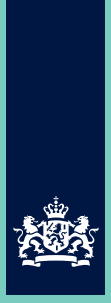

National Institute for Public Health
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Interpretation and implications of the European Commission Recommendation on the definition of nanomaterial

RIVM Letter Report 601358001/2012
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E.A.J. Bleeker et al.

Colophon

Eric A.J. Bleeker

Flemming R. Cassee

Robert E. Geertsma

Wim H. de Jong

Evelyn H. W. Heugens

Marjorie Koers-Jacquemijns

Dik van de Meent

Agnes G. Oomen

Jan Popma

Anton G. Rietveld

Susan W.P. Wijnhoven

Contact:

Eric A.J. Bleeker

Expertise Centre for Substances

eric.bleeker@rivm.nl

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Abstract

Interpretation and implications of the European Commission definition on nanomaterials

In October 2011, the European Commission published the Recommendation on the Definition of Nanomaterial. RIVM considers this definition to be a good basis for further discussion that should focus on two aspects of the definition: the proposed size limits for nanoparticles (1 to 100 nanometres); and the requirement that at least 50 % of the number of particles should be in this size range. According to RIVM, further scientific research would contribute to better understanding the implications of these threshold values. In addition, reliable and standardised measurement techniques are needed to determine particle number and size distributions. The European Commission will review the definition in 2014 in the light of experience and developments in science and technology.

Understanding potential risks important

In recent years, an increasing number of applications and products containing or using nanomaterials have become available. However, the small size of the particles in nanomaterials gives these materials different properties relative to materials with larger sizes. A univocal definition of the term 'nanomaterial' is essential in EU legislation and regulations, particularly with regard to the management of potential risks of nanomaterials to humans and the environment.

Once the definition of a nanomaterial has been established, it has to be incorporated in the appropriate legislative frameworks. Subsequently, further amendments may be required with regard to specific provisions for certain types of nanomaterials to ensure safe use.

Particles outside the definition are not automatically safe

RIVM agrees with the Commission's principle that a nanomaterial should not automatically be considered as hazardous. Conversely, materials not covered by the definition should not automatically be considered as safe. Such materials may pose a nano-sized related risk, if a substantial number of the particles is in the nano-size range, depending on the degree of human and environmental exposure.

Keywords:

nanomaterial, definition, risk assessment, regulation, legislation

Rapport in het kort

Interpretatie en implicaties van de door de Europese Commissie aanbevolen definitie van nanomaterialen

In oktober 2011 heeft de Europese Commissie Aanbeveling Inzake de Definitie van Nanomateriaal vastgesteld. Het RIVM beschouwt deze definitie als een goede basis voor verdere discussie. De discussie zou zich vooral moeten richten op twee uitgangspunten van de definitie: de grenzen voor de afmeting van nanodeeltjes (van 1 tot 100 nanometer), en de eis voor nanomaterialen dat minimaal 50 procent van de deeltjes binnen de gestelde afmeting voor nanodeeltjes vallen. Volgens het RIVM kan wetenschappelijk onderzoek helpen om implicaties van de keuzes van deze uitgangspunten in te schatten. Verder is het van belang om betrouwbare en gestandaardiseerde methoden te hebben om de aantallen nanodeeltjes en de grootte ervan te kunnen meten. De Europese Commissie zal de definitie herzien in 2014 in het licht van de ervaringen en de wetenschappelijke en technologische ontwikkelingen.

Inzicht in potentiële risico's van belang

De laatste jaren is een toenemend aantal toepassingen en producten beschikbaar gekomen waarin of waarvoor nanomaterialen worden gebruikt. Vanwege de geringe afmeting van de deeltjes hebben ze andere eigenschappen dan materialen met grotere deeltjes. Een eenduidige definitie is een belangrijke stap om de term 'nanomateriaal' voor Europese wet- en regelgeving vast te stellen. Het uiteindelijk doel van de definitie is om de potentiële risico's van nanomaterialen voor mens en milieu te beheersen.

Nu de definitie van een nanomateriaal nader is bepaald, is de volgende stap om deze in te passen in de diverse kaders van wet- en regelgeving. Dan kan ook worden vastgesteld voor welke typen nanomaterialen specifieke maatregelen nodig zijn om te kunnen waarborgen dat ze op een veilige manier worden geproduceerd en toegepast.

Deeltjes buiten definitie: niet automatisch veilig

Het RIVM onderschrijft het uitgangspunt van de Commissie dat een nanomateriaal niet automatisch als gevaarlijk moet worden beschouwd. Tegelijkertijd benadrukt het instituut dat materialen met deeltjes die buiten de definitie vallen, niet automatisch als veilig moeten worden beschouwd. Zo kunnen materialen met deeltjes die net buiten de limieten vallen toch een risico vormen afhankelijk van de blootstelling van mens en milieu.

Trefwoorden:

nanomateriaal, definitie, risicobeheersing, wetgeving, regelgeving

Contents

Summary

Rapid developments in nanoscience and nanotechnology have lead to an increasing number of applications and products containing or using nanomaterials. This has raised concerns that some of these materials may introduce new risks when workers, consumers, or the environment is exposed. These potential risks of nanomaterials may not be sufficiently controlled by current legislation.

Where adaptation of legislation would be appropriate, the European Parliament recognises that a clear definition is needed to distinguish between nanomaterials and other materials. In its response, the Commission published the 'Recommendation on the Definition of a Nanomaterial', primarily to provide clear and precise criteria to identify materials which may require specific legal provisions. The definition also aims to promote consistency in the interpretation of the term 'nanomaterial' in legal frameworks.

The Dutch ministries have requested RIVM to interpret the meaning and implications of the Recommendation from a scientific perspective and to consider the implications for use in legislation. This report provides the basis for discussions by policy makers and stakeholders on the use and further implementation of the recommended definition in national and international legal frameworks.

Commission Recommendation

'Nanomaterial' means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm.

In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.

In addition, a material is within the definition if its specific surface area by volume is greater than 60 m^2/cm^3.

The Recommendation also includes definitions of 'particle', 'agglomerate' and 'aggregate'. A review of the definition, focusing on the appropriateness of the 50 % limit is foreseen by December 2014.

The Commission solely aims to identify substances within a specific size range and does not aim to classify nanomaterials as intrinsically hazardous. The Commission definition together with background information is presented in Chapter 2 and the key elements of the recommended definition are discussed from a scientific perspective in Chapter 3.

The Recommendation states that a ''*nanomaterial' means a natural, incidental or manufactured material* […]'. RIVM agrees that a distinction should be made between natural, incidental or manufactured materials in the appropriate legislation, if necessary.

Particle size distribution

RIVM acknowledges the Commission reasons for limiting the size range to between 1 and 100 nm in the absence of scientific arguments for other thresholds. However, scientific evidence would contribute to better understanding the implications of the chosen threshold values.

The inclusion of size distribution in the definition is acknowledgement that individual particles of a material differ in size. RIVM also acknowledges the Commission's choice of the number size distribution in the definition of a nanomaterial. This implies that a particulate material can be defined as nanomaterial when only some of the particles are in the 1-100 nm size range.

The selection of a 50 % particle number threshold has no scientific basis but has the advantage that the threshold can be determined by the median without knowing the details of the size distribution. However, this 50 % threshold might obscure relevant information on the size distribution. Yet allowing deviation from this threshold raises questions about what valid concerns require deviation from the 50 % threshold.

In addition, the definition of an aggregate may lead to misinterpretation of the nanomaterial definition (see Section 3.3). It is therefore recommended that the definition of an aggregate be reconsidered, or further guidance is provided to ensure univocal interpretation.

The definition of nanomaterial is intended for use in legal frameworks to address assessment on potential environmental, health and safety risks. The Commission explicitly states that a nanomaterial is not intrinsically hazardous. Conversely, materials not covered by the definition, may exhibit a size related hazard, for example when different (hazardous) properties arise in a specific material at particle sizes larger than 100 nm. The potential hazards of materials not considered to be nanomaterials need to be assessed in the appropriate legal framework.

In addition, the definition does not relate to use or exposure to nanomaterials. Thus, a material with most particles larger than 100 nm is not classified as a nanomaterial, even though exposure to the particles smaller than 100 nm may be considerable. A threshold needs to be defined for nanomaterial. Regardless of the threshold chosen, nano-sized related risks will always be present and thus better insight into such risks is required to ensure safe use.

Measurement techniques

For practical application of the definition and for adequate risk assessment of nanomaterials, measurement techniques for number-based size distribution need to be further developed and clear guidance provided on their application. At present, the most suitable method to measure nanomaterials depends on the type of nanomaterial and the matrix in which the nanomaterial is present, for instance liquid or air.

In addition, various measurement techniques are available to determine different dimensions such as geometric, hydrodynamic and aerodynamic dimensions but many methods do not distinguish between agglomerates/ aggregates and single particles. Thus, it is recommended that at least two measurement techniques are used, one of which should be electron microscopy. Finally, the measurement of nanomaterials is further complicated by changes that can occur during the life cycle of nanomaterials.

Implications for legislation

The implications of the recommended definition for legislation are presented in Chapter 4, specifically for biocides, plant protection products, cosmetics, food,

medicinal products, medical devices, REACH[1], CLP[2], and occupational health and safety.

In addition to specific legislation, a number of general issues were addressed. Concern is raised because nanomaterials may introduce new risks during occupational, consumer and/or environmental exposure. Thus as well as the need for adequate measurement techniques for particle size distribution, other more specific information may be required for hazard assessment. Such requirements are related to 'nano-specific' properties that make nanomaterials behave differently from other nanomaterials, influencing both their fate and their effects. This includes the determination of 'nano-specific' properties and the development of methods to measure these properties, including possible additional effects.

Risk assessment of nanomaterials is further complicated by surface treatment, particularly when a nanolayer of another material is applied. Although it would seem reasonable not to include this aspect in a definition, surface treatment may complicate decisions on whether the coating is part of a material, a formulation, a mixture or product in some legislation, for instance in REACH. Thus, the extent to which the surface treatment does define a material or substance needs to be considered.

Several legal frameworks have been updated or are being updated to explicitly include nanomaterials, for instance regulations on cosmetics, biocides, and novel foods. Nanomaterials are also being discussed in other legal frameworks (e.g., REACH, medical devices) but the extent to which legislation will be adapted is not yet clear. The recommended definition may contribute to these deliberations.

Conclusion

Finally, it is concluded that the recommendation contains the relevant aspects, but that further guidance is needed to ensure the definition is interpreted consistently. The definition is important in promoting consistency between legal frameworks with regard to the interpretation of the term nanomaterial. The next step is to incorporate this definition into these legal frameworks. This will lead to the collection of 'nano-specific' data that will contribute to further insight into the 'nano-specific' properties and the fate, kinetics and effects of nanomaterials. Such insights can help focus on specific needs for risk assessment and risk management of nanomaterials.

[1] Registration, Evaluation, Authorisation and registration of Chemicals.

[2] Classification, Labelling and Packaging.

1 Introduction

In October 2011 the European Commission published the 'Recommendation on the definition of a nanomaterial' (EU, 2011a) that states that nanomaterial is a material containing particles of which at least 50 % are within a size range of 1–100 nm. By publishing this Recommendation, the Commission responds to the call by the European Parliament for a comprehensive science-based definition of nanomaterials in legislation of the European Union (EP, 2009).

Rapid development in nanoscience and nanotechnologies is leading to an increasing number of applications and products containing or using nanomaterials (see, for instance, the Project on Emerging Nanotechnologies[3]). Concerns have been raised that the potential hazards of these materials and technologies for workers, consumers, and the environment may not be sufficiently covered under current legislation.

Nanomaterials complicate the product life cycle which is generally divided into four phases: production of the raw materials, product formulation/manufacture, product use, and disposal of the end product. For instance, dissolution processes may change particle size during the life cycle so that a material produced as a nanomaterial may not meet the criteria of the definition after product formulation. Moreover, a product not considered to be nanomaterial may release or form nanomaterials during the product use phase. A nanomaterial may even undergo significant changes in properties during transport, for instance, due to dissolution processes or formation/disintegration of coatings.

Each stage in a product life cycle such as production and waste disposal is regulated by legislation (e.g. EU, 2003a; EU, 2003b, 2006a). In addition, different uses of the same material or product may be covered by different regulations, for instance, for professional or consumer use. Although legislation covers potential health, safety and environmental risks in relation to nanomaterials (EC, 2008), these materials are not mentioned specifically and thus legislation may need to be adapted. For this purpose, the adoption of the recommended definition is an important step.

Most Dutch ministries are cooperating to develop a national policy on nanotechnology and are contributing to EU policy on risk assessment and management of nanomaterials. In line with both a high level of safety and European innovation policy, a project group has been set up to consider nanotechnology and a subgroup, the Interdepartmental Working Group on Risks of Nanotechnology (IWR), is considering the risks of nanomaterials. IWR has requested RIVM to interpret the European Commission Recommendation on the Definition of a Nanomaterial and to evaluate the Recommendation from both a scientific and policy perspective. The evaluation covered various legislative frameworks including biocides, plant protection products, cosmetics, food, medicinal products, medical devices, REACH[4], CLP[5], and occupational health and safety. The usefulness of the recommended definition is being considered from

[3] See http://www.nanotechproject.org.

[4] Registration, Evaluation, Authorisation and registration of Chemicals.

[5] Classification, Labelling and Packaging.

the point of view of different stakeholders including scientists, regulators, and industrial companies.

This report is intended as a basis for further discussion by policy makers and other stakeholders on the use and further implementation of the recommended definition in national and international legal frameworks.

2 Commission Recommendation on the definition of nanomaterial

On 18 October 2011, the European Commission (EC) published the Recommendation on the Definition of a Nanomaterial (EU, 2011a). The main parts of this recommendation are cited in this chapter, together with further clarifications given by the Commission in a list of nineteen questions and answers published on the webpages of the EC[6].

As explained on these webpages, the Commission considers the definition in this recommendation for use as a reference in determining whether a material should be considered to be nanomaterial for legislative and policy purposes in the European Union. The definition is primarily intended to provide clear criteria to identify materials for which special legal provisions may apply. Such provisions are part of the specific legislation in which the definition is used. Another purpose for the definition is to promote consistency so that a material considered to be a nanomaterial in one legal framework will also be considered as such in other legal frameworks.

The recommended definition is mainly based on a reference report by the European Commission Joint Research Centre (Lövestam et al., 2010) and an opinion by the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR, 2010).

Following an introductory section, the recommendation comprises seven statements:

1. *Member States, the Union agencies and economic operators are invited to use the following definition of the term 'nanomaterial' in the adoption and implementation of legislation and policy and research programmes concerning products of nanotechnologies.*

2. *'Nanomaterial' means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm.*

   In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.

3. *By derogation from point 2, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials.*

4. *For the purposes of point 2, 'particle', 'agglomerate' and 'aggregate' are defined as follows:*

   (a)'particle' means a minute piece of matter with defined physical boundaries;

[6] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm.

(b) 'agglomerate' means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components;

(c) 'aggregate' means a particle comprising of strongly bound or fused particles.

5. *Where technically feasible and requested in specific legislation, compliance with the definition in point 2 may be determined on the basis of the specific surface area by volume. A material should be considered as falling under the definition in point 2 where the specific surface area by volume of the material is greater than 60 m^2/cm^3. However, a material which, based on its number size distribution, is a nanomaterial should be considered as complying with the definition in point 2 even if the material has a specific surface area lower than 60 m^2/cm^3.*
6. *By December 2014, the definition set out in points 1 to 5 will be reviewed in the light of experience and of scientific and technological developments. The review should particularly focus on whether the number size distribution threshold of 50 % should be increased or decreased.*
7. *This Recommendation is addressed to the Member States, Union agencies and economic operators.*

The Commission states[7] that the definition aims to identify substances within a specific size range. It is not intended to classify nanomaterials as a group of compounds exhibiting an increased risk to health or the environment. Nanomaterials are not intrinsically hazardous but specific considerations may need to be taken into account in their risk assessment.

2.1 Background and other definitions

The International Organisation for Standardisation (ISO) published its first document containing a definition in 2008 (ISO, 2008), in which the term nanomaterial is defined as '*material with any external dimensions in the nanoscale or having internal structure or surface structure in the nanoscale*'. The term nanoscale is defined as '*size range from approximately 1 nm to 100 nm*'. Based on this definition, ISO defines a range of related terms[8], such as nanofibre, nanoplate, nanowire, and quantum dot.

This ISO definition has been used as a basis for working definitions in various regulatory contexts in various countries within and outside the EU. These countries include Australia[9], Canada[10], Denmark[11], United Kingdom[12], and United States of America[13]. The ISO definition has also been used by international organisations such as the Organisation for Economic Co-operation and

[7] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm.

[8] See https://cdb.iso.org.

[9] See http://www.nicnas.gov.au/Publications/Chemical_Gazette/pdf/2010oct_whole.pdf#page=14.

[10] See http://www.hc-sc.gc.ca/sr-sr/pubs/nano/pol-eng.php.

[11] See http://www.mst.dk/English/Chemicals/Substances_and_materials/Nanomaterials.

[12] See http://archive.defra.gov.uk/environment/quality/chemicals.

[13] See http://www.epa.gov/oppt/nano/nmsp-conceptpaper.pdf.

Development (OECD), and EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR).

The Commission considered a more precise definition was needed in the EU regulatory context. Most countries outside the EU use their definitions of nanomaterials in a different regulatory context. These definitions are mainly intended to identify individual substances on a case-by-case basis, which may be subject to specific data provision or risk assessment or risk management obligations. Provisions in EU legislation, such as ingredient labelling, prior notification, and authorisation, apply directly to all manufacturers of products containing nanomaterials. Thus, the Commission considered a more precise definition is required to provide legal clarity in the EU.

The main difference between the EC Recommendation and definitions in non-EU countries such as Canada and Australia is that the EU definition does not include the specific properties of nanomaterials. However, such properties are not well defined in those definitions that do include such properties. For instance, Canada uses the term nanoscale properties/phenomena which is defined as '*properties which are attributable to size and their effects; these properties are distinguishable from the chemical or physical properties of individual atoms, individual molecules and bulk material*'[14].

Another difference with other definitions is that the EU recommendation also takes into consideration size distribution. The consequences of these differences are discussed in Section 4.11.

[14] See http://www.hc-sc.gc.ca/sr-sr/pubs/nano/pol-eng.php.

3 Elements of the Recommendation and their scientific implications

The Commission Recommendation is an important first step in providing clarity on nanomaterials in a regulatory context. In this chapter, the key elements of the recommended definition are discussed from a scientific perspective, focusing on potential applicability in risk assessment frameworks. The regulatory consequences of the Recommendation are discussed in Chapter 4.

As indicated in Chapter 2, the Recommendation defines a nanomaterial as 'a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm. In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.'

The key elements of the Recommendation are discussed as follows: natural, incidental or manufactured material in Section 3.1; unbound state or as an aggregate or as an agglomerate in Section 3.3; 50 % or more of the particles in Section 3.5; the number size distribution in Section 3.4, the size range 1 nm–100 nm in Section 3.2, and the specific cases in Section 3.7.

In addition, the volume specific surface area element (point 5 of the recommended definition) is discussed in Section 3.8, availability of necessary measurement techniques in Section 3.6, and additional implications of the definition in Section 3.9. Finally, the implications are summarised in Section 3.10.

3.1 Natural, incidental or manufactured material

The Recommendation states that a ''*nanomaterial' means a natural, incidental or manufactured material* […]'. This raises the question why the definition is not limited to, for instance, manufactured materials. This issue is addressed by the Commission in one of the 19 Questions & Answers[15]:

'The Recommendation only identifies a nanomaterial on the basis of its particle size. The justification for this choice is that properties or risks posed by a nano-sized material are not determined by the intention of the manufacturer and do not differ depending on whether the nanomaterial is natural, produced incidentally, or the result of a manufacturing process with or without the explicit intention to produce a nanomaterial. There are many naturally occurring nanomaterials and they may exhibit similar properties to those that are manufactured. From a definition point of view it is therefore not logical to omit certain types of materials on the basis of their genesis.

However, when it comes to potential legislative requirements it is expected that nanomaterials will be treated like other materials. This means that if a specific

[15] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm, question 6.

piece of legislation only addresses manufactured materials, the same limitation would also apply to nanomaterials.'

RIVM supports the Commission's decision that the origin of nanomaterials should not be part of a definition of nanomaterials. This approach results in the inclusion of many different materials in the definition. A distinction between natural, incidental, and manufactured materials needs to be made in specific legislation, as is the case with other materials. The need for distinction is often related to the purpose of the legislation.

3.2 Size range 1 nm–100 nm

Size is considered to be an important element in distinguishing nanomaterials from non-nanomaterials. The concern about nanomaterials is primarily related to changing in properties due to change in particle size, as reflected by the inclusion of size in all proposed definitions. The prefix 'nano' relates to the size range of 1 to 999 nm (the size range between picometer and micrometer). In choosing a range, a compromise needs to be sought between including many materials that exhibit 'nano-specific' properties and excluding many materials that do not exhibit such properties.

For this purpose, ISO suggested an upper limit of approximately 100 nm because many of the specific properties of nanomaterials (those properties that are not extrapolations from a larger size) occur at sizes below this limit, but materials may have such properties well above 100 nm. Based on the ISO definition, standardised nanomaterials in this size range were manufactured for use in scientific programmes including OECD sponsorship programme, and materials stored in the repository of the European Commission Joint Research Centre.

Auffan et al. (2009) identified unique properties in a group of nanoparticles (metals and metal oxides) when the diameter of nanoparticles was less than 30 nm. This was due to changes in crystalline structure or surface-to-volume ratio that enhanced their interfacial reactivity. For other compounds, changes in conduction bands and redox activity have been observed at larger particle sizes (Gilbert and Banfield, 2005). In addition, other physicochemical properties have been found to show a continuous effect (without a strong rise or decline) in relation to size (Herzer, 1995; Siow et al., 2004; Wen et al., 2004). For this reason, higher upper limits have also been proposed (for example, 200 nm by DEFRA[16]; and 1000 nm by EMA[17]).

The lower limit of 1 nm to distinguish nanomaterials from atoms and molecules can be debated because some molecules may be larger (e.g., certain proteins can be ~5 nm in size). However, most atoms and molecules are smaller, for instance the largest atom (caesium) has a radius of 0.6 nm.

RIVM supports the reasoning of the Commission to follow the most commonly used size range between 1 and 100 nm in the absence of better arguments for other thresholds. Science plays a role in understanding the implications of choosing certain size thresholds for nanomaterials. RIVM is exploring the relationship between changes in physicochemical properties and particle size.

[16] See http://archive.defra.gov.uk/environment/quality/chemicals.

[17] See http://www.ema.europa.eu under 'special topics' the topic 'Nanotechnology' under 'Medicines and emerging science'.

The outcome of this literature survey may help place the size limit of 1 and 100 nm in perspective.

3.3 Unbound state or as an aggregate or as an agglomerate

As indicated in the Commission Recommendation on the definition of nanomaterial, 'agglomerate' means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components. 'Aggregate' means a particle comprising of strongly bound or fused particles (EU, 2011a).

Although the Commission definition of agglomerate is related to a measurable unit (external surface area), this issue needs to be debated. This assessment requires comparison of the surface area of the material and aggregates/agglomerates to the surface area without them. The latter is difficult to measure because of the rapid formation of aggregates/agglomerates, and is thus generally estimated mathematically from the size distribution of the primary particles. Mathematical estimation of the surface area depends heavily on the quality of the information available on the primary particle size.

Furthermore, measurement of surface area is common practice for powders, but a straightforward technique is not yet available for particles dispersed in liquid. In addition, no guidance is provided on when the surface area of the aggregate/agglomerate can be considered to be the same or similar to that of the individual components.

In the Questions and Answers that accompany the Recommendation[18], aggregates and agglomerates are considered to be nanomaterials when the constituent particles are in the size range 1–100 nm. This is based on the fact that agglomerated or aggregated particles may exhibit the same properties as unbound particles. Moreover, during the life cycle of a nanomaterial, particles may be released from weakly bound agglomerates or under certain conditions from more strongly bound aggregates.

Nevertheless, the first sentence of the definition that a nanomaterial is 'a […] material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles […] is in the size range 1 nm – 100 nm' could be misinterpreted. An aggregate is defined as 'a particle comprising of strongly bound or fused particles'.

Defining an aggregate as a particle could lead to interpreting the statement '50 % or more of the particles' as referring to '50 % or more of the aggregates'. To avoid misinterpretation, RIVM recommends that this sentence and/or the definition of an aggregate be reconsidered in the revision in 2014. Alternatively, guidance on interpretation of 'aggregate' may be provided and linked to a standardised measurement procedure, for instance, related to measurement of the primary particles.

3.4 Number size distribution

The inclusion of size distribution in the Commission definition recognises that particles differ in size. When a material contains a collection of particles, the median size and distribution width can be determined. Without specifying the size distribution, it would be difficult to determine whether a material with some

[18] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm, question 10.

particles less than 100 nm complies with the definition. Nevertheless, the proposed definition is the first to include a size distribution.

The recommendation that the nanomaterial definition should be based on the number size distribution rather than a mass-based size distribution may have far reaching implications.

Most importantly, more materials will be classified as nanomaterial. When a material contains both very small (nano) particles and larger (micro) particles, the mass-based size distribution is dominated by a relatively small number of larger and heavier particles (see in Figure 1), while the number-based size distribution is dominated by the smaller (nano) particles.

A definition based on particle number is required to minimise the chance of defining a material as non-nanomaterial, while the majority of particles are below the threshold size. This is in line with the SCENIHR recommendation (SCENIHR, 2010). RIVM supports the use of the number-size distribution in the definition to designate a material as a nanomaterial.

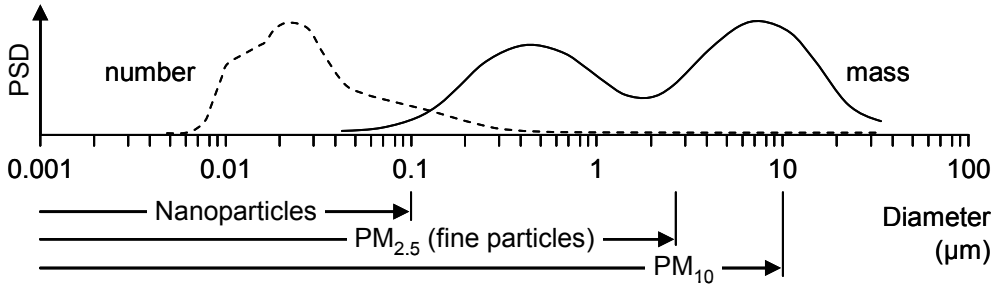

Figure 1 – Example of a particle size distribution (PSD: relative contribution to particle size distribution) expressed as number (dotted line) and mass (adapted from http://www.dmu.dk/en/news/artikel/size_matters/).

3.5 Number distribution threshold of 50 %

The choice of 50 % of the number of particles as a criterion for defining a material as a nanomaterial has no scientific basis. It indicates a material can be defined as nanomaterial if the majority of particles are in the size range of 1 nm–100 nm.

SCENIHR (2010) suggested a threshold of 0.15 % of the number of particles based on a margin of plus/minus three times the standard deviation of the geometric mean of the particle size distribution. A 0.15 % threshold would ensure that the median of the size distribution[19] is above 100 nm. SCENIHR acknowledges that different distribution thresholds might be required for specific areas of application. However as at this stage, science can only provide a statistically based rationale, SCENIHR indicated that threshold determination would need be a political decision.

The 50 % threshold now chosen will cover fewer materials than a threshold of 0.15 % or 1 %. No information is available on the number and type of materials to be included in the threshold levels and will depend on the number-based particle size distribution of a given material.

[19] The median statistically represents the numerical value separating the higher half of the distribution from the lower half, i.e. the 50 % value.

When the particle size distribution does not deviate strongly from a normal or log-normal distribution, the median can be determined relatively easily and checked against the definition's size range. However, determining the median becomes more challenging when other types of distribution are found such as bimodal distributions. This will require the use of specific statistical software.

Nevertheless, the median can be determined without details of the particle size distribution. When a different threshold (between 1 and 50 % as indicated in the Recommendation) is required, further details on the particle size distribution are required to determine whether a material is a nanomaterial. The extent to which this is feasible depends on the availability of measurement techniques.

The second phrase under point 2 of the recommended definition reads '*In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.'* While this raises questions about these concerns, lowering the threshold will broaden the definition to include more materials[20]. This may be done in certain frameworks to include materials with a median particle size outside the 1–100 nm range. As indicated above, the feasibility of such deviations depends on the availability of measurement techniques.

Measurement of the commonly used food additive E171 (titanium dioxide) showed that 36 % of particles in the sample were at least in one dimension below 100 nm (Weir et al., 2012). If this measurement is representative for this food additive, this material would not be classified as nanomaterial under the 50 % threshold. Production volumes and use of E171 are probably high and thus exposure to titanium dioxide particles smaller than 100 nm may be significant. Hence, this example might justify considering a lower threshold due to the considerable exposure to nano-sized particles, even if only 36 % of particles are less than 100 nm.

Whether these results are representative of nanomaterials is not as yet known. It would be premature to replace the 50 % threshold by a general threshold between 1 and 50 %, based on this one observation alone. It may very well depend on the type and use of a specific nanomaterial. Furthermore, any decision on a threshold level will be challenged by borderline cases.

3.6 Measurement techniques

For practical application of the definition, guidance and further development of measurement techniques for a number-based size distribution are required. Two aspects are considered for guidance on measurement techniques.

Firstly, the most suitable method to measure nanomaterials may vary between cases, and depends on the type of nanomaterial and the matrix in which the nanomaterial is present (for instance, liquid or air). Secondly, different measurement techniques are used to determine different dimensions such as geometric, hydrodynamic and aerodynamic dimensions. The numerical value of a hydrodynamic or aerodynamic diameter is usually larger than the geometric diameter, for example, because of water molecules around the particle that are also included in the size determination (cf. Bootz et al., 2004). Thus, the

[20] To put these percentages in perspective, for example for titanium dioxide particles with a diameter of 35 nm the number density is in the order of 10^{16} per gram: the range of 1–50 % of this value equals $0.1 \cdot 10^{15} - 5 \cdot 10^{15}$ per gram (He et al., 2011).

measurement technique can influence the particle size distribution, and the assessment of whether a material meets the nanomaterial definition (e.g. Tiede et al., 2008; Domingos et al., 2009).

In addition, many methods cannot distinguish between agglomerates/ aggregates and single particles. To date, electron microscopy is the only technique that can distinguish between primary particles and agglomerates, and determine the size of particles based on visualisation. Electron microscopy techniques also have disadvantages (see below).

Measuring nanomaterials is further complicated by the fact that nanomaterials can change during their life cycle. For instance, aggregates/agglomerates may form or disintegrate, particles may bind to other types of materials, coatings may form or disintegrate, and particles may dissolve. In some regulatory frameworks, it may be relevant to determine the steps in the life cycle and measure nanomaterials and/or their size distributions in each of these steps.

European Food Safety Authority (EFSA) recommends using at least two different analytical methods, one of which should be electron microscopy (Antunović et al., 2011). RIVM recommends the same approach to be used in guidance on application of the definition. At present, electron microscopy techniques are the only methods that can give precise information on shape and size of the primary nanoparticles. However, this information cannot be used directly for exposure assessment, because air or liquid aggregation and agglomeration may change the behaviour of the nanomaterial.

Other techniques are more feasible in determining particle size distributions, such as light scattering in combination with separation techniques such as chromatography and centrifugation. EFSA provides an overview of available measurement methods (Antunović et al., 2011). Electron microscopy techniques are feasible for pristine material, but such measurements are very tedious to carry out in relevant matrices in toxicity tests or in estimation of exposure. However, development of measurement techniques is continuing to advance.

Currently, work on measurement techniques for nanomaterials has been taken up by ISO and in European projects, such as NANODEVICE[21], NANOVALID[22], MARINA[23], NanoLyse[24], in which experience in measuring airborne fine dust may serve as a starting point.

Regardless of the measurement methods, further guidance is needed to ensure consistent application of the definition as well as enforcement of legislation that uses the definition. Recently, ECHA has adapted its guidance with appendices on nanomaterials, based on the work done in the REACH Implementation Plans on Nanomaterials[25]. This includes an overview of the advantages and disadvantages of the measurement methods. These appendices were published 30 April 2012[26].

[21] See http://www.nano-device.eu.

[22] See http://www.nanovalid.eu.

[23] See http://www.marina-fp7.eu.

[24] See http://www.nanolyse.eu.

[25] See http://ec.europa.eu/environment/chemicals/nanotech/index.htm#ripon.

[26] See http://echa.europa.eu/web/guest/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment.

3.7 Derogations for specific substances

The Commission definition includes a specific exception for *dimensions below 1 nm* for a number of carbon substances (fullerenes, graphene flakes and single wall carbon nanotubes). However, no explanation is given on the background to this exception. The carbon substances mentioned are generally considered to be nanomaterials, but it is not clear whether other non-carbon substances could show similar properties. By specifically mentioning these carbon substances, it becomes difficult to include other such substances and is in contrast with the broad intention of the recommended definition. Clarification is necessary, for instance on the Questions and Answers page, and the list of derogations may need to be addressed in the 2014 revision.

3.8 Volume-specific surface area

The emphasis in the definition on external dimensions may exclude materials with an internal structure (e.g., porous materials with relatively large internal surface area) or materials with a surface structure at the nanoscale. The Commission recognises this by including the specific surface area by volume as an additional parameter.

However, a generally accepted method to measure the volume specific surface area is only available for dry powders, the BET method (Brunauer et al., 1938). For nanomaterials in suspension or other liquid or solid matrices, methodology and measurement techniques are in an early stage of development. In the short-term, this criterion can be used for dry particles, but further development of methodology and techniques is needed for the practicality of the surface area criterion in liquid or solid matrices.

3.9 Additional scientific implications

The Commission states that the scope of the Recommendation covers nanomaterials that are substances or mixtures, but implicitly not as final products[27]. This limitation is similar to that introduced by ISO: 'End products containing nanomaterials (e.g. tyres, electronic equipment, coated DVDs) are not themselves nanomaterials' (ISO, 2008). This means that if a nanomaterial is used with other ingredients in a formulation the entire product will not become a nanomaterial[27].

There are analytical challenges in determining the presence of nanomaterials in products (cf. Oomen et al., 2011). For instance, sample preparation may change the particle size distribution. Yet, inclusion of most products as nanoproducts in various databases (e.g., the Project on Emerging Nanotechnologies[28]) is based on the word 'nano' used by manufacturers on product labels and website rather than based on analytical evidence that nanomaterials are present. At present, a 'nano' label does not necessarily mean that the product contains nanomaterials. Similarly, the absence of a 'nano' label does not necessarily mean that a product does not contain nanomaterials according to the definition. To gain insight into how many products on the market contain nanomaterials, additional information is needed including measurement of nanomaterials in products, and taking into consideration manufacturing and production processes.

[27] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm, question 13.

[28] See http://www.nanotechproject.org.

A further complicating factor is that nanomaterials are known to change characteristics during their lifetime, including during product formulation and production phases. A nanomaterial may no longer be considered to be such when used in product formulation, or a product considered not to be a nanomaterial may release or form nanomaterials in the product use phase. A nanomaterial may change significantly in properties during transport, for instance due to aggregation or dissolution processes.

This suggests that the kinetics, fate, and hazard of nanomaterials, and thus the potential risk may vary during their lifetime. In risk assessment, the presence of nanomaterials needs to be determined at several stages in the material's life cycle. This requires the development of suitable methods and guidance in selecting the appropriate method. Sample treatment for measurements may lead to changes in particle size distribution and in the determination of a nanomaterial.

3.10 Summary of the scientific considerations

The recommended definition is a good starting point but future improvements may be needed on some aspects.

At present, the particle size range of 1nm–100 nm has no scientific basis. Further insight into 'nano-specific' properties (those that cannot be extrapolated from a larger size) and the specific size at which these properties occur could contribute to understanding the implications of the choices for these threshold values. However, the final decision on the particle size range will remain a political one.

From a scientific perspective, inclusion of the particle size distribution in the definition is appreciated because particle size is very likely to vary in a material and thus an indicator of this variability is required. The 50 % threshold for the number of particles in the size range for nanomaterials has been a political decision because no scientific reasoning can be given for a threshold value (50 % or other). Yet, allowing for deviation from this threshold (second part of Point 2) raises questions about what valid concerns require deviation from the 50 % threshold.

Defining an aggregate as a particle leads to confusion in interpretation of the definition of a nanomaterial that refers both to particles and aggregates. Thus, RIVM recommends that the definition of a nanomaterial and/or the definition of an aggregate be reconsidered, or at least guidance is provided on the interpretation of these definitions.

The definitions include an exception for '*dimensions below 1 nm*' for certain carbon substances. Clarification is needed on why the exception is restricted to these specific substances, and the list of derogations may need to be reconsidered in the 2014 revision.

However, the main challenge to the practical application of the recommended definition in legislation and its enforcement is the availability of measurement techniques to determine accurately the number-based particle size distribution and/or volume specific surface area in different matrices including liquid and air matrices as well as in products. Currently, a range of measurement techniques is available (Antunović et al., 2011) and guidance and development of measurement techniques is necessary, especially for measurement in final products and identification of specific nanomaterials. Continuous advancements suggest that such techniques will become available in the near future.

Nanomaterials are known to change in characteristics during their lifetime, including during formulation and production phases. A nanomaterial may no longer be considered to be such when used in product formulation, or a product considered not to be a nanomaterial may release or form nanomaterials in the use phase. Science has a role to play a role in determining the relevant steps in the life cycle and in developing measurement techniques for nanomaterials and their size distributions in each of these life cycle stages.

4 Implications for legislation

Much legislation on controlling risks is based on the 'precautionary principle' that products can only placed on the market if the potential health, safety and environmental risks are controlled sufficiently (EU, 2001b, 2003a, b). The rapid development of nanomaterials in combination with their potentially different behaviour has raised concerns that these materials may introduce new hazards during occupational, consumer and/or environmental exposure. In addition to new hazards, regulation of nanomaterials may be further complicated by the fact that nanomaterials can change during their life cycle. A material may not necessarily be considered to be a nanomaterial in all stages of its life cycle.

Based partly on these observations, the Commission concluded that although the legislation covers potential environmental, health and safety risks in relation to nanomaterials (EC, 2008), nanomaterials are not specifically mentioned and legislation may need to be adapted. Currently, nanomaterials are mentioned specifically only in the Cosmetics Regulation (see Section 4.4) and currently in draft revisions of the Biocides and Novel Food Regulations (see Sections 4.2 and 4.5).

Specific legislation for nanomaterials could be developed that includes reference to existing legislation. However, in the light of the previous statement, existing legislation, regardless of the stage in life cycle of a nanomaterial, covers risks in relation to nanomaterials. Thus, adaptation of legislation with specific provisions for nanomaterials is the preferred route, as indicated by the revision of the Cosmetics Regulation. For some regulations, stand-alone legislation for nanosubstances parallel and linked to and coherent with specific relevant legislation (e.g., REACH) may be more feasible (cf. Azoulay, 2012).

The first step in adapting legislation is a definition to make the distinction between nanomaterials and non-nanomaterials. Preferably, such a definition should be formulated in a separate document and referred to in appropriate legislation. This would ensure consistency in legal frameworks with regard to the interpretation of the term nanomaterial. In addition, such an approach will ensure that changes in the definition are directly incorporated into legal frameworks. The Commission intends the recommended definition to be used in this way[29].

However, the recommended definition is ambiguous because of the inclusion of the second phrase under point 2: '*In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.'* This ambiguity severely hampers reference to the definition in its entirety.

Furthermore, the Commission acknowledges that it may be necessary in some cases to exclude certain materials from the scope of application of specific legislation or legislative provisions even if within the definition. It may likewise be necessary to include additional materials, such as materials smaller than 1 nm or greater than 100 nm in the scope of specific legislation or legislative

[29] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm, question 1.

provisions for a nanomaterial (preamble 16; EU, 2011a). Regardless of how a definition for nanomaterials is incorporated, whether a distinction as nanomaterials has legal consequences will depend on the specific legal framework.

The need for specific provisions is discussed in Section 4.1, followed by discussions on relevant legal frameworks. This report focuses on those frameworks which currently address nanomaterials or will do so in the near future, either in specific regulations or directives, or in accompanying guidance documents. Many of the issues identified may be relevant in other frameworks (e.g., EU, 2001b, 2003a, b).

The focus in the sections below is on the need to treat nanomaterials differently from other materials, and the usefulness of the recommended definition in this respect. In addition, 'nano-specific' implications for the legal framework are indicated where possible. Limitations of legislation applicable to both nanomaterials and non-nanomaterials (e.g., exclusion of natural and/or unintentionally produced materials) are not discussed.

4.1 Specific provisions for nanomaterials

Irrespective of the legal framework, the following observations are made regarding specific provisions for nanomaterials. A distinction between nanomaterials and non-nanomaterials is only useful where specific provisions for nanomaterials are envisaged within a legal framework and where such provisions can be adequately enforced.

In addition to establishing a definition, methods are needed to determine whether a material fulfils the criteria of the definition. For the recommended definition, the number-based particle size distribution of the nanoparticles must be adequately determined, either measured or estimated.

For risk assessment, information on exposure and hazard should be available. To assess the exposure and hazard, measurements of size distribution or other relevant properties, for example in relation to dose metrics of specific nanomaterials, should be reliable. Furthermore, additional information may be required for hazard assessment, such as on kinetics (cf. Pronk et al., 2009). Information may be required on 'nano-specific' properties that make nanomaterials behave differently to non-nanomaterials, influencing both their fate and their effects.

In addition to determining the 'nano-specific' properties, methods should be developed or adapted to measure these properties including effects presently not assessed in hazard assessment.

The Commission states specifically that if a nanomaterial is used with other ingredients in a formulation, the entire product will not be a nanomaterial[30]. For risk assessment, this implies that the potential environmental, health and safety risks of a product are adequately covered in determining and managing the potential risks of the nanomaterial ingredients. This may be questionable because nanomaterials may change during their life cycle, specifically when changes involve characteristics known to be relevant for the kinetics, fate and hazard of nanomaterials, and thus to the potential risk (e.g., aggregation and dissolution).

[30] See http://ec.europa.eu/environment/chemicals/nanotech/questions_answers.htm, question 13.

In addition, some products exist for which specific circumstances result in the intentional formation of nanomaterial. For example, this may be the result of mixing different components, or spraying a coating that forms a nanolayer. It may not be feasible in the legal frameworks on specific product groups (Cosmetic Directive, Novel Food, Consumer Products) to request information on each product that may contain a nanomaterial. It will be difficult to establish a link between the risk characteristics of the nanomaterial as a substance and the presence of characteristics relevant for risk assessment of the end product.

At present, no guidance is available on the extent to which hazard information on nanomaterials with slightly different physiochemical characteristics can be used in read-across or extrapolation, or when information on exposure and hazard of slightly different nanomaterials can be combined.

Another issue is the coating of nanomaterials, which is also commonly referred to as surface treatment. Such treatment is often applied to add or enhance properties of the nanoparticles, for instance to increase water solubility but may result in undesired effects. For instance, reducing cytotoxicity by surface treatment may increase genotoxicity (Yin et al., 2010). Specifically in REACH, surface treatment may complicate decisions on whether the coating is part of a material, a formulation, a mixture or a product, and thus to what extent a nanocoating defines the substance (cf. JRC, 2011).

RIVM considers it reasonable to exclude surface treatment from a definition of nanomaterials that focuses on particle size. However, acknowledgement of surface treatment and the possible related complications may be necessary in some legislation. These issues may be of less importance for products coated with a layer of nanomaterial, unless the nanolayer is released as nanomaterials during the life cycle of the product, for example by wear and tear, or specific effects may be expected related to the coating.

4.2 Biocides

Directive 98/8/EC which regulates biocidal products in the EU (EU, 1998b) does not specifically mention nanomaterials, nor does it provide a basis for separate assessment of particles.

On 19 January 2012, a new regulation for biocidal products was agreed between the Council and Parliament[31]. This Regulation will enter into force on 1 September 2013. The new definition on nanomaterials has been included in the text to distinguish between nanomaterials and non-nanoforms of the same substance that require separate assessment. As a result, a separate risk assessment of nanomaterials will be required if used as the active ingredient. Nanomaterials that are not the active substance may require risk assessment for product authorisation.

Deviation from the 50 % threshold as mentioned in the definition document is not included in the draft regulation. The following sentence is included which may open the way to define specific criteria for nanomaterials in biocides. '*The Commission may, at the request of a Member State, decide, by means of implementing acts, whether a substance is a nanomaterial, having regard, in particular to Recommendation 2011/696. Those implementing acts shall be*

[31] See http://www.europarl.europa.eu/plenary/en/texts-adopted.html.

adopted in accordance with the examination procedure referred to in Article 82(3)'.

However, the current directive will be in force until September 2013. This directive provides the possibility to include risk assessment of nanomaterials in case-by-case assessment of both active ingredients and substances of concern in biocidal products. According to Article 14 of the Directive (EU, 1998b), information that may affect continuing authorisation should be notified, such as changes in the source or composition of the active substance. For this purpose, a definition of a nanomaterial is beneficial, for instance in recognising changes to the nanoscale in the composition of the active ingredient.

4.3 Plant protection products

Current European legislation on plant protection products falls under Regulation (EC) No 1107/2009 (EU, 2009b). Even though updated relatively recently, the Regulation does not specifically mention nanomaterials. Similar to the current legislation on biocides, active substances and products are assessed on a case-by-case basis, which provides the possibility for risk assessment of nanomaterials as active substance or as substance of concern (see Section 4.2).

4.4 Cosmetics

The current Cosmetics Directive (76/768/EEC; EU, 1976) does not provide a legal basis for specific assessment of nanomaterials, but states that a selection of ingredients in cosmetics should be evaluated by the Scientific Committee on Consumer Safety (SCCS). These ingredients include UV filters, colorants and preservatives (listed in the Annexes to the Cosmetics Directive). In addition, Member States can express their concern about specific ingredients and request an evaluation by the SCCS. Such ingredients could potentially include nanomaterials.

As of 11 July 2013, a new Cosmetics Regulation (EC No 1223/2009; EU, 2009c) will be fully implemented in which nanomaterials should be notified. Nanomaterials are defined with the provision that the definition should be adapted according to 'an agreement on a definition in appropriate international fora'. This indicates that the new recommended definition will be incorporated in the Regulation.

In the Cosmetics Regulation (EU, 2009c) nanomaterials are limited to biopersistent and intentionally manufactured materials. There is no reason to change this limitation when the recommended definition is adopted.

The following provisions apply to nanomaterials:

- A selection of ingredients should be evaluated by the SCCS, including nanomaterials.
- Nanoparticles may only be used when notified before placing on the market (at the EC registry, at least 6 months in advance).
- Nanomaterials in cosmetics products should be included in the list of ingredients on the label.

Currently, the Working Group on Nanomaterials in Cosmetic Products is developing a guidance document on safety assessment dossiers of

nanomaterials. DG SANCO[32] is planning to set up a sub-working group (Nanomaterials in Cosmetics) to the Cosmetics Working Group to consider the implications of the definition for the Cosmetics Directive and Regulation. RIVM will participate in this sub-working group.

4.5 Food

Food safety is covered by a range of regulations for which the general principles are laid down in Regulation (EC) No 178/2002 (EU, 2002). For nanomaterials, the regulations on novel foods, food additives, and food contact materials are most relevant.

Recently, the Regulation (EU) No 1169/2011 (EU, 2011c) was published on the provision of food information to consumers. It amends Regulations 1924 and 1925 from 2006 (EU, 2006b, c) and repeals several older directives. This regulation states that '*all ingredients present in the form of engineered nanomaterials shall be clearly indicated in the list of ingredients. The names of such ingredients shall be followed by the word 'nano' in brackets*' to inform consumers about the presence of engineered nanomaterials in food. This regulation entered into force by November 2011 but manufacturers have a three-year transition period to comply with it.

The regulation includes the provision that the Commission will adapt the definition[33] of engineered nanomaterials referred to technical and scientific progress or to definitions agreed at international level. This suggests that the recommended definition will be incorporated in this legislation, although it is likely that the restriction to "engineered" nanomaterials will remain. It can be further anticipated that a distinction between natural nanomaterials and nano-structured materials from engineered nanomaterials will be considered for the entire legal framework on food safety. Products with oil-in-water or water-in-oil droplets (e.g., mayonnaise) are likely to come within the present recommended definition of nanomaterials.

Authorisation of food additives is regulated at the European level. The European Food Safety Authority (EFSA) evaluates the safety of food additives and advises the European Commission (EC). The EC decides on authorisation and prepares a proposal for authorisation including maximum permitted levels for specific food categories. The EC proposal is presented to the Council and the European Parliament.

A common authorisation procedure for food additives, food enzymes and food flavourings is laid down in Regulation (EC) No 1331/2008 (EU, 2008b). This is accompanied by specific regulations on food additives (Regulation (EC) No 1333/2008; EU, 2008d), food enzymes (Regulation (EC) No 1332/2008; EU, 2008c) and food flavourings (Regulation (EC) No 1334/2008; EU, 2008e). The additives authorised in foodstuffs and conditions of use are listed in Annex II to Regulation (EC) No 1333/2008 (EU, 2008d) on food additives.

[32] Directorate General Health and Consumers (Santé et Consommateurs).

[33] Currently, the definition of an 'engineered nanomaterial' in this Regulation differs from the EU-Recommendation. Currently size is only defined as "one or more dimensions of the order of 100 nm or less", i.e. no lower limit is set, nor is a reference to the particle size distribution included (EU, 2011c). In addition, a reference is made to "properties that are characteristic of the nanoscale", which are defined as "those related to the large specific surface area of the materials considered and/or specific physicochemical properties that are different from those of the non-nanoform of the same material" (EU, 2011c).

Article 12 of this Regulation states that 'when a food additive is already included in a Community list and there is […] a change in particle size, for example through nanotechnology, the food additive prepared […] shall be considered as a different additive and a new entry in the Community lists or a change in the specifications shall be required before it can be placed on the market.' This case-by-case approach ensures that a new safety evaluation is carried out by EFSA for new nanomaterials, which can ensure risk assessment in this context.

The recommended definition may help focus this case-by-case approach with respect to nanomaterials. In addition, some currently authorised food additives may be nanomaterials (e.g., silica E551). Previous evaluations may not have included nano-related risks (Dekkers et al., 2011; 2012). However, Commission Regulation (EU) No 257/2010 (EU, 2010) sets up a re-evaluation programme for all food additives authorised before 20 January 2009. These food additives have to be re-evaluated by EFSA by 2020 (with the exception of 17 additives recently re-evaluated by EFSA).

In the calls for data for the re-evaluations, information on specifications including particle size and particle size distribution is requested. For example, calls for data on the food colours silver and gold were launched in 2011 (EFSA, 2011). A recent study (Weir et al., 2012) has shown a measurement on E171 (titanium dioxide) that indicates 36 % of particles are less than 100 nm in size. The recommended definition would not define E171 as a nanomaterial, but consumers could be exposed to a substantial amount of nanomaterial. It is not clear how representative the measurements by Weir et al. (2012) are, but they raise questions about inclusion of nanomaterials in the current Community list of authorised food additives and whether the potential risks are sufficiently assessed. Titanium dioxide will have to be re-evaluated by EFSA before 31 December 2015 (EU, 2010). This should put the observations of Weir et al. (2012) in perspective and shed further light on potential 'nano-specific' risks of titanium dioxide.

Food contact materials are generally covered by Regulation (EC) No 1935/2004 (EU, 2004b), but there are specific regulations for certain materials such as plastics in Regulation (EC) No 10/2011 (EU, 2011b). The general principle in food contact materials with regard to safety focuses on minimising exposure by minimising leakage of ingredients from food packaging or other food contact materials. This requires adequate measurement techniques.

As part of the authorisation procedure, substances have to be evaluated by the European Food Safety Authority (EFSA) before use in the EU can be authorised. Regulation (EC) No 450/2009 (EU, 2009a) sets out rules for active and intelligent materials and articles intended for contact with foodstuffs to be applied in addition to the general requirements established in Regulation (EC) No 1935/2004 (EU, 2004b) for their safe use. EFSA also provides guidance on submission of a dossier for authorisation.

The general Regulation (EU, 2004b) does not specifically mention nanomaterials, but Regulation (EC) No 10/2011 (EU, 2011b) states that '*substances in nanoform shall only be used if explicitly authorised*' and that '*authorisations which are based on the risk assessment of the conventional particle size of a substance do not cover engineered nanoparticles*'. Furthermore, nanoparticles *should be assessed on a case-by-case basis as regards their risk until more information is known about such new technology. Therefore, they should not be*

covered by the functional barrier concept.'[34] This case-by-case approach can ensure adequate risk assessment in this context. Regulation (EC) No 10/2011 (EU, 2011b) does not include a definition of nanomaterials, but the recommended definition will be sufficient for food contact materials. At present, 'nano-specific' provisions are mentioned specifically in relation to plastics. The EU is currently harmonising legislation on food contact materials to ensure food safety and it is anticipated that similar provisions will be included for other materials.

Novel foods and novel food ingredients are covered by the Novel Food Regulation. In the current Regulation (EC) 258-97 (EU, 1997), no specific provisions are made for nanomaterials as novel food ingredients, but a new regulation is in preparation.

In March 2011, the Commission failed to adopt a new Regulation because of the debate on the sections on cloned animals. In the proposal for a new regulation on novel foods, one of the criteria that defines a novel food is "food containing or consisting of engineered nanomaterials". The definition of an engineered nanomaterial is the same as in Regulation (EU) No 1169/2011 (EU, 2011c) and thus differs from the recommended definition (see above). The proposal also includes the provision for the Commission to adapt the definition of engineered nanomaterials referring to technical and scientific progress or to definitions agreed at international level. Thus, it is likely that the recommended definition will be included in the new novel food regulation.

This regulation is likely to remain restricted to engineered nanomaterials. Thus, nanomaterials and nano-structured materials (e.g., mayonnaise, margarine, and ice cream) can be exempted from specific provisions for nanomaterials. This exemption is reasonable in the light of the abundance of natural nano-sized ingredients and the long history of consumption of both natural nanomaterials and manufactured nanostructures. For nanoparticles that can be shown to be easily digestible, nano-specific evaluation may not be relevant. EFSA has recently published "Guidance on the risk assessment of the application of nanosciences and nanotechnologies in the food and feed chain", which sets out considerations for the safety evaluation of nanomaterials in food and feed (Antunović et al., 2011).

4.6 Medicinal products

The regulatory system for medicinal products is based on the provisions of Directive 2001/83/EC (EU, 2001a) that details the EU marketing authorisation system. This directive is supplemented with 13 Directives, 21 Commission Regulations and several legal reference documents. Specific rules govern medicinal products for paediatric use, orphan drugs, herbal medicinal products, blood products and advanced therapy medicinal products. The legislation is supported by a series of Community guidelines published in 'The rules governing medicinal products in the European Union'[35] which includes both regulatory and scientific guidelines.

[34] In this context a functional barrier is "a layer within food contact materials or articles preventing the migration of substances from behind that barrier into the food. Behind a functional barrier, non-authorised substances may be used, provided they fulfil certain criteria and their migration remains below a given detection limit" (EU, 2011b).

[35] See http://ec.europa.eu/health/documents/eudralex/index_en.htm.

The current regulatory framework has no specific provisions for nanomaterials. The European Medicines Agency (EMA)[36] has published 'Reflection Papers' on nanomedicine in general (EMEA, 2006), and for a specific product class (products based on iron nanoparticles; EMA, 2011a). A third Reflection paper is being drafted for another product class (liposomes; EMA, 2011b). The EMA has established the Ad Hoc Expert Group on Nanomedicines to support the Agency's activities with specialist input on new scientific knowledge and to contribute to the review of guidelines on nanomedicines.

Legislation on medicinal products requires careful risk assessment and risk management on a case-by-case basis before products can be brought to the market. Even though the specific risks of nanomedicine products are not as yet fully known, they are to be thoroughly evaluated in registration dossiers. The availability of alternatives and the clinical benefits of the products will also be taken into account in this process.

In the preamble (17) to the Recommendation, the Commission states that there are '*special circumstances* […] *in the pharmaceutical sector*', and that the definition '*should not prejudice the use of the term 'nano' when defining certain pharmaceuticals and medical devices*'. Although the 2006 Reflection Paper (EMEA, 2006) states that the nanometre scale ranges from the atomic level at around 0.2 nm (2 Å) up to around 100 nm, the EMA currently states on its website[37] that '*nanotechnology is the use of tiny structures - less than 1,000 nanometres across - that are designed to have specific properties'*. The website introduces two major differences: a limit of 1,000 nm instead of 100 nm, and the mention of 'specific properties'. Some product classes considered to be nanomedicines by the EMA contain products with particle sizes larger than 100 nm, for instance liposomes. Furthermore, the Reflection Paper (EMEA, 2006) diverges from the new EC definition with regard to the lower limit (0.2 nm as opposed to 1.0 nm). As these are considerable differences, further discussion in the medicinal products sector is required to decide whether and how the recommended definition will be incorporated in the regulatory system for medicinal products.

4.7 Medical Devices

Currently, procedures for market access of medical devices are set out in three Directives:

- Active Implantable Medical Devices Directive (90/385/EEC; EU, 1990)
- Medical Devices Directive (93/42/EEC; EU, 1993)
- In-Vitro Diagnostic Medical Devices Directive (98/79/EC; EU, 1998c)

These directives are supplemented by seven amending or implementing Directives, two Commission Regulations and several other legal reference documents. Medical devices manufactured utilising tissues of animal origin are governed by specific rules. The legislation is supported by a series of (MEDDEV) guidelines[38], consensus statements[39] and interpretative documents[40]. Also, there is an important role for 'harmonised standards'.

[36] See http://www.ema.europa.eu.

[37] See http://www.ema.europa.eu under 'special topics' the topic 'Nanotechnology' under 'Medicines and emerging science'.

[38] See http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm.

The current regulatory framework contains no specific provisions for nanomaterials. Legislation for medical devices requires that careful risk assessment and risk management is carried out on a case-by-case basis before products are brought onto the market. Even though the specific risks of nanomedicine products are not as yet fully known, they should be thoroughly evaluated in the technical documentation required by the directives. The availability of alternatives and the clinical benefits of the products are also be taken into account in this process.

The 2007 report by the EC New & Emerging Technologies Working Group (N&ET WG)[41] on medical devices manufactured utilising nanotechnology concluded that the framework was suitable for such products (N&ET WG, 2007). However, the Working Group recommended introducing a classification placing nanoproducts in the highest risk class: '*All devices incorporating or consisting of particles, components or devices at the nanoscale are in Class III unless they are encapsulated or bound in such a manner that they cannot be released to the patient's organs, tissues, cells or molecules*'.

The Working Group also recommended developing regulatory guidance because risks are partly new and not known to all stakeholders. A 'Meddev guidance document' for medical devices manufactured utilising nanomaterials is currently being prepared. Furthermore, a working group has been created as part of the International Organisation for Standardisation (ISO/TC194/WG17[42]) to develop harmonised standards for biological evaluation of medical devices utilising nanomaterials.

The Commission is currently working on a revision of the regulatory framework[43] and the first proposal is expected in the second half of 2012. The new regulation will contain provisions for innovative medical devices, which could potentially include specific requirements for nanomaterials.

The preamble (17) to the Commission Recommendation on the definition of nanomaterial states that there are '*special circumstances* […] *in the pharmaceutical sector*', and that the definition '*should not prejudice the use of the term 'nano' when defining certain pharmaceuticals and medical devices*'.

The 2007 report of the N&ET WG (N&ET WG, 2007) did not present a definition, but noted working definitions at the time, mentioning a scale from 1-100 nm, while stating that '*There is no scientifically based cut-off point to define nanoscale. The size below which materials can display specific properties varies for different materials'*. If the revision of the medical devices regulatory framework introduces specific requirements for nanomaterials, discussion might arise on the need for amendments to the Commission Recommendation to address specific needs of this sector.

[39] See http://ec.europa.eu/health/medical-devices/documents/consensus-statements/index_en.htm.

[40] See http://ec.europa.eu/health/medical-devices/documents/interpretative-documents/index_en.htm.

[41] See http://ec.europa.eu/health/medical-devices/scientific-technical-assessment/working-group/

[42] This working group on 'Nanomaterials' is part of the technical committee on 'Biological Evaluation of Medical Devices' (http://isotc.iso.org/livelink/livelink/open/tc194).

[43] See http://ec.europa.eu/health/medical-devices/documents/revision/index_en.htm.

4.8 REACH

The REACH Regulation (EC 1907/2006; EU, 2006a) defines a substance as '*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*'. Nanomaterials fall within this definition.

However, there are no provisions in REACH specifically for nanomaterials. REACH deals with substances, in whatever the size, shape or physical state and thus covers substances on the nanoscale. If it is decided to make a distinction between nanomaterials and non-nanomaterials and that nanomaterials should be assessed (separately or together with its non-nanomaterial counterpart), it would be preferable to have the option to register them separately under REACH.

The recommended definition accommodated in REACH or referred to by REACH will help to determine whether specific materials should be considered to be nanomaterials. Separate registration under REACH would be limited to materials imported or produced in volumes of more than one tonne per year, unless the current volume limits are amended to include nanomaterials with lower production volumes.

At present, requirements for substances under REACH are listed in Annexes (e.g., Annex VI, Section 2 on substance identification). However, only a limited number of endpoints in these Annexes are considered relevant for nanomaterials and there are no 'nano-specific' endpoints.

The recommended definition will only apply to the REACH legislation if the legislation is amended to accommodate or refer to the definition of nanomaterials; and to include the specific information or registration requirements for the nanomaterials. Without this amendment, separate registration of nanomaterials will be voluntary on the part of industry. If REACH is amended, supplementary guidance will be needed to help registrants comply with REACH. In addition, the current IUCLID format will have to be adapted to accommodate registration templates for nanomaterials. Currently, ECHA is adapting its guidance with appendices on nanomaterials, based on the work done in the REACH Implementation Plans on Nanomaterials[44]. These appendices are to be published at the end of May 2012.

Even when the three changes mentioned above have been implemented, the question remains whether all REACH instruments are suitable for nanomaterials (for instance, REACH art. 57f related to 'equivalent level of concern'). This needs to be further explored. In addition, the requirements in REACH Annex II may have to be adapted (e.g., with the addition of specific requirements for nanomaterials). The Annexes can be amended by a comitology procedure, which is easier that adapting the REACH regulation.

4.9 CLP

The CLP Regulation (EC No 1272/2008; EU, 2008a) on classification, labelling and packaging of substances and mixtures aims to ensure a high level of protection of human health and the environment as well as the free movement

[44] See http://ec.europa.eu/environment/chemicals/nanotech/index.htm#ripon.

of substances, mixtures and articles. The information relates to the forms or physical states in which a substance is placed on the market and in which it can reasonably be expected to be used.

The recommended definition of nanomaterials is based on physical states, so a connection can be made to the classification of substances in nanoform. This does not imply that nanomaterials will be mentioned separately, but if information on the properties of nanomaterials is available, it should be reflected in the classification. It is possible to have more than one entry for one substance. For instance, if a substance is on the market as a grain and as a fine powder, two entries with a different classification are possible. However, at present it is not obligatory to test a different physical form. This makes it doubtful whether the CLP requirements will provide specific information on nanomaterials. As high concentrations of nano-sized particles in the air can be highly explosive, the CLP regulation needs to be elaborated further.

If specific regulation for nanomaterials is in place (under REACH or separately) physicochemical and toxicological data for man and the environment will become available and nanomaterials can be classified separately under CLP.

4.10 Occupational Health and Safety

Occupational health and safety (OHS) are regulated by several directives (EU, 1989, 1998a, 2004a, 2006a, 2008a) and also by the REACH and CLP regulations (EU, 2006a, 2008a).

The philosophy of the OHS Directives is that a duty of care is imposed on employers to protect the health and safety of their employees. The directives also impose general requirements such as minimising risks and instructing employers on the remaining risks. The Substances Directives (EU, 1998a, 2004a) also contain an requirement to develop Occupational Exposure Limits.

The scope of the duty of care, in general, depends on the specific risks on the work floor (e.g., the risks of working with nanomaterials), which are to be determined by the employer in a mandatory risk inventory and evaluation. This risk assessment should include the risks of *any* chemical agents that may present a risk to the safety and health of workers because of their physicochemical, chemical or toxicological properties, usage and/or present in the workplace, irrespective of particle size.

Although not specifically mentioned, nanomaterials fall under the definition of a chemical agent (art. 2, sub b, sub iii; EU, 1998a) and should be included in a risk assessment. The definition also implies that a full life cycle assessment should be conducted, according to the specific use or exposure in the workplace. Where nanomaterials are emitted unintentionally but foreseeable, this exposure should also be addressed in the risk assessment.

Basic information on probable risks of chemical agents is to be obtained from the risk information produced in the chemical safety assessment in REACH or under CLP. However, the OHS Directives do not limit the employer duty to assess the risks of chemicals only on the information produced under REACH/CLP. The OHS Directives impose a broader obligation on employers. To what extent additional information should be provided in specific cases (e.g., nanomaterials) is unclear and will ultimately have to be determined by case law. Adaptation of REACH and/or CLP regulations to include information requirements on nanomaterials will help to clarify the scope of the employer risk assessment obligations under the OHS regulations.

Based on a broad, precautionary interpretation of the employer duty of care, it could be argued that the employers should also take into consideration the possibility of *uncertain* risks (WRR, 2008; Vogelezang-Stoute et al., 2010). Any uncertainty surrounding the presence or probability of risks (e.g., nanomaterials) should at least be addressed by an employer in the risk assessment.

An employer is required to inform employees of the risks of the chemical agents in the workplace, including the identity of the agent. Identity of the agent could include the composition of the substance (including the percentage of nanomaterials), although this is not clearly stated in the regulations and not required in Annex VI, section 2 of the REACH Regulation. The definition of a nanomaterial could be helpful in determining whether and when the 'identity of the agent' should include specific information on nanomaterials.

In some cases, OHS Directives require the development of a statutory Occupational Exposure Limit (OEL)[45] and employers should reduce worker exposure to below these limits. Currently at a European level, there are no specific OELs for nanomaterials[46], although recently NIOSH[47] proposed an OEL for ultrafine (including engineered nanoscale) titanium dioxide (NIOSH, 2011). In addition, various attempts have been made to devise provisional nano-reference values (NRVs). These NRVs may be used as pragmatic benchmark levels to reduce the exposure of employees to nanomaterials (cf. van Broekhuizen, 2011). However, these NRVs must *not* be considered to be scientific, health-based limits that guarantee the health and safety of workers (Dekkers and de Heer, 2010).

In deriving specific OELs for nanomaterials, a distinction between nanomaterials and non-nanomaterials (definition of 'nanomaterial') is essential.

4.11 Additional regulatory impacts

As indicated in Chapter 2, the recommended definition by the Commission differs in two ways from definitions used in non-EU countries. Firstly, the specific properties of nanomaterials are not included in the EU definition, and secondly, the EU recommended definition explicitly take into consideration the size distribution. These differences could have an impact on the level playing field for industry and market.

At present, this impact is difficult to predict. The Recommendation indicates that the specific requirements to distinguish nanomaterials from other materials depend on the framework in which the definition is used. Similarly, the impact is difficult to predict for those definitions that include specific properties of nanomaterials, because the properties are not specified and the consequences are not indicated. The specific properties vary for each nanomaterial and it is often unclear whether these properties relate to the nano size, to the chemical

[45] For all cases the Directives do not impose such a statutory OEL, the Dutch Working Conditions Decree does impose an obligation upon the individual employer to derive *private* OELs for all substances that are being used on the shop floor level. This is a national elaboration of article 4 paragraph 1 and article 5 paragraph 6 of Directive 98/24/EEC (EU, 1998a).

[46] No OEL is indicated at the website of the Scientific Committee on Occupational Exposure Limits (SCOEL): http://ec.europa.eu/social/main.jsp?catId=153&langId=en&intPageId=684 (visited on 20 April 2012).

[47] United States National Institute for Occupational Safety and Health.

nature of the material, or a combination of both. This greatly hampers enforcement of a definition that includes such properties.

Based on the opinion of SCENIHR (2010), the Commission considers that size is the only universally applicable, clear and measurable criterion to identify materials that may exhibit specific properties or risks because of their particle size. These materials should be characterised as nanomaterials, and special considerations may apply. Another reason for not including properties specific to nanomaterials is legal clarity. The Commission considers that including material properties in the definition would render the definition subjective, because it would be unclear which properties and what thresholds would be used to distinguish nanomaterials from non-nanomaterials.

Moreover, a definition based on properties bears the risk of circular reasoning. This is because size is relatively straightforward to measure compared to other properties. Information on other 'nano-specific' properties may not be available before testing but only after analysis. Therefore, with a definition based on properties, it may only be possible to identify whether a material is a nanomaterial after the testing for those properties. Yet, one of the main purposes of the definition is to identify materials relatively easily and clearly for which specific testing considerations might apply.

Establishing a definition in legislation ensures a level playing field at a European level, although discussions may still arise at the global level. Such discussions are premature if based on the definition alone, although relevant in discussion of the consequences of 'nano-specific' requirements.

4.12 Summary of legislation

An overview of progress in incorporating nanomaterials into the legal frameworks discussed is presented in Table 1.

The recommended definition is suitable for incorporation in legal frameworks, albeit different additional conditions can be anticipated. Especially the ambiguity of Point 2 of the recommendation hampers reference to the definition in its entirety. This is illustrated by those frameworks that currently include a definition on nanomaterials (such as the Cosmetics Regulation) or that will include a definition after the current revisions (Biocides and Novel Food Directives). In the Cosmetics Regulation, for instance, the definition is restricted to biopersistent materials and nanomaterials. Similarly, the recommended definition can form a basis for incorporating nanomaterials into legal frameworks that currently do not specifically mention these materials.

The main challenge is to decide on additional provisions for nanomaterials and the extent to which these are needed in addition to adequate characterisation to enable a comparison with the definition of a nanomaterial. This may largely influence the need to re-evaluate risk assessments of materials currently on the market as well as the impact of specific 'nano-provisions'.

For food/feed ingredient evaluation, EFSA has published separate guidance on the use and risk assessment of nanomaterials. Yet, most discussion on additional hazard criteria will probably not be restricted to a specific framework. It may even be essential to have consensus on criteria within the different legal frameworks.

Table 1 – Overview of the legal frameworks governing nanomaterials[a)]

Legislation	Definition available	Label required	Specific provisions	Further discussion/ development anticipated on
Biocides[b)]	Yes	Yes	Separate assessment	Guidance
PPP[c)]	No	No	None	Guidance
Cosmetics[d)]	Yes	Yes	Separate assessment	Guidance
Food				
Information to consumers[e)]	Yes	Yes	None	None
Contact materials[f)]	No[g)]	No	Separate assessment	Guidance
Novel foods/feeds[h)]	Yes	Yes	Separate assessment	Guidance
Additives[i)]	No	No	Separate assessment	Re-evaluation of authorised food additives; guidance
Medicinal products	No[j)]	No	None	Definition; guidance
Medical devices	No	No	None	Definition, risk classification, specific provisions, guidance[k)]
REACH[l)]	No	No	None	Additional or adaptation of legislation and guidance
CLP[m)]	No	No	None	Additional or adaptation of legislation and guidance
OHS[n)]	No	No	None	Guidance and OELs[o)]

a) For further details, see Sections 4.2 – 4.10.
b) This refers to the new Biocides Regulation (Section 4.2)
c) Plant protection products (Regulation (EC) No 1107/2009; EU, 2009b)
d) Cosmetics Regulation (EC No 1223/2009; EU, 2009c)
e) Regulation (EU) No 1169/2011 (EU, 2011c)
f) This refers to Regulation (EC) No 10/2011 (EU, 2011b)
g) Nanoforms are mentioned but the term is not defined.
h) This refers to the new draft Regulation on novel foods (Section 4.5)
i) Regulation (EC) No 1331/2008 (EU, 2008b) and related Regulations
j) The legislation does not include a definition, but the European Medicines Agency provides a definition on its website.
k) The EC New & Emerging Technologies Working Group recommended the addition of "all devices incorporating or consisting of particles, components or devices at the nanoscale" in the highest risk class (Section 4.7); currently a revision of the regulatory framework for medical devices is being carried out.
l) Registration, Evaluation, Authorisation and Restriction of Chemicals
m) Classification, Labelling and Packaging
n) Occupational Health and Safety
o) Occupational Exposure Limits

5 Conclusions

The publication of the 'Recommendation on the definition of a nanomaterial' by the European Commission was greatly needed by stakeholders for risk assessment and regulation. This Recommendation provides more clarity on the term nanomaterial within a regulatory context. Based on our evaluation of the definition from a scientific and legislative perspective it is concluded that the recommendation contains the relevant aspects but that further guidance and some adaptations are needed to ensure consistent interpretation.

The practicality of the definition depends on accurate and reproducible measurement of the key elements and, where necessary, this should be performed with more than one analytical method. Adequate methods are currently available for pristine nanomaterials but measurement in all relevant matrices is not always necessarily straightforward and the outcome may depend on the matrix itself.

Standardised measurement methods are being developed and adequate methods should be available in the foreseeable future. Simultaneously, guidance is needed with regard to equipment, methods, and matrices used, as well as for interpretation of analytical results.

The recommendation provides a sound basis to initiate debate among stakeholders that may lead to further refinement of the definition in 2014 when it is reviewed by the Commission. One topic for debate is the 50 % threshold as indicated by the Commission, and the special limit between 1 and 50 % for 'specific cases'. A second topic for debate is the proposed particle size range of 1–100 nm (including the list of derogations) as this range has no scientific basis. Additional issues for debate may also arise from practical application of the definition.

Reference to the Recommendation in legislative documents will promote consistency with regard to interpretation of the term nanomaterial, more so than including the wording of the definition in the legal frameworks.

Specific provisions may be introduced for nanomaterials in legal frameworks. Certain nanomaterials may be exempted from these provisions, for instance natural nano-sized ingredients in food that disintegrate when ingested (such as oil-in-water dispersions). Moreover, some non-nanomaterials can be identified to which 'nano-specific' provisions apply. The need for such exemptions depends on the requirements in the individual frameworks.

The definition has already been implemented in some frameworks (e.g., Cosmetics Regulation) and is currently under discussion in the revision of other legal frameworks such as biocides and novel foods. In this way, 'nano-specific' data will be generated which will contribute to further insight into 'nano-specific' properties and the related fate and effects of nanomaterials. These insights can help to focus on specific needs of risk assessment of nanomaterials, and provide input for the review of the definition as foreseen in December 2014.

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National Institute for Public Health and the Environment
P.O. Box 1 | 3720 BA Bilthoven
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