:

ISO TS 27687 Definition for Nano-object- a material with one, two or three external dimensions in the nanoscale, where nanoscale is defined as the size range from approximately 1 nm to 100 nm

» Existing regulations are generally based on substances, therefore in a regulatory context any definition should focus on solid particulate substances (as defined by chemical regulations) instead of materials in general.

» The definition should cover nano-object as defined by ISO, their agglomerates and aggregates. The further specification on solid particulate substances containing nano-objects and their aggregates and agglomerates ensures that any potential risk of disintegration of the larger structures are adequately addressed and at the same time avoids macroscopic (non-nano) substances having an internal nanostructure like e.g. activated carbon from inappropriately being included in the definition.

» ICCA strongly advocates using weight concentration rather than particle number concentration to determine the cut of criterion for the definition of nanomaterials. Weight-% is generally used in all chemical legislation and test procedures and should therefore be the preferred choice instead of particle number concentration. In addition most identified modes of action in biological responses to nanomaterials suggest that the dose/response relationship is based on mass and not on particle number and hazard characterization is generally conducted in studies that meter out doses by weight.

» A cut-off criterion is indispensable because all solid particulate substances will have a particle size distribution that is likely to have a certain fraction at the nanoscale. In addition the cut-off should reflect the current manufacturing processes (top down / bottom up) and should not limit the quantification to a specific measurement technique. Particle measurements at the nanoscale depend strongly on the use of the appropriate methods. Results vary based on the equipment, the dispersion unit, the dispersion energy, the media of dispersion, the concentration of the nanomaterials, and the stability of the generated aerosols.

Based on these key principles, five internationally harmonized core elements have been agreed by the global chemical industry and endorsed by ICCA for a definition of manufactured nanomaterials in a regulatory context (for further information please refer to Annex 1).

ISO TS 27687 Definition for Nano-object- a material with one, two or three external dimensions in the nanoscale, where nanoscale is defined as the size range from approximately 1 nm to 100 nm

1. Solid, particulate substances
2. Intentionally manufactured at the nano-scale
3. Consisting of nano-objects with at least one dimension between 1 and 100nm on the basis of ISO
4. And their aggregates and agglomerates
5. With a weight based cut-off of either
   - 10 wt.-% or more of nano-objects as defined by ISO or
   - 50 wt % or more of aggregates / agglomerates consisting of nano-objects.

The state of science around nanomaterials is constantly evolving and knowledge about potential and perceived risks and benefits related to nanomaterials continues to develop. The global chemical industry is at the forefront of international efforts to improve understanding towards the responsible development of nanotechnology and actively engages in research efforts focused on identifying, understanding and managing any potential risks.

ICCA is strongly committed to ensuring – as with all products of our industry – that nanomaterials are manufactured, handled and used in a safe and environmentally sound manner throughout their lifecycles.

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Annex 1: ICCA Core Elements of a Regulatory Definition of 'Manufactured Nanomaterial' (Approved on 27. October 2010)

Core Elements	Substantiation
Solid, particulate substances	Substance as defined by chemical regulations. For example in the REACH regulation (Article 3, Definition 1): Substance means a chemical element and its compounds, in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent, which may be separated without affecting the stability of the substance or changing its composition. The substance definition in REACH is identical to the definition of a substance that was used in the 7th amendment of the Dangerous Substances Directive (Directive 92/32/EEC amending Directive 67/548/EEC).
Intentionally manufactured at the nano-scale	Intentionally manufactured nanomaterials are materials engineered to take advantage of their small size. Naturally occurring (e.g. sea salt nanocrystals) and unintentionally produced (e.g. diesel soot) substances are not included.
Consisting of nano-objects on the basis of ISO	ISO definition: A material with one, two or three external dimensions in the nanoscale (nanoparticles, nanofibres, and nanoplates), where nanoscale is defined as the size range from approximately 1 nm to 100 nm. The lower limit in this definition (1 nm) is introduced to avoid molecules from being designated as nano-objects which would be implied by the absence of a lower

	limit. The upper limit is a common and internationally accepted limit for the definition of a nanomaterial and test cases revealed that most size-dependent properties of nanomaterials have been shown to occur below 30nm (Auffan et al 2009).. Thus 100nm represents a conservative limit that allows the definition to focus on the materials of interest. *Auffan M, Rose J, Bottero J-Y, Lowry GV, Jolivet J-P, Wiesner MR. Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. Nat Nanotechnol 2009; 4:634-641.*
And their aggregates and agglomerates	Nano-objects typically form aggregates and agglomerates larger than 100 nm in the course of the production process. Although they are covered in a different ISO technical specification than the nano-objects and placed under the over-arching category "nano-structured materials" it is commonly accepted that they should be included in a regulatory relevant definition.
With a cut-off of either	A cut-off criterion is indispensable because all solid particulate substances will have a particle size distribution that may have a certain fraction at the nanoscale. To simply define a material by its mean particle diameter may be inappropriate as a sample with a mean particle size greater than 100 nm may have a significant portion of the particulate population in the nanoscale (less than 100 nm). At the same time, if one applies the definition without a cut-off, all particulate matters will likely be defined as nanomaterials as they likely contain some small fraction of particulates in the nanoscale range. The cut-off criterion should be based on weight% instead of

	number%. Weight-% is generally used in all chemical legislation to characterize dose/response relationships and should therefore be the preferred choice compared to number concentration. ICCA strongly advocates using weight concentration rather than particle number concentration as most identified modes of action in biological responses to nanomaterials suggest that the dose/response relationship is based on mass and not on particle number. Nanomaterials can generally be produced using a top-down or bottom-up approach. This is reflected in the two cut-off criteria.
10 wt.-% or more of nano-objects as defined by ISO	<u>Cut-Off 1 (to account for top down manufacturing processes):</u> 10 wt.-% or more of nano-objects as defined by ISO (includes aggregates / agglomerates that are below 100nm as per the ISO definition)) Most conventional manufacturing processes are "top down," in which material is produced in bulk (large primary particles) and grinded or milled down to a smaller particle size (broken into smaller pieces). Depending on the process and the applied forces / energy the final content of particles at nano size can vary. Any top down process even if not intentionally manufactured is likely to result in a certain fraction of nano-objects. However, intentionally manufactured nanomaterials typically need to exceed in most cases at least 10wt% of nano-objects in order to have a significant impact on functionality of the material. Weight percentages below 10% are not sufficient to change / improve functionality of the material and are generally unintended side products of the manufacturing process (similar to impurities).
or	
50 wt % or more of aggregates / agglomerates consisting of nano-objects	<u>Cut-Off 2 (to account for bottom up manufacturing processes):</u> 50 wt % or more of aggregates / agglomerates consisting of nano-objects By contrast, "bottom up" manufacturing processes are those in which atoms are intentionally controlled during the manufacturing operation to result in nano-objects and their aggregates and/or

	agglomerates. The material is synthesized from atomic or molecular species via chemical reactions, allowing for the precursor particles to grow in size. By nature of this synthesis process, one intentionally starts with nano-sized particles. These nano-scale building blocks can join together to form aggregates and agglomerates. Besides reflecting the predominant "nano based" nature of a material that has been synthesized through a "bottom up" process, the cut off is also seen as conservative, as the value in most cases almost corresponds to the Volume Specific Surface Area (VSSA) value of 60 m2/cm3. The two cut-offs are linked with an "or" meaning that if either condition is fulfilled, the substance would be considered as a nanomaterial according to the definition. Note: Use appropriate methods to quantify the cut offs (technical guidance under development)